# PMS & PMCF: Creating integrated solutions

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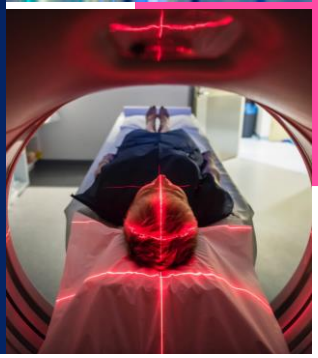
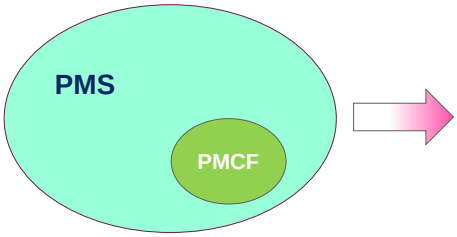



## Topics

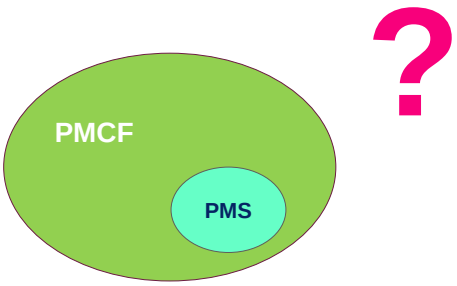
01 PMS vs PMCF – what's the difference under EU MDR?
02 A few notes on document logistics
03 Recap of frequent NB findings
04 Case study

# PMS vs PMCF– what's the difference?

**Pre-MDR**




**Post-MDR**

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# PMS vs PMCF – Annex III vs Annex XIV

## Annex III

(a) The post-market surveillance plan shall address the collection and utilization of available information, in particular:

— information concerning serious incidents, including information from PSURs, and field safety corrective actions;

— records referring to non-serious incidents and data on any undesirable side-effects;

— information from trend reporting;

— relevant specialist or technical literature, databases and/or registers;

— information, including feedbacks and complaints, provided by users, distributors and importers; and

— publicly available information about similar medical devices.

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# PMS vs PMCF – Annex III vs Annex XIV

## Annex XIV

6.1. The PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

(a) confirming the safety and performance of the device throughout its expected lifetime,

(b) identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

(c) identifying and analysing emergent risks on the basis of factual evidence,

(d) ensuring the continued acceptability of the benefit-risk ratio referred to in Sections 1 and 9 of Annex I, and

(e) identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.

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# PMS vs PMCF – Annex III vs Annex XIV

## Annex III

(b) The post-market surveillance plan shall cover at least:

— a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterisation of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market;

— effective and appropriate methods and processes to assess the collected data;

— suitable indicators and threshold values that shall be used in the continuous reassessment of the benefit-risk analysis and of the risk management as referred to in Section 3 of Annex I;

— effective and appropriate methods and tools to investigate complaints and analyse market-related experience collected in the field;

— methods and protocols to manage the events subject to the trend report as provided for in Article 88, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period;

— methods and protocols to communicate effectively with competent authorities, notified bodies, economic operators and users;

— reference to procedures to fulfil the manufacturers obligations laid down in Articles 83, 84 and 86;

— systematic procedures to identify and initiate appropriate measures including corrective actions;

— effective tools to trace and identify devices for which corrective actions might be necessary; and

— a PMCF plan as referred to in Part B of Annex XIV, or a justification as to why a PMCF is not applicable.

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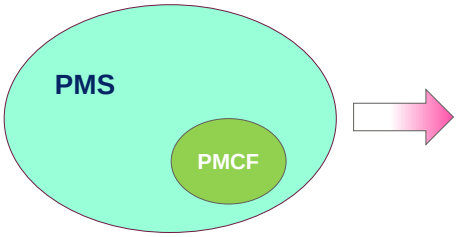
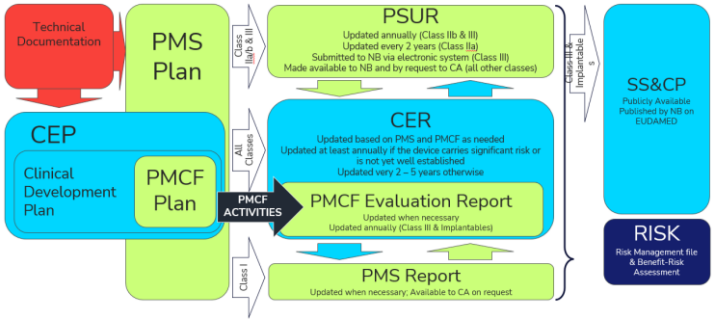
# PMS vs PMCF– what's the difference?

