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# PMCF in 5 steps

## How Castor EDC can help you achieve MDR compliance (Part II)

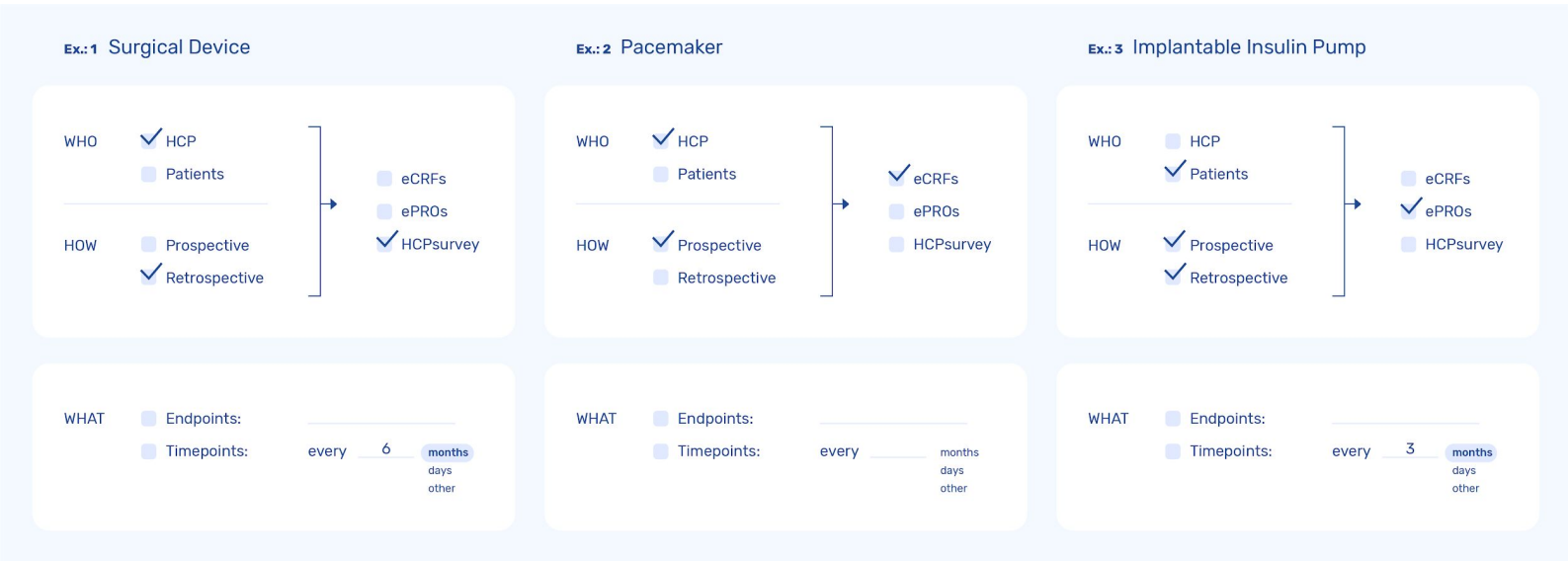
This document provides a brief overview of how Castor's 5-step approach to PMCF can be used to fulfill MDR requirements

## Contents

# Executive Summary

Under the MDR, manufacturers are mandated to routinely collect and evaluate data on their high-risk CE-marked devices with PMCF activities. Although these activities can be costly, PMCF processes can be optimized to significantly reduce costs. With Castor, manufacturers can create and execute PMCF activities smoothly and effectively in just 5 steps.

A user-friendly interface guides users to determine PMCF design - by indicating endpoints and whether the data are submitted by a HCP or patients, and whether the data are collected prospectively or retrospectively.




With this step, forms are automatically generated. Next, Castor's interface guides users to define enrollment strategy and then validate the model and forms created. Once PMCF activities have been launched, users can continuously track progress, and finally, extract the data into charts to be used in reports and submissions.

