METRC Policy & Procedure Manual

Title: Standards & Procedures for Clinical Site Certification

General Description & Purpose: This document describes the METRC Coordinating Center's standards and procedures for certifying a METRC site to begin screening and enrollment activities for a given METRC study.

Corresponding Documents:

A. Clinical Site Certification Documentation Checklist Template
B. Clinical Site Certification Form Template
C. Clinical Site Certification Approval Email Template

I. Site Certification Definition and Purpose

METRC Policy Regarding Clinical Site Certification

Clinical Site Certification is the process by which the clinical site, and specific individuals within the site, are reviewed and approved to engage in study activities for the given METRC study. A site may not initiate formal screening and enrollment activity prior to receipt of Clinical Site Certification approval from the METRC Coordinating Center. As part of the Certification approval, the MCC will specify which individuals at the clinical site are certified and approved to engage in which study activities.

Purpose of Clinical Site Certification

Clinical Site Certification is the final step is the regulatory review and approval process for clinical sites participating in METRC Studies. The overall purpose of MCC Site Certification processes is to ensure that all sites participating in a given METRC study are fully prepared to begin screening and enrollment and to implement all study procedures as described in the study protocol. More specifically, Certification processes facilitate the following communication and planning between the MCC and the sites:

- Verification that the site has met all necessary regulatory review and approval requirements, e.g., approval by the local IRB or centralized IRB, approval by other sponsoring agencies such as the DoD HRPO, etc.
- Verification that the site has fully developed plans for implementing all key study procedures
- Identification of who on the site research team will be responsible for carrying out specific study procedures, who will collect or contribute key data elements, and who will make key decisions if necessary over the course of study implementation
- Verification that all study personnel have received adequate training and that they have appropriate levels of access to the institutional resources which will be necessary for study conduct, e.g., the Electronic Medical Record, Outpatient/Clinic Records, Billing Data, etc.
- Verification that the site has identified the necessary facilities and equipment necessary for carrying out the study

II. Documentation Submitted and/or Reviewed in Support of Certification

In order to fulfill the purpose of Clinical Site Certification (described in the above section), the site must submit documentation to the MCC which demonstrates the site and the study team's preparedness for study implementation. Some of the required documentation is submitted to the MCC indirectly at earlier phases of the Regulatory Review and Approval process. Other pieces of documentation must be submitted specifically for Certification purposes, after all other required approvals have been obtained. Finally, there are some pieces of documentation already on-file at the MCC and these documents do not require re-submission for every new study certification.

Each piece of documentation minimally required for Clinical Site Certification Approval is described in the table below. Also noted is the typical time at which the documentation is submitted; actual submission times may vary.

Document/ Documentation	**Description**	**When Documentation is Usually Submitted**
IRB Application Materials	IRB Application materials include the local or single IRB application, the study protocol submitted to the local or single IRB, consent Form(s), HIPAA Authorization, study advertisements such as brochure inserts, etc.	For DoD sponsored studies, the IRB Application Materials are submitted at the time of DoD HRPO Submission. For non-DoD sponsored studies, materials are submitted to the MCC upon approval. For studies using the JHM SIRB, the MCC will retrieve the materials directly form the eIRB application.
IRB Approval Letter(s)	Official approval letter from the local or Single IRB	For DoD sponsored studies, the IRB Approval Letter is submitted at the time of DoD HRPO Submission. For non-DoD sponsored studies, the letter is submitted to the MCC upon approval. For studies using the JHM SIRB, the MCC will retrieve the letter directly form the eIRB application.
For DoD Sponsored Studies only: DoD Human Research Protections Office (DoD HRPO) Approval Letter	Official approval memo from the DoD HRPO. This memo is sent via email by the DoD HRPO reviewer to the site PI and other study team members at the site and the MCC.	The MCC study team is typically carbon copied on the DoD HRPO approval memo. The site does not need to forward or submit the approval memo to the MCC unless the site notices that the appropriate contacts at the MCC were not cc'ed on the memo; in this case the site should also request that the reviewer updates his or her distribution list. Likewise, the MCC will verify that the appropriate contacts at the clinical site were cc'ed on the memo and will rectify the distribution list with the HRPO reviewer as necessary.
Clinical Site Certification Form	This is a study specific form on which the study team must document certification-specific information, e.g., basic descriptions of study implementation plans, dates of submission of other documentation, which individuals will conduct which study activities, etc.	The Clinical Site Certification Form may be submitted to the MCC once IRB approval (by local IRB or single IRB) is obtained. For DoD sponsored studies, this form may be completed and submitted even if the HRPO approval is pending.

