

## METRC Policy & Procedure Manual

**Title:** Regulatory Review & Approval

**General Description & Purpose:** This document describes the METRC Coordinating Center's standards and processes for regulatory review and approval.

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### **I. Master/ Parent IRB Approval**

#### *Selecting a single IRB of Record*

Multicenter studies sponsored by government agencies that are signatories to the Common Rule (including DoD, NIH) are required to use a single IRB. METRC does not dictate which single IRB must be used. Some single IRBs METRC has used in the past include the Johns Hopkins School of Medicine Single IRB, Advarra, Pearl, Chesapeake, and Western IRB. Each single IRB service provider has advantages and disadvantages related to cost, the user experience within their electronic platform, and efficiency of reviews.

The MCC has developed some decision-support tools, e.g., a single IRB cost calculator, but ultimately the final selection of single IRB is left to the study PI.

#### *Master Single IRB Application*

Once a study protocol is finalized and approved by the Protocol Committee, the MCC study team prepares and submits the master IRB Application, often referred to by the single IRB providers as the "parent application". Application requirements are dependent upon which single IRB is used. The MCC study team consults the specific single IRB to confirm the requirements prior to initiating the application.

#### *Master Study Materials*

Regardless of which single IRB provider is used, the MCC study team always develops a Master Study Protocol and Master Informed Consent Form(s). METRC maintains templates for these essential documents, however, the study team is responsible for confirming that they are using the correct template and correct version as these templates are occasionally updated.

Other master study materials include but are not limited to: HIPAA waivers, case report form portfolios, study-specific SOPs, and intervention manuals. Some single IRB providers require submission of these documents as part of the IRB application while others do not. The MCC study team will confirm which documents are required prior to application submission.

Regardless of whether they are submitted to the single IRB, master study materials repositories are maintained for each METRC study on the password-protected Study Materials section of the METRC website. Access to this section of the website is granted by the MCC Informatics Core when appropriate.

### **III. Study Site IRB Approval**

As with the parent IRB application, there are some differences across single IRB providers related to the study site applications. The study site applications are often, but not always, referred to as “p-sites” where the “p” is intended to stand for “participating”. Some single IRBs allow p-sites to generate their own logins and to submit their own materials; other sites require that this is done via the MCC. The MCC confirms and provides clear guidance to study sites on how to obtain p-Site approval once the master approval is obtained.

METRC requires that study sites understand and adhere to their local institutional policies regarding participation in multicenter studies and reliance on outside IRBs. In some cases, sites are required to submit a pared-down version of an IRB application to their local IRB or other local review body, prior to pursuing p-Site approval. The MCC defers responsibility for adherence to these requirements to the study sites; the MCC will ask the p-Site to confirm that they’ve taken all necessary steps at the local level prior to (or during) their IRB application.

#### **IV. DoD HRPO Approval**

The majority of METRC studies are sponsored by the Department of Defense (DoD). The DoD requires a secondary approval of every IRB-approved application, both master and p-site. The Human Research Protections Office (HRPO) within the United States Army Medical Research and Materiel Command is the group that conducts these reviews. Different reviewers are assigned to every METRC study. Prior to conducting the initial study training, the MCC study team will consult with the primary HRPO liaison to confirm the name and contact information of the assigned HRPO reviewer. The initial study training will incorporate this information as well as specific instructions for obtaining HRPO approval at the site level.

Even though multicenter studies are now approved by a single IRB, the DoD HRPO still reviews and approves every p-site separately. Study sites are responsible for submitting their materials to DoD HRPO upon p-site approval from the single IRB. HRPO reviewer assignments and submission instructions change periodically. The MCC maintains reference documents for HRPO contacts and submissions on the METRC website.

#### **V. Continuing Reviews**

##### *Single IRB Continuing Review Approval*

Under the single IRB model, continuing review for multicenter studies is consolidated into one annual review. All p-sites that are part of the IRB application as of the time of the continuing review are approved for the continuing review, regardless of when they were initially approved as a p-site.

##### *DoD HRPO Continuing Review Approval*

The DoD HRPO requirements for continuing review approval are different from the initial approval requirements in that all sites are reviewed and granted continuing review approval at the same time. The MCC study team is responsible for submitting the continuing review materials to the DoD HRPO upon receipt of continuing review approval from the single IRB.

#### **VI. Master Protocol Amendments**

##### *Single IRB Master Protocol Amendment Approval*

Under the single IRB model, when a master protocol amendment (sometimes called a Change in Research) is approved by the single IRB, all p-sites automatically receive approval. In some cases, p-sites are asked to make updates to site-specific documents like Informed Consent Forms that are transferred onto templates with local institutional information. The MCC is responsible for submitting master protocol amendments to the single IRB. The MCC notifies the study sites if they are required to do anything in support of the master protocol amendment application.

*DoD HRPO Master Protocol Amendment Approval*

The DoD HRPO reviews and approves master protocol amendments for the master and p-sites all at the same time. The MCC study team is responsible for submitting the master protocol amendment materials to the DoD HRPO upon receipt of master protocol amendment approval from the single IRB.

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**Last Updated:** September 2021