# Background

Clinical trials come with a high price tag, and the quality of clinical data resulting from such trials is often low compared to what manufacturers pay to generate the data. Low-quality clinical data makes healthcare decision-making significantly more difficult, which ultimately impacts patient safety (Meeker-O' Connell, et al. 2016). In contrast, real-world data (RWD) have the potential to provide insight into larger patient populations, and more comprehensive treatment options than data collected in randomized, controlled settings (Miksad et al. 2017; Singh et al. 2018).

In recent years, to protect patient safety and ensure the clinical benefits of available treatments, government agencies have attempted to overcome these challenges by requiring medical device manufacturers to proactively gather post-market clinical data. Post-Market Clinical Follow-Up (PMCF) studies constitute one such example. As discussed in the European Medical Device Regulation (MDR), PMCF studies are part of Post-Market Surveillance activities and should be aimed at capturing safety and performance outcomes for high-risk devices during their entire lifetime. These PMCF activities should be a continuous, proactive process. As a consequence, manufacturers are mandated to routinely collect and evaluate clinical data derived from the use of their CE-marked devices in humans.

The objective of PMCF requirements is to confirm the safety and performance of those devices "throughout the expected lifetime of the device, [thus] ensuring the continued acceptability of identified risks and detecting emerging risks on the basis of factual evidence" (EU MDR, Annex XIV Part B par. 5). Results derived from PMCF activities feed into the Clinical Evaluations Reports (CER) that manufacturers prepare to obtain or renew CE marks on their medical devices.

# The PMCF challenge

The EU MDR is scheduled to go into full effect by May 26, 2020. Following MDR full implementation, PMCF activities will be mandated as part of medical device surveillance programs. As a result, manufacturers will be tasked to plan and execute PMCF activities to gather the clinical data needed to confirm the safety and effectiveness of certain high-risk devices.

PMCF activities may include clinical studies, surveys and questionnaires, as well as focus groups. While these options appear as the gold standard, they can be costly. Planning and executing ad hoc PMCF studies is generally appropriate, insofar as the subject device uses new technologies that make it worth the extra scrutiny. However, a more common scenario is that of legacy devices lacking high-quality clinical evidence. In this case, running a dedicated PMCF study might be excessively burdensome for manufacturers, especially when these devices have been historically associated with low complaint rates. While protecting patients' health through continuous scrutiny of medical devices to confirm their safety and effectiveness is a necessary requirement, this process should be reasonably optimized.

To address the PMCF challenges arising from EU MDR implementation, Castor developed a 5-step approach to PMCF. This document illustrates how Castor can help your organization meet PMCF requirements through a cost-effective, MDR-compliant solution .

# PMCF in 5 steps

Although no two medical devices are the same, Castor's 5-step solution to PMCF is easily adaptable to suit different types of devices as well as different types of study design and data collection approaches. The result is a cost-effective solution that enables manufacturers to meet regulatory requirements and increase patient safety.

The 5 steps are as follows:

**STEP 1:** Decide on your approach

**STEP 2:** Define enrollment strategy

**STEP 3:** Validate model

**STEP 4:** Track progress

**STEP 5:** Extract PMCF data

# STEP 1: Decide on your approach

At the beginning of the process, manufacturers will determine their preferred approach and make a selection to indicate:

- Who will submit the data (either Health Care Professionals (HCPs) or patients/guardians)
- How the data will be collected (either prospectively or retrospectively)
- Which endpoints will be assessed and how often

