mantrasystems

# Post-Market Surveillance in the MDR

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# About the author and Mantra Systems Ltd

Mantra Systems Ltd delivers a completely new form of medical device regulatory support. Unlike any other provider of MDR support services, we have a team of specially-trained medical doctors who apply their clinical acumen and industry expertise to your medical device compliance challenges. With the new MDR focusing heavily on clinical evidence, our knowledge will provide the support you need to ensure your devices meet the requirements of the MDR.

This White Paper is part of a series written by Dr Paul Hercock, the CEO & founder of Mantra Systems Ltd. Paul is dual-trained in medicine and law. He spent 14 years working for the NHS as a front-line clinician and then obtained a Graduate Diploma in Law with distinction from Nottingham Law School. While at law school, Paul established a medical device start-up. He then went on to specialise in providing medical and regulatory support to multi-national medical device companies from across the industry.

**Leveraging Paul's expertise, Mantra Systems comprises an infrastructure of specially-trained medical doctors who apply their clinical knowledge to support medical device manufacturers working to achieve MDR compliance of their medical devices.**

# Introduction - PMS in the MDR

On 26th May 2021 the Medical Device Regulations (EU) 2017/745 will formally replace the Medical Devices Directive 93/42/EEC (MDD) after a transition period that was extended to four years due to the COVID-19 crisis. The MDR places an increased burden on manufacturers in many areas, including in requirements for the design, implementation and reporting of Post Market Surveillance (PMS) systems.

Post-Market Surveillance (PMS) is defined by the MDR as:

> *"the structured process of monitoring the safety of a medical device after its release on the market."*

Post-Market Surveillance involves proactive collection and review of data relating to clinical experience with the device. PMS is an essential component of the regulatory framework for every medical device under the MDR, regardless of risk class. PMS systems must be designed in accordance with MDR requirements in order to successfully gain device accreditation under the MDR, so it is essential that all manufacturers become familiar with the MDR's requirements and rules for PMS systems.

**This White Paper offers guidance on the requirements for PMS in the MDR.**

It is absolutely essential that all medical device manufacturers have a thorough understanding of the MDR. For a detailed guide to the MDR as an instrument, please ***download our "Mastering the MDR" White Paper.***

## Post-Market Surveillance - Knowing the rules

The MDR is organised into Chapters and Annexes, each of which is devoted to a specific topic. **Constructing an MDR-compliant PMS system begins with a detailed understanding of these parts of the MDR.**

**Chapter VII** contains Articles relating to Post-market surveillance, vigilance and market surveillance.

**Annex III** lists technical documentation requirements relating to PMS, **Annex XIV** concerns clinical evaluation and PMCF and **Annex XV** details expectations for conducting clinical investigations.

# MDR Chapter VII: Rules on Post-Market Surveillance (PMS), Vigilance, and Market Surveillance

This Chapter of the MDR outlines requirements for planning, implementing and reporting Post-Market Surveillance (PMS) systems.

Article 83 requires the manufacturer to plan, establish, document, implement, maintain and update a PMS system for every medical device and document the system in a **PMS plan**. In other words, the PMS system must be prospectively designed, implemented on a planned basis, and then constantly updated according to a structured assessment of how well it is working.

Article 83 lists the areas where data from PMS should "in particular" be used. This list can be used to begin defining the scope of the PMS plan for each medical device. Areas include:

- To update the benefit-risk analysis
- To feed improvements to risk management
- To update device design, Instructions For Use (IFU) and device labels
- To update clinical evaluation
- To identify needs for PACAs or field safety corrective actions (FSCAs)

Knowing what is expected of the PMS system allows it to be designed with these specific objectives in mind.

Article 84 states that the PMS plan must comply with the detailed PMS plan requirements specified in Annex III MDR, discussed later in this White Paper.

Articles 85 & 86 explain that PMS reporting requirements differ according to the risk Class of the device in question. For Class I devices (Article 85) a **PMS Surveillance Report** must be prepared that summarises relevant results, conclusions, and any Preventive and Corrective Actions (PACAs), updated as necessary. For devices in all other risk Classes (Article 86) a more detailed **Periodic Safety Update Report (PSUR)** must be prepared that forms part of the technical documentation for that device.

