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Satisfying PMCF requirements by utilizing IIS data

How Castor EDC can help you achieve MDR compliance

This document provides details on an approach to re-use anonymous data from Investigator Initiated Studies (IIS) to fulfill MDR (PMCF) requirements

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Background

It has been estimated that 85% of the millions of dollars spent on clinical research fails to be useful; however, there is an increasing mandate for clinical data to help inform meaningful, pragmatic approaches to disease management. The costs associated with conducting clinical trials to generate new insights is often too high when compared to the slim returns, especially in terms of quality of the clinical data collected (Ioannidis J 2016). Yet maximizing the quality and variety of clinical data collection is a medical necessity, and a desirable business objective.

In general, the medical device industry spends hundreds of millions on Investigator Initiated Studies (IIS) or External Research Programs (ERP) each year, but there is limited quality control, monitoring and/or reuse of data generated in these studies. Studies focused on the "Value for Money" perspective on clinical trials indicate that 90% of the expenditures on these trials could be saved as inconclusive and inefficient (Ioannidis J 2016). A common failure is that investigators use tools not suited for data capture in a clinical study, for example, MS Excel or SPSS, rendering those projects non-compliant with GCP and 21 CFR Part 11. Furthermore, sponsors often have limited return on investment from IIS projects because they have little insight or control into how and when these projects produce a deliverable that adds value for their business.

To help resolve these challenges we propose a solution in which data generated through IIS will be of higher quality and should satisfy regulatory requirements for medical research such as those outlined in GCP and the MDR. Furthermore, our solution can maximize the impact of these IIS data for the investigator through successful scientific publications, and the sponsor through real-time progress reports and reuse of anonymous study data. The latter is particularly valuable in the context of the EU MDR, where substantially more Post-Market Clinical Follow-up (PMCF) data will be required to keep devices on the market.

Below we describe an approach that would enable medical device manufacturers to leverage anonymous data from IIS projects to support the fulfillment of PMCF data requirements.

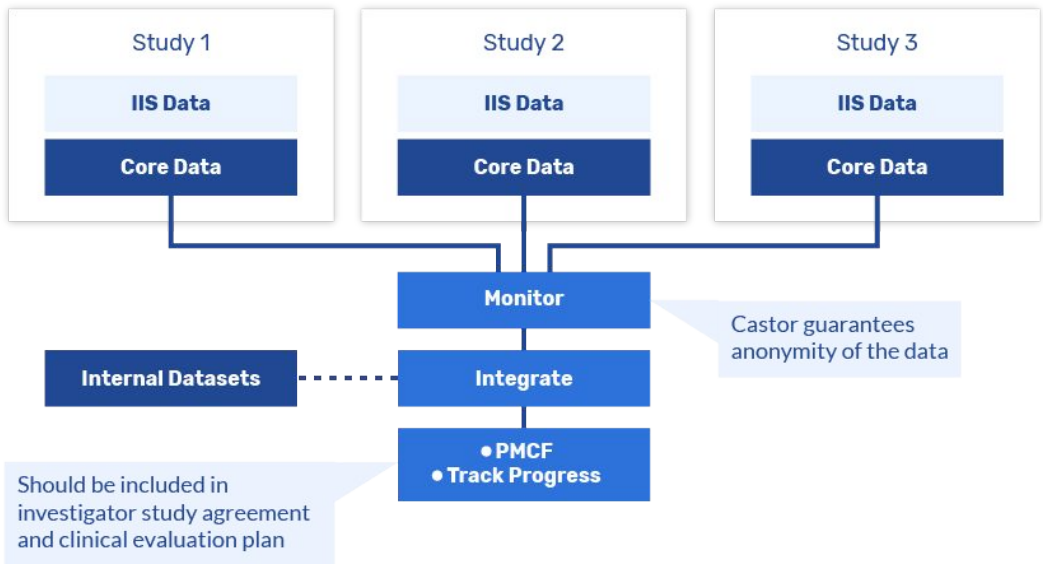
Outline of the Solution

Core dataset and clinical evaluation plan

The basic prerequisite for this solution is to provide investigators on IIS projects with a commercial-grade EDC platform (Castor EDC) that ensures captured data are of the highest possible quality and also meet all regulatory requirements. These regulatory requirements include GCP and 21 CFR Part 11, as well as ISO 14155 and ISO 14971, compliance to which is especially relevant for IIS-generated data to be acceptable within the context of the MDR.