## Pre-MDR




## Post-MDR

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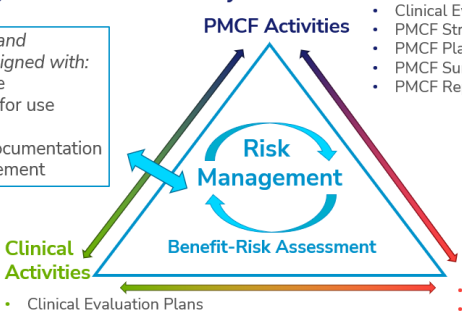
# PMS vs PMCF– and what are the logistics?

## Cross-Functional Integration

*Presenting a Consistent Story*

*Overall safety and performance aligned with:*
- Intended use
- Instructions for use
- Claims
- Technical documentation
- Risk management




- Clinical Evidence Matrix
- PMCF Strategy
- PMCF Plans
- PMCF Surveys
- PMCF Reports

- Clinical Evaluation Plans
- CERs
- Literature Search Protocols and Searches
- Literature Reviews

- PMS Procedures
- PMS Plans
- PMS Reports/PSURs
- Complaint analysis and trending

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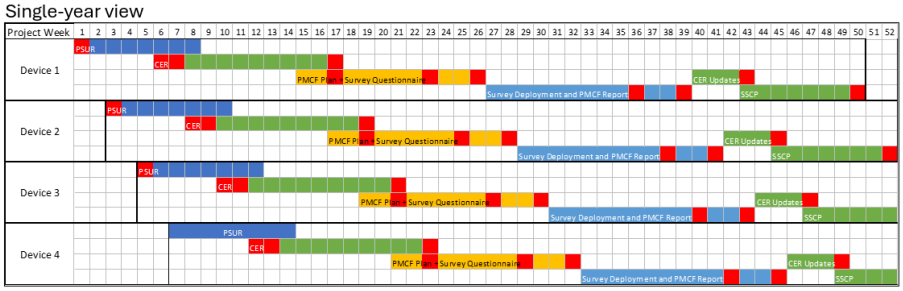
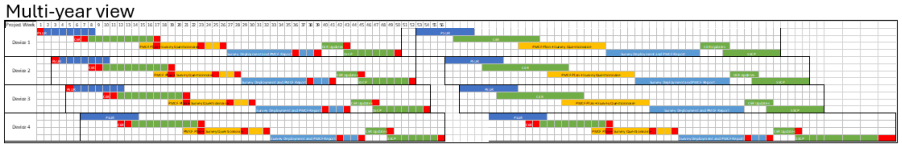
# PMS vs PMCF– and what are the logistics?

Single-year view

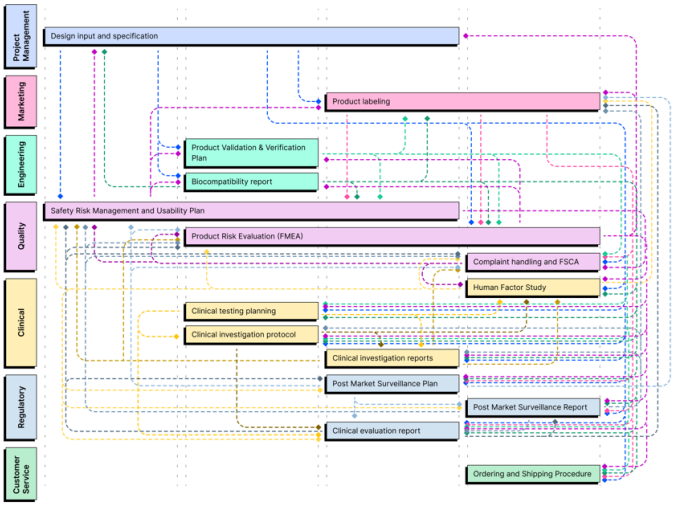



Multi-year view





# PMS vs PMCF– and what are the logistics?



## Top 5 Notified Body Findings

- Lack of alignment between PMS/PMCF activities and CER outputs
- Poor / absent interaction with risk management
- Ineffective trending mechanisms
- Inadequate justification for PMCF study design
- Cadence of document updates not satisfactory