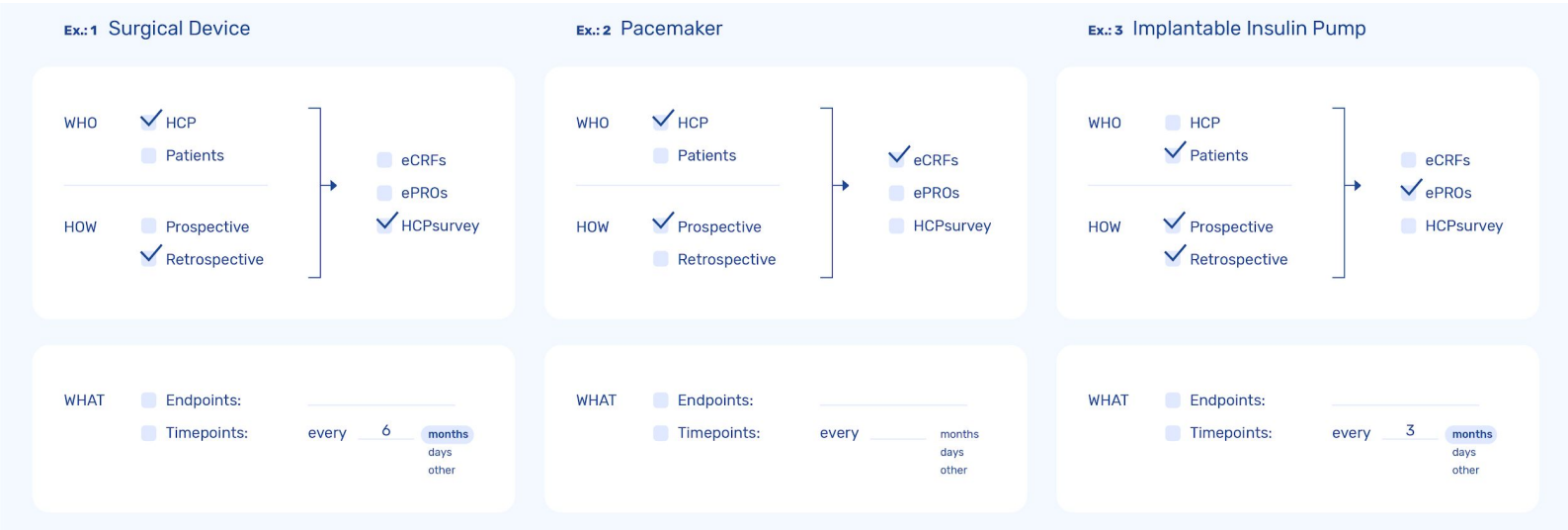



*Figure 1. Examples of PMCF approach selections in Castor*

Making the right initial choices is crucial, as PMCF activities can be leveraged to not only gather data that satisfy regulatory requirements, but also to gain a more comprehensive market experience on a specific device.

For example, if the subject device is an angioplasty balloon, PMCF data should be submitted by HCPs because properly trained practitioners are generally the sole users of these devices and patients tend to have a very limited experience--and therefore understanding--of the device.

Similarly, PMCF data on a device that is used in a specific medical procedure should be submitted preferably by HCPs rather than by patients. Clinicians may be better suited for assessing whether an adverse event was device-related or procedural, whereas patients might introduce higher rates of inaccuracies or biases into such assessments.

Conversely, patients might be the best candidates to submit PMCF data on certain wearable or implantable devices. For instance, with intrauterine devices (IUD) HCPs might not be a manufacturer's best bet with respect to submitting relevant PMCF data whereas patients could be more likely to provide clinical data on device performance as well as on potential adverse events. In addition, when choice on who should submit the PMCF data is strategically and appropriately done, the burden of missing data and lost-to-follow-up is minimized, which improves cost-effectiveness of PMCF activities.

The choice between prospective and retrospective PMCF design also depends on the specifics of the device under evaluation.

### Prospective PMCF Studies

In general, devices used within certain medical procedures will benefit from prospective submission of the PMCF data as safety and performance outcomes are usually available peri-procedurally and submission of those data is generally time-sensitive.

In contrast, wearable and implantable devices could benefit from patients retrospectively submitting relevant PMCF data to improve assessment of the medium- and long-term clinical outcomes while minimizing the potential for missing data.

Finally, specifying the endpoints to be assessed through PMCFs is another important choice for manufacturers, along with the frequency of the PMCF data collection. While clinical trial design is generally handled by clinical affairs departments, PMCF design might benefit from deeper collaborations and use of cross-functional teams to identify crucial, meaningful PMCF endpoints.

These choices feed into the creation of PMCF-tailored forms. By leveraging Castor's user-friendly EDC platform, manufacturers will be able to plan prospective PMCF data collection by embedding a Core Dataset (CD) into relevant studies in which their subject devices are used.