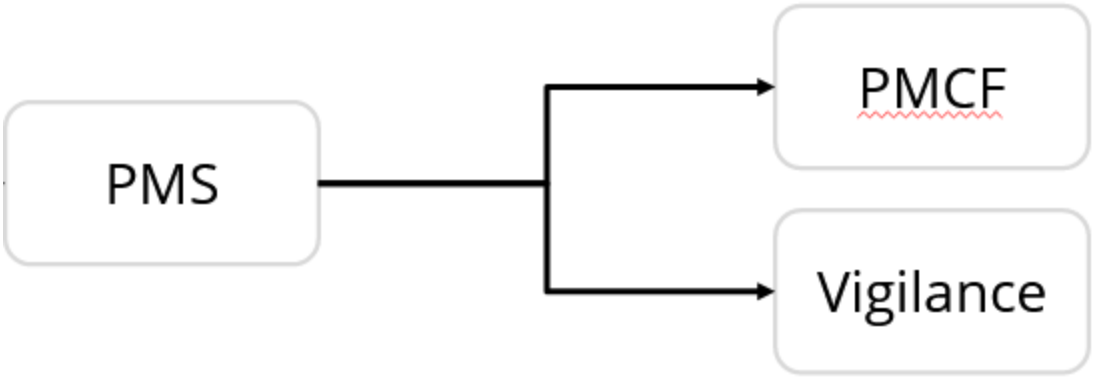
The **PSUR** must contain:

- A summary of the results and conclusions from PMS
- A rationale for and description of any PACAs
- Conclusions of benefit-risk determination
- Main findings of Post-Market Clinical Follow-up (PMCF)
- Volume of sales, estimated use population, and usage frequency of device (e.g. sold 1000 units that have been used on 100,000 patients, with each device contacting a patient twice per day)

For Class IIb and Class III devices the PSUR must be updated annually. For Class IIa devices the PSUR must be updated at least once every two years.

## What are the elements of PMS?

PMS can be thought of as comprising two major elements: Post-Market Clinical Follow-up (PMCF) and Vigilance:




**Post-Market Clinical Follow-Up (PMCF)** is a continuous process that involves the proactive collection and evaluation of clinical data relating to the safety and performance of a medical device throughout its entire lifetime. Effective PMCF systems generate **Real World Evidence** that provides data on device performance outside the constraints of a formal clinical trial. PMCF is discussed in detail below.

**Vigilance** concerns the collection and reporting of data on serious incidents, Field Safety Corrective Actions (FSCAs), and the monitoring of trends of expected side-effects.

A distinction must be made between serious incidents and expected side-effects. Manufacturers must specify how this determination has been made in the PMS plan.

- **Serious incidents** are unexpected or “new” incidents that take or threaten life or limb. Article 87 requires that they are reported to the competent authority as soon as a causal relationship between the device and the incident has been identified.
- **Expected side-effects** are undesirable clinical effects related to use of the device that are not 'new' and have already been addressed in risk management processes. Each known side-effect should be detailed in product literature such as the IFU and should be mitigated against as far as possible. Article 88 requires manufacturers to monitor all known side-effects and report any statistically significant increase in the frequency or severity of them.

Article 89 describes the expected process for following up on serious incidents and details what is required when undertaking a **Field Safety Corrective Action (FSCA)** - a corrective action designed to prevent the recurrence of a serious incident. The follow-up process shall include:

- An investigation on the facts
- A risk assessment focused on the event
- Co-operation with notified body and competent authority
- Not making changes to or sampling any devices that are under investigation – they must be supplied for examination “as is”.

If a FSCA becomes necessary, the manufacturer must bring it to the attention of users of the device through a **Field Safety Notice (FSN)** that must include:

- Unique identification (UDI) of devices affected
- Manufacturer details
- Reasons for FSCA
- Details of risks to patients, users or others
- Actions to be taken - i.e. what actions the users of the device must take to reduce the risk of the serious incident occurring in future.

# MDR Annex III: Technical documentation on PMS

MDR Annex III lists the requirements for the technical documentation that must be produced in relation to the Post-Market Surveillance (PMS) system for every medical device under the MDR. It is a short Annex that is easy to read and work with.

Annex III specifies that PMS technical documents must include:

- A **PMS Plan**
- A **Periodic Safety Update Report** (PSUR – Article 86) if Class IIa, IIb or III
- A **PMS report** (Article 85) if Class I

The Annex provides useful detail about the requirements for writing a **PMS Plan**. Combining this detail with the expected uses of the PMS system defined in Article 83 helps to ensure that the PMS plan is correctly constructed for compliance with the MDR.

