METRC Policy & Procedure Manual

Title: METRC Study Site Management

General Description & Purpose: This document describes the METRC Coordinating Center's standards and procedures for working with sites throughout their participation in METRC studies.

I. Study Sites

METRC's network of clinical sites is composed of more than 70 Level 1 or Level 2 civilian trauma centers and 6 Military Treatment Facilities. A subset of clinical sites from METRC's network is selected for participation in any given METRC study; these are considered the "study sites".

II. Study Site Personnel

Minimally, every study site identifies a local Study PI and Research Coordinator who are responsible for the conduct of the study at the study site. Sites may identify one or more associate investigators, other practitioners such as physical therapists, or additional research personnel. The METRC Coordinating Center maintains records of these individuals and their respective roles in its Administrative Database. These records are used to generate distribution lists for study memos, communications with specific sites, etc.

All investigators and personnel working on a given study must be certified by the METRC Coordinating Center before initiating screening and enrollment for the study. Site certification procedures are described in detail in the Site Certification SOP.

III. Ongoing Review of Study Site Status

MCC study teams meet weekly or biweekly to review overall study progress and the progress of each individual study site. During these meetings, the Study Manager, the MCC study team member primarily responsible for managing and assisting the study sites, provides a status update for each site. This update includes a description of what progress the site has made since the last study team meeting, what challenges the site is experiencing, if any, and other pertinent information. As appropriate, the MCC study team identifies specific actions for the MCC study team and/or the study site team to take to overcome challenges or to maintain study progress.

IV. Study Phase-Based Approach to Site Management

The METRC Coordinating Center provides training and assistance for study sites during every phase of study implementation.

Regulatory Review and Approval

Prior to releasing master study materials to sites, the MCC conducts an initial study training. The purpose of the initial training is to provide a high-level overview of the study to the study sites and to prepare them for the regulatory review and approval process; this process is now tied to the single IRB.

The initial study training includes but is not limited to:

- Introduction of MCC study team members, Study PI, and other key contacts for sites
- Brief background information and focus area for the study, e.g., precision medicine, infection, etc.
- Description of main objective, specific aims, and hypotheses
- Description of patient population, inclusion and exclusion criteria
- Overview of study design and schedule
- Overview of data collection and outcomes
- Description of intervention(s), if applicable
- Overview of procedures for screening, enrollment, and follow-up
- Overview of regulatory review and approval process

Upon completion of the initial training, the MCC provides tailored, one-on-one assistance to sites via phone calls and email as the sites proceed with procedures for obtaining IRB, and as necessary, DoD HRPO approval. The regulatory review and approval process is described in a separate SOP.

Training and Certification

While study sites are awaiting approval from the IRB and/or DoD HRPO, the MCC provides additional training and assists the study sites in preparing for study certification. The most appropriate additional training activities are determined on a study-by-study basis. They typically include but are not limited to:

- A second training to provide a more in-depth overview of study procedures, data collection, and follow-up procedures
- Working with study sites to develop local SOPs which describe implementation-related procedures that are specific to the site, e.g., where, when, and with what data/information sites will conduct screening
- Study certification/ initiation calls with the site PI and research team, the MCC study team, and the study PI (of the overall study)

On a rolling basis, as study sites receive all required regulatory approvals, the MCC study team certifies the sites to begin study implementation. Site Certification procedure are described thoroughly in the Site Certification SOP.

Study Initiation, Screening, and Enrollment

Study sites that are certified by the MCC are permitted to begin screening and enrollment. After study initiation, the MCC study team continues to have frequent contact with sites, tailoring the approach and level of support to the specific and changing needs of each site. Site management focus areas for this phase of study implementation are related to:

- Ensuring that sites are screening consistently and at a volume consistent with their projected screening volume

- Ensuring that the conversion rate of screened-to-enrolled participants is within expected thresholds; this includes ensuring that sites are appropriately applying screening criteria and documenting screen failures in the study database
- Ensuring that the sites are equipped with all required study materials and supplies
- Ensuring adherence to randomization and blinding procedures as appropriate
- Ensuring that sites are obtaining complete and accurate data for all enrolled participants

The MCC study teams have multiple strategies for providing support and monitoring sites during study initiation. The study teams tailor these strategies to the needs of the study and the study sites. Some examples include:

- Requesting that the site provide billing data records to assess thoroughness of site screening volume
- Establishing benchmarks or screening and enrollment goals
- Developing a repository of "tips and tricks" for screening and enrollment
- Implementing a "Provisional Certification" or "Provisional Enrollment" phase during which the site must demonstrate that it has the knowledge and capacity to conduct the study
- An escalation plan for managing sites that are failing to make adequate progress, up to and including terminating a study site's participation in the study

Follow-up

Most METRC studies are longitudinal and include at least one follow-up visit. Once study sites are screening and enrolling at an adequate threshold, the MCC study teams expand their site management focus to include ensuring complete follow-up.

During the Site Certification process, study sites are required to explain how they will maintain contact with study participants and how they will ensure complete follow-up. The MCC study team reviews sites' plans for follow-up and, during regular communications with the sites, ensures that the plans are thoroughly executed and updated or enhanced as appropriate.

The MCC provides extensive guidance on follow-up best practices and tools such as follow-up calculators to assist sites with follow-up. Also, the MCC maintains a comprehensive protocol for 'Hard to Reach' participants. The MCC study team revisits this protocol with sites that have participants who are lost to follow-up. For sites with concerning follow-up rates, the MCC study team may require the site to have regular calls to review the status of all follow-ups that are due or soon due; in some cases, the local study PI is asked to join these calls.

Close out

Upon study completion, the MCC study team assists sites in executing the Study Close Out Checklist. This checklist and more thorough close out procedures are described in a separate Study Close Out SOP.

V. Monitoring & Data Quality Assurance

Study data is monitored prospectively through regular reports which track study progress and data quality and completeness. The MCC study team, in conjunction with the study Data Analyst and MCC Informatics Core, develop study-specific queries which are programmed into METRC's customized, state-of-the-art, automated querying application. Study sites are sent data queries prospectively and the

MCC study teams monitor sites' attendance to these queries. The querying application is described in a separate Data Queries SOP. In general, queries are designed to most closely monitor data that are most closely tied to each study primary and secondary outcome and covariates.

Sites that fail to adequately address data queries, or sites that do not address data queries in a timely fashion, may be required to have regular calls with the MCC study team to resolve queries in real-time.

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