In this scenario, the PMCF CD can be captured by a clinician (ClinRO), a patient (PRO), a non-clinician observer such as a guardian (ObsRO), through a performance-based (PerfO) assessment or directly from the medical device using Castor's API, forms and surveys.

In addition, HCPs may be required to enter PMCF-relevant data into an electronic Case Report Form (eCRF) if PMCF activities were planned as part of an Investigator Initiated Study (IIS).

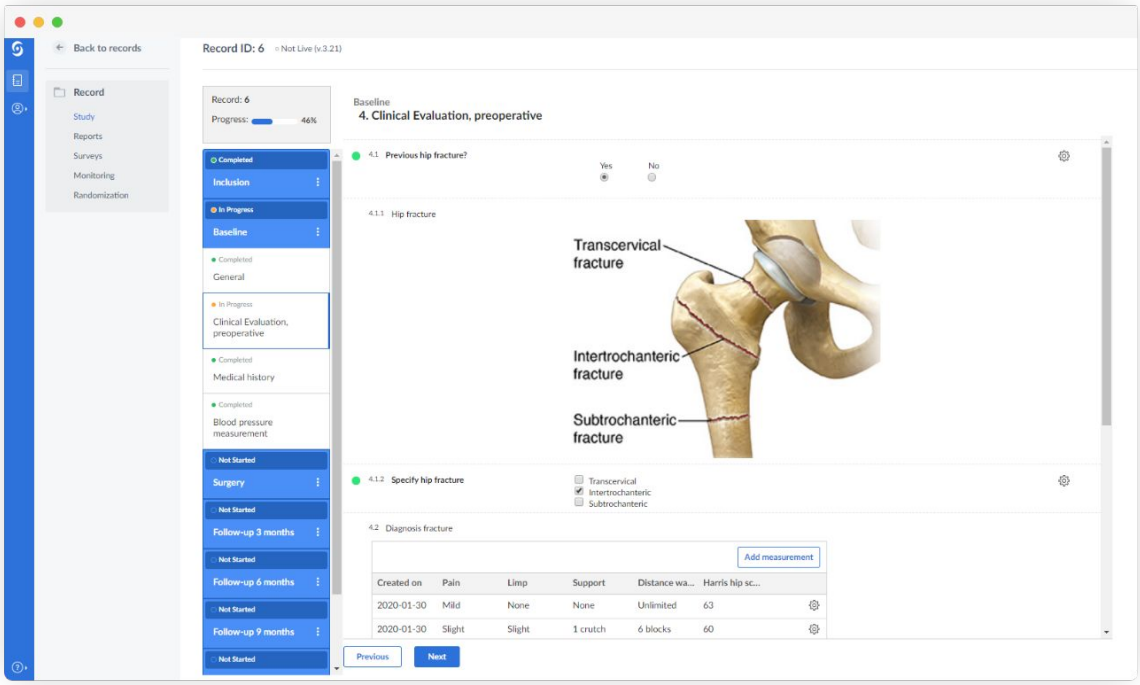



*Figure 2. Example of a form in Castor*

## Retrospective PMCF Studies

When collecting retrospective PMCF data, manufacturers will be able to use tailored surveys focused on PMCF-relevant endpoints and administered to patients (through ePRO forms), during a study, or occasionally to HCPs (through physician survey forms).

Surveys are built using a user-friendly form builder (by your team or using Castor's expert services) or by using Castor's proprietary PMCF templates with device-specific endpoints.

# STEP 2: Define enrollment strategy

## Enrollment of study participants can be an unpredictable and time-consuming phase of clinical studies

Manufacturers enroll participants in different ways. Both HCPs and patients can be enrolled based on the manufacturer's PMCF strategy. A sales roster can be provided to facilitate outreach to device users; alternatively, manufacturers can launch campaigns to solicit participants' interest and then upload candidate rosters to Castor. When participants have been identified, PMCF enrollment can be completed either through HCPs on their own, on their patient's behalf, or through patients depending on who will submit PMCF data.

Alternatively, when PMCF data are collected as part of an Investigator initiated study (IIS), the principal investigator (PI) initiating the study will complete the patients' concurrent enrollment in the PMCF activities.