The **PMS plan** needs to describe how data will be collected and used from sources including:

- Serious incidents, PSURs, FSCAs
- Records of non-serious incidences and side-effects
- Trend reporting information
- Specialist or technical literature
- Databases and/or registers
- Feedback and complaints
- Public information about similar devices (e.g. newspaper reports)

The **PMS plan** must contain the following aspects:

- A documented process to collect information from the above sources
- Methods to assess collected data
- Indicators/thresholds/rationale used during risk analysis

- Methods for collecting and investigating complaints
- Methods for statistical analysis of trends
- Methods for communicating with competent authorities, notified bodies and others
- Methods for tracing devices
- PMCF plan

**Structuring a PMS Plan is made easier by the detail outlined in Annex III MDR. However, designing the underlying processes and methods requires considerable clinical expertise. Mantra Systems' expert team of specially-trained medical professionals build and implement MDR-compliant PMS systems for all types and risk class of medical device. Contact a member of our team today to discuss your requirements.**

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# MDR Annex XIV Part B: Post-Market Clinical Follow-up (PMCF)

Post-Market Clinical Follow-Up (PMCF) is an important component of PMS systems under the MDR. It concerns the running of clinical investigations (often specialised in form) to collect data on the performance of a medical device in normal use.

**MDR Article 2** defines PMCF as:

> *"a continuous process that comprises the proactive collection and evaluation of clinical data from the use of CE-marked medical devices in humans according to intended use."*

Effective PMCF generates **real world evidence** that reflects device performance in normal use in the hands of real customers. PMCF data must confirm the safety and performance of the device ***throughout its entire lifetime*** therefore 'formal' clinical trials of limited duration are less useful for PMCF than a well-designed **medical device product registry.**

**MDR Annex XIV Part B** provides some detail about requirements for PMCF under the MDR. It specifies the need for summarising the outcome of PMCF in the form of a **PMCF report** that, in turn, will be part of the **Clinical Evaluation Report (CER)** for that medical device. It does not go into detail about what the PMCF report must contain because this will be informed by the type, quality and periodicity of data generated through PMCF activities.

MDR Annex XIV Part B does provide detailed requirements for writing **PMCF plans**. PMCF must be performed in accordance with a method described prospectively in a PMCF plan, which forms part of the technical documentation referred to in Annex III.

The **PMCF plan** must specify how it will:

- Confirm safety and performance of the device throughout its expected lifetime
- Identify previously unknown side-effects and monitor the rate and severity of known side-effects
- Identify and analyse any emergent risks
- Ensure continued benefit-risk acceptability
- Identify any systematic misuse or off-label use

Annex XIV Part B states that the **PMCF Plan** must include at least:

- General methods to be applied, e.g. gathering clinical data or literature searching
- Specific methods to be used, e.g. medical device product registry
- Rationale for chosen general and specific methods
- A reference to relevant parts of the CER that contain a summary of PMCF data, an appraisal of the PMCF system, and results of data analysis.
- Specific objectives addressed by PMCF
- Evaluation of clinical data from equivalent/similar devices
- Reference to any harmonised standards/CSs used
- Timescale of PMCF activities

Clinical expertise is required in order to develop an effective PMCF plan that will pass regulatory scrutiny and produce data of sufficient detail, quality and periodicity to meet requirements. The choice of method for generating data will be subject to assessment. Care must be taken to ensure that PMCF methods:

- will minimise sources of bias
- can be implemented in practice
- will be effective throughout the lifetime of the device
- will meet the objectives specified in the Annex.

PMCF activities must also conform to the relevant requirements in **Annex XV** for the conduct of clinical investigations. These requirements include the need for detailed study protocols, investigator's brochure, and other technical documents. Further, broader legislative requirements such as GDPR require careful handling of patient consent for data capture, data processing, and data storage.

Clinical expertise, legal insight and extensive experience working with such requirements is a pre-requisite for ensuring that PMCF activities will pass regulatory scrutiny.

**At Mantra Systems, this is where we excel. Our team of specially-trained medical doctors are experts at writing Annex III- compliant technical documents and building medical device product registries that meet all requirements for PMCF under the MDR. Contact Mantra Systems today to work with one of our expert clinicians in designing your PMCF system.**

# Summary

This concludes our commentary on MDR requirements for PMS systems. Our hope is that this document has served to clarify and contextualise what is required of PMS under the new legislation.

At Mantra Systems, we offer a range of services to help you implement a PMS system that will ensure compliance of your products both now and in the future. Our services include:

- Planning, designing, implementing and monitoring the performance of **medical device product registries** to generate **real world evidence** for robust PMCF
- Writing **PMS Plans, PSURs and PMS reports** to MDR Annex III standards
- Designing, implementing and overseeing **Vigilance systems** that comply with MDR Article 87, with services including:-
    - investigation, analysis and reporting of medical complaints
    - investigation, medical analysis and reporting of serious incidents
    - frequency and severity trends analysis for product complaints and side-effects

We also offer a range of training packages designed to ensure that your team is ready for the MDR implementation deadline in May 2021.

**Contact a member of our team today to learn more about our range of services and training:-**

- **Tel:** +44 114 386 3349
- **Email:** contact@mantrasystems.co.uk

For further information on these and our other services please visit our website **www.mantrasystems.co.uk.**