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## Process

- Identify clinical evidence objectives
- Map existing data against these objectives
- Identify areas requiring confirming or additional granularity
- Select appropriate PMS / PMCF activities based on data needs and residual risk
- Select appropriate hypotheses
- Plan interim data analysis of SOTA and DUE data
- Create provisional PMS / PMCF plans based on interim analysis

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# Case study

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## Case study: Advanced wound dressing

| | |
|---|---|
| **Device Type** | Primary wound dressing |
| **Risk Classification** | Class III |
| **Indication** | The device is intended for use in management of clean, contaminated, or infected wounds with moderate to high exudate, including surgical wounds, traumatic wounds, partial-thickness burns and pressure ulcers<br>**(NOTE: does not include diabetic foot ulcers).**<br>**(Replace gauze every ≤7 days)** |
| **Clinical Benefit** | Manage the wound environment and promotes wound healing |
| **Clinical Outcomes** | • Wound bed size reduction<br>• Reduction in exudate levels<br>• Reduction in bacterial burden<br>• Any reported safety outcomes |
| **Years on market** | 15 years |
| **Device description** | Sterile, single-use gauze |
| **Device materials** | Cellulose, contains silver as antimicrobial |
| **Marketing region** | European Union, US, Canada |
| **Available data** | ***Simplified summary on next slide…*** |
| **Expected Lifetime** | - Per dressing (gauze), benefit is offered for up to 7 days<br>- However, benefit is offered for (months) when replaced with identical device(s)<br>- (Worst case) Residual (safety) risk is biocompatibility-related, for the cumulative continuous use period (months) |

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# Case study: Advanced wound dressing

| Study Type | Data Quality | # Patients | Reported Clinical outcomes | Clinical Outcome results (performance) | Clinical Outcome results (safety) |
|---|---|---|---|---|---|
| Case series study | 4 | 10 | • Wound bed size reduction<br>• Reduction in exudate levels<br>• Any reported safety outcomes | • Wound depth reduction by 10%-75%<br>• Exudate reduction | 0 |
| Prospective, non-randomised comparative study | 2 | 200 | • Wound bed size reduction<br>• Reduction in bacterial burden<br>• Any reported safety outcomes | • Wound healing (ASEPSIS scoring system)<br>• Reduction in SSI rate | Infection (3 mild and 1 moderate case) |
| Observational single-centre study | 4 | 50 | • Reduction in bacterial burden<br>• Any reported safety outcomes | • Statistically significant reduction in bacterial load in patients with pressure ulcers | 0* |
| Prospective RCT | 1 | 300 | • Wound bed size reduction<br>• Reduction in exudate levels<br>• Any reported safety outcomes | • Wound depth reduction by 60-85% vs control group (standard care) | 0* |
| Patient chart review | 4 | 300 | • Wound bed size reduction<br>• Reduction in exudate levels<br>• Reduction in bacterial burden<br>• Any reported safety outcomes | • Wound depth reduction by 20%-90%<br>• Exudate reduction<br>• Reduction of bacterial bioburden with time | Infection (2 moderate cases) |

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# Case study: Advanced wound dressing

## Manufacturer conclusions:

- Data on 860 patients covering all indications, patient populations
- Statistically significant outcomes relevant to claims and intended clinical benefits
- 15 year clinical history with no safety issues
- Common design with well established risk profile; no significant risks if used as intended
- “General” PMCF methods satisfactory

## NB request for additional info:

- Stratify data across specific indications and high-risk patient populations
- Provide statistical justification for acceptability of stratified data
- Provide evidence to support specific marketing claims
- Explain how you monitor for off-label use
- Provide justification for PMCF mechanisms, based on conclusions of revised evaluation

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# Case study: Advanced wound dressing

## Manufacturer conclusions:

- Data on 860 patients covering all indications, patient populations
- Statistically significant outcomes relevant to claims and intended clinical benefits
- 15 year clinical history with ne…
- …k
- …

These kinds of questions are NB-speak for: “You’re probably going to have to generate more evidence, or remove some indications / add more contraindications / warnings”

## NB request for additional info:

- Stratify data across specific indications and high-risk patient populations
- Provide statistical justification for acceptability of stratified data
- Provide evidence to support specific marketing claims
- Explain how you monitor for off-label use
- Provide justification for PMCF mechanisms, based on conclusions of revised evaluation