## To shorten enrollment time and simplify the process, participants can be recruited online

For example, Castor technology enables users to enroll using eConsent forms.

In addition, whether or not PMCF data are being collected within an IIS, field encryption can also be used to protect personally identifiable information (PII) and facilitate re-use of clinical data for PMCF purposes. As an optional feature and as applicable to subject devices, during this step it will be possible to connect the device to the Castor platform--using the Internet of Things (IoT) device connectivity technology--to facilitate product surveillance when devices use a software component.

# STEP 3: Validate model

To validate that the model is set up for relevant PMCF activities, users can complete a feasibility or a pilot trial.

A feasibility trial enables model testing and provides users with an opportunity to make revisions to the forms generated as well as to the way these forms are administered to study participants. This type of trial can be run as a demo without collection of clinical data solely for model validation purposes.

As an alternative, if study participants such as HCPs/patients are enrolled, the trial can be run as a pilot PMCF study to collect small-scale datasets. The ease of use and flexibility of Castor's form builder allows users to build and test multiple form variations--quickly and without technical knowledge.

# STEP 4: Track progress

After the launch of a PMCF study, users have the opportunity to track PMCF study enrollment and progress, as well as to access real-time charts using an interactive dashboard in Castor's platform. These dashboards will enable users to monitor the quality of the data and to visualize provisional study outcomes, fulfilling the obligation to continuously detect "emerging risks on the basis of factual evidence" (EU MDR, Annex XIV Part B par. 5). Depending on the manufacturer's preference, ad hoc read-only access to adverse event reports can also be granted to Notified Bodies (NB) to facilitate audits.

Data entry, monitoring and PI sign-off progress can be tracked using Castor's built-in dashboards and integrated reports. Suspect data can be marked up and reviewed, and queries can be raised to solicit discussion between team members. Notifications can also be configured to immediately trigger emails for critical events, ensuring surveillance of emerging risks in a timely manner.


*Figure 3. Example of a study progress dashboard in Castor*

For companies with more technical capabilities, Castor's extensive API allows for the collection of data directly from devices, as well as real-time access to all data collected for more extensive analyses. Additionally, Castor's FHIR importer can be connected directly to EHR/EMR systems, which facilitates the automated, secure transfer of anonymized clinical data to the study records.

# STEP 5: Extract PMCF data

When planned PMCF activities are complete or at specific timepoints during the process, users can extract device-specific data to be used in support of the devices under PMCF evaluation.

The collected PMCF data can be extracted to suit specific outcome measures that support the "continued acceptability of identified risks" (EU MDR, Annex XIV Part B par. 5). Users can download these charts for use in PMCF reports as well as for use in other types of documentation.

One such example includes Periodic Safety Update Reports (PSUR), which manufacturers must compile under the MDR for their higher risk devices. In addition, manufacturers will be able to extract the results of PMCF activities to ultimately update CERs for CE mark renewal.

It is worth noting that, conducting PMCF activities provides an opportunity for manufacturers to gain further insight into the user experience and usability of their products. Thus, data collected in the context of PMCF can potentially contribute to identifying new research and development opportunities. We previously published a blog article that summarizes some of the benefits of PMCF and how it can produce value.

# About Castor

A global healthtech company, Castor enables manufacturers and research organizations to optimize clinical trials through the capture of high-quality clinical data that are reusable, thus maximizing their impact.

Since 2012, Castor has delivered solutions to support over 4,000 studies in collaboration with medical device, biotech, contract research, and academic organizations.

Castor's capabilities include:

- Electronic Data Capture (EDC) to maximize productivity in clinical studies and integrate data from different sources
- Electronic Patient Reported Outcome (ePRO) forms to administer surveys and collect clinical data into a centralized platform
- Integrations to capture data directly from multiple sources, including patients, clinicians, devices, wearables, and EHR systems
- eConsent to facilitate and automate patient enrollment processes
- Services for study set up and study conduct to help reduce study build time, capture higher quality data, and get to market faster

## Get in touch

For more information regarding Castor's 5-step approach to PMCF, please contact Floris Morang at floris.morang@castoredc.com

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