In addition to ensuring IIS projects are conducted in a compliant and secure research infrastructure, this approach allows for the integration of a "Core Dataset" (CD) defined by the medical device manufacturer. The CD contains the most important outcomes relevant for monitoring the safety and performance of a device. Since manufacturers are typically not involved in defining what data will be captured in IIS projects, Castor will work directly with the investigators, acting as a liaison to support the integration of the CD in their projects.

Investigators will be able to build their study on top of the CD, as illustrated below.



The EU MDR describes PMCF activities as a proactive approach to "collect and evaluate clinical data from the use in or on humans of a device [...] throughout the expected lifetime of the device" (Annex XIV Part B par. 5). In the spirit of the MDR, PMCF activities should be aimed at gathering data from clinical experiences and on a patient-level. Therefore, integrating a CD that is tailored to collect PMCF-specific data from upcoming IIS may be a cost-effective solution to achieve regulatory compliance with PMCF requirements as described in the MDR.

Investigator Agreement and Informed Consent

To ensure full transparency towards investigators and patients, and to meet MDR requirements for proactively capturing these safety and performance data, the investigator agreement should clearly reflect the intended use of the anonymous CD. The investigator can include this purpose in the patient informed consent form, explaining that anonymous performance and safety data will be transmitted to the device manufacturer for regulatory purposes (Art. 63). Technically this additional statement is not required when anonymization is guaranteed, but for the sake of full transparency and in the spirit of GDPR, Castor's position is that this is the preferred approach.

Technical Specifications

The sponsor will work with Castor to define the CD. Castor will support the sponsor in annotating the CD so that it can produce standardized output. Castor will ensure the combined data points in this dataset cannot lead to direct or indirect identification of patients.

To allow data from the CD to be used in a PMCF context, these outcomes should be described in the PMCF plan (Art. 83, 84: PMS and Annex II + III, Annex XIV-B 6.1 & 6.2). The plan should describe an approach to proactively capturing these outcomes by embedding the defined CD in any new IIS projects going forward.

Castor will act as a third party with complete independence of the sponsor and provide guaranteed anonymous access to the CD. The investigator may disclose use of the CD for PMCF purposes in the published trial protocol (either in a (local) trial registry or in a peer-reviewed journal that fits this purpose), to ensure complete transparency as to which projects generated the data in the PMCF reports. Castor will support audits by a notified body to confirm that all data from IIS projects were included in the PMCF reports. We recommend that manufacturers state that these data are auditable in the technical documentation for the notified body.

When a new IIS project is identified, the sponsor outlines the approach described above. This means the following steps need to be completed:

- Use of the CD and access to these anonymous data are agreed upon in the investigator agreement
- Implementation of the anonymous CD is included in the Trial Protocol
- The trial protocol is registered through a local trial registry or peer-reviewed journal

After these steps have been completed, Castor developers will work directly with the investigator to build the study database on the EDC platform. This ensures a high quality data capture process and that sponsor has no direct access to any elements of the investigator study. This has the additional benefit of reducing the risk of costly study amendments when issues with the study build arise.

Castor will ensure that the CD is correctly embedded and may set up restricted, read-only access for both the sponsor and the Notified Body. The opportunity to access the data should allow both parties to monitor study progress (number of participants included), and the manufacturer to store and integrate these data with data from other IIS projects in progress, along with their internal datasets for use in Clinical Investigation reporting and PMCF.

Notified Body Reporting (Annex XIV-B Section 7)

When required, Castor may create PDF reports with statistics on combined safety and performance data from embedded CDs across multiple IIS projects. These PDF reports can be included in the technical documentation provided to the Notified Body (as required in Annex XIV-B Section 7).

Additional Capabilities

In addition to the CD capability described above, offering the Castor platform to investigators brings additional benefits, such as eliminating potential errors that result from manual entry by researchers, which increases the quantity and quality of clinical data as a return on investment. Furthermore, a solid grounding in clinical research in the academic setting enables Castor to smoothly and successfully set up contracts with investigators, a step that is often a challenge for medical device manufacturers. We have listed additional capabilities below.