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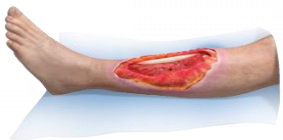
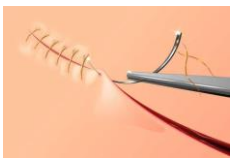
# Case study: Advanced wound dressing

**Indication**

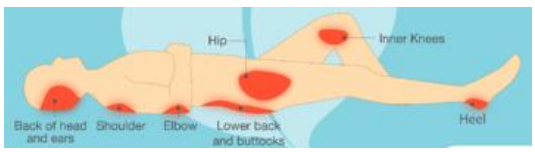
Traumatic wound



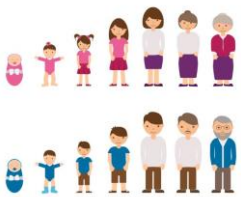
Surgical wound



Pressure ulcers




**Population**




**Follow-up**


**Safety**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# Case study: Advanced wound dressing

Suitable for sensitive skin

Painless removal

Does not stick to the wound

**Proven by available data !**

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# Case study: Advanced wound dressing

## Limited data / Weak areas

| Indication | Patient Populations | | | Mean follow-up time |
|---|---|---|---|---|
| | Pediatrics (<18) | Adults (18-64) | Geriatric (≥65) | |
| Surgical Wounds | 2 | 138 | 70 | 30 days |
| Traumatic Wounds | 0 | 300 | 0 | 15 – 90 days |
| Pressure Ulcers | 0 | 50 | 300 | 3 months |
| **Total** | **2** | **488** | **370** | NA |

Adequacy of data justified based on similar devices and SOTA:
- pediatric and geriatric populations for traumatic wounds
- pediatric populations for pressure ulcers
- follow-up time for pressure ulcers (3 months vs 6 months)

Note: warnings added to IFU re: risks in paediatric populations and contraindication in neonates

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# Case study: Advanced wound dressing

## PMCF specific methods - Study design options:

- Prospective clinical study
- Registries
- Retrospective data mining
- Surveys

## PMCF general methods:

- Literature review
- Vigilance (DUE and similar devices)
- Other user feedback

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# Case study: Advanced wound dressing

| Input Requirements | CIs | Registries | Retrospective Data-Mining | Surveys |
|---|---|---|---|---|
| Ability to cover all indications for balanced approach | Yes | Potentially | Potentially | Potentially |
| Ability to focus PMCF study on collecting data from pediatric and geriatric populations | Yes | Yes | Yes | Yes |
| Ability to collect patient data at 6 month follow-up for pressure ulcer indication | Yes | Yes | Potentially | No |
| Ability to ask participants in PMCF study about off-label use | No | No | Yes | Yes |
| Ability to collect occurrence rate and severity of adverse events to better estimate probability of harm / risk management updates | Yes | Yes | Yes | No |
| Activity cost | $$$$ | $$$ | $$ | $ |
| Activity time-scale | >1 year | 1 year to set up then ongoing | 6 months – 1 year | <6 months |
| Level of data quality per MDCG 2020-6 | 1 or 2 | 3 | 4 | 4 or 8 |

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# Case study: Advanced wound dressing

| Input Requirements | CIs | Registries | Retrospective Data-Mining | Surveys |
|---|---|---|---|---|
| Level of data quality per MDCG 2020-6 | 1 or 2 | 3 | 4 | 4 or 8 |
| Overall recommendation | Although “gold standard” approach, very expensive and time consuming, would not collect information on off-label use so not pragmatic for this device type | Unlikely scenario for this device not realistic to design registry for disposable product with this use case | Best case scenario; if well-designed able to collect data to meet all input requirements, cost-effective, efficient, and high quality data to meet requirements | Unlikely to produce high quality data to inform on enough PMCF study input requirements |

Justification:
- 15 years’ market history
- Proactive PMS under MDD; no trends or safety signals
- Pre-existing clinical data at levels 1 and 2 (RCT and prospective study)
- Usage consistent with SOTA and clinical best practice
- Given above, data collection based on RW usage more appropriate in the post-market phase

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# Case study: Advanced wound dressing

## How did it turn out?

- Accepted by NB
- No additional warnings limitations on intended use
- Systemic off-label use for diabetic foot ulcers detected – prompting review of RM, labelling, and follow-on study

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