ePRO

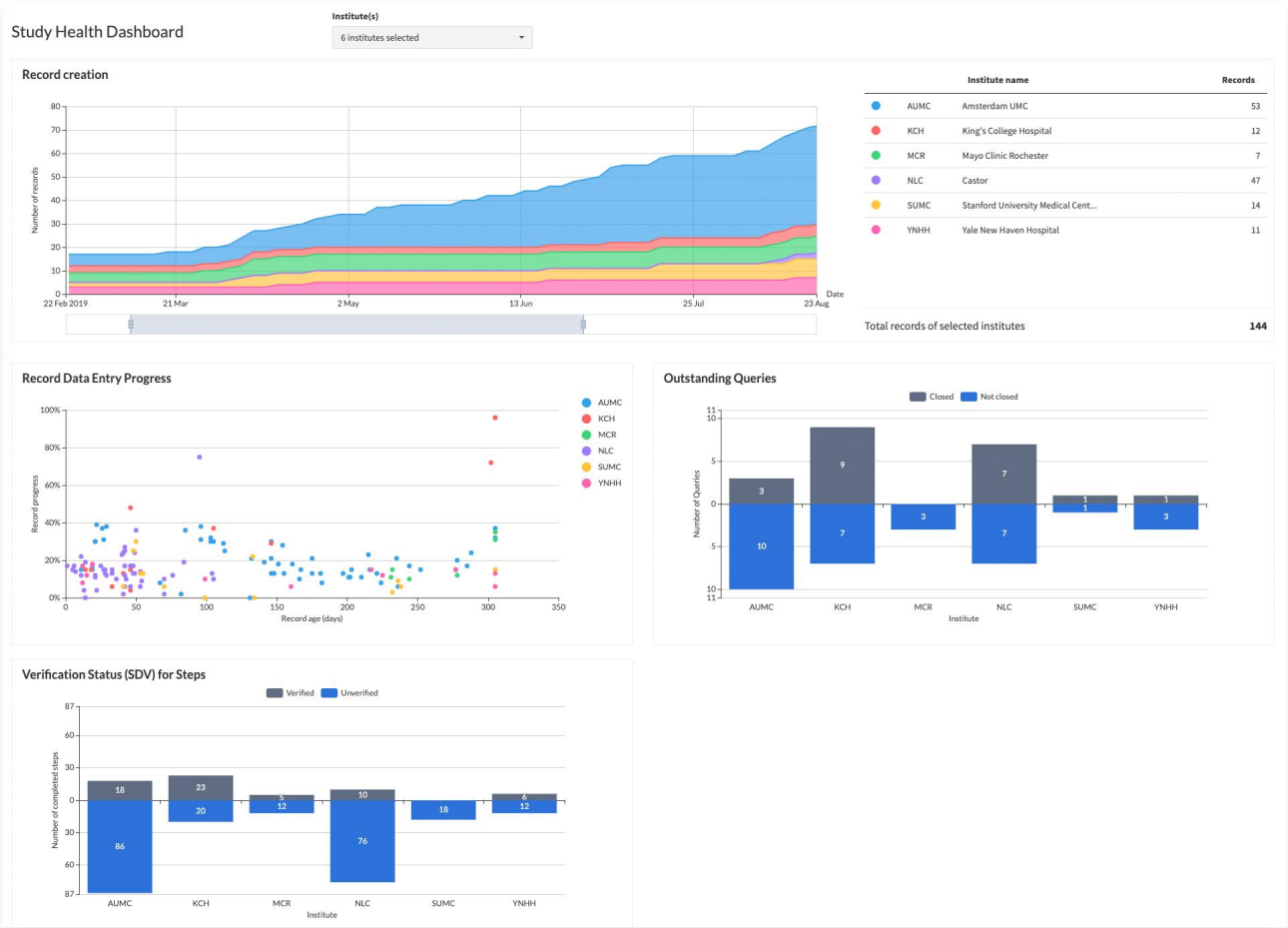
ePRO is our most popular module and is being used in over 2000 live projects to securely capture patient data without the need for paper. With higher data quality and significantly increased efficiency, ePRO is widely recognized as the standard for capturing patient data remotely. Castor's module enables investigators to easily define and manage questionnaires that can include Quality of Life and product efficacy data.

API device integration

Data can be directly pushed from your devices into the investigator's study database through Castor's API. This greatly increases data quality and study efficiency. Both raw data and interpreted data can be pushed to support an investigator's project.

Study Progress Dashboard

Our study progress dashboard allows sponsors to gain insights into IIS study progress with an aggregated, real-time data view. This dashboard will be available across the IIS portfolio, ensuring manufacturers can check-in with their running IIS projects at any time.



Example of a study progress dashboard

Contact

For more information regarding the use of Castor's platform for IIS studies, please contact our team at sales@castoredc.com.

References

Ioannidis JPA (2016) Why Most Clinical Research Is Not Useful. PLoS Med 13(6): e1002049. https://doi.org/10.1371/journal.pmed.1002049

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

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