	Please note: If certification approval is being requested for study team members who have never before been certified for a METRC study, it is important to include their complete contact information on the Clinical Site Certification Form.	**More information about when and how this form is submitted is included in a later section of this PPM document.*
Medical Licenses (clinicians only)	Each study surgeon/clinician must submit a current medical license, if not previously submitted to the MCC as part of certification for another METRC study.	The MCC maintains a "Certification Document Repository" in which it files non-study-specific documents submitted in support of certification. If the MCC already has copies of the clinicians' current medical licenses, they do not need to be re-submitted at the time of certification for the given study. Otherwise, the licenses may be submitted at any time during the regulatory review and approval process, prior to certification.
Curriculum Vitae or Resume	Each member of the study team seeking certification approval must submit a CV or resume, if not previously submitted to the MCC as part of certification for another METRC study.	CVs and Resumes are filed in the MCC's "Certification Document Repository" (described in the row above). If the MCC already has copies of the study team members CVs or resumes, they do not need to be re-submitted at the time of certification for the given study. Otherwise, the CVs or resumes may be submitted at any time during the regulatory review and approval process, prior to certification.
Basic Human Subjects Research Training Completion Certificate	Each member of the study team seeking certification approval must submit a Basic Human Subjects Research Training Completion Certificate. This may be a CITI-training certificate (Collaborative IRB Training Initiative), or a certificate from an institutional training equivalent to CITI. Certificates must be current within 3 years; individuals must take a Refresher course upon expiration of their previous certificate.	Human Subjects training certificates are filed in the MCC's "Certification Document Repository" (described in the rows above). If the MCC already has copies of the certificates, and if those previously-submitted certificates are not expired, they do not need to be re-submitted at the time of certification for the given study. Otherwise, the certificates may be submitted at any time during the regulatory review and approval process, prior to certification.
Good Clinical Practice (GCP) Training Completion Certificate	The Site PI and all Research Coordinators and Research Assistants seeking certification approval must submit a Good Clinical Practice Training Completion Certificate. This may be a CITI-training certificate, or a certificate from an institutional training equivalent to CITI. There are multiple options for GCP trainings, e.g., GCP for social and behavioral research, GCP for drug and device trials, etc. Any of these trainings meet the MCC requirement; it does not matter which GCP training was taken. Certificates must be current within 3 years; individuals must take a Refresher course upon expiration of their previous certificate.	GCP training certificates are filed in the MCC's "Certification Document Repository" (described in the rows above). If the MCC already has copies of the certificates, and if those previously-submitted certificates are not expired, they do not need to be re-submitted at the time of certification for the given study. Otherwise, the certificates may be submitted at any time during the regulatory review and approval process, prior to certification.

	**Research Coordinators or Research Assistants who are <u>only</u> involved in regulatory work, e.g., submitting continuing reviews, etc., do not need to submit GCP certificates.*	
Conflict of Interest (COI) Disclosures	Each member of the study team seeking certification approval must have COI disclosure current within the year. For investigators on the study team who are members of the American Academy of Orthopaedic Surgeons (AAOS), the annual required disclosure to AAOS will suffice; this disclosure is publicly searchable, includes the date of disclosure, and is renewed every year. For non-AAOS members, disclosure may happen via the AAOS mechanism (it is available to the public, regardless of AAOS membership) or via a METRC-specific REDCap COI disclosure report form. Conflict of Interest reporting is described in further detail in other METRC PPM documents.	Conflict of Interest reporting occurs on an ongoing basis. Study team members may confirm that their COI disclosures are complete and up-to-date at any time prior to certification. If an individual has not submitted a COI disclosure, s/he must do so prior to certification using the AAOS-mechanism or the METRC-specific REDCap COI disclosure report form.

The above table may also be found on the Clinical Site Certification Documentation Checklist (Corresponding Document A). This Checklist version of the table exists as a resource for the clinical site and the MCC study team to ensure that all minimally required documents have been submitted in support of the clinical site's Certification.

III. The Clinical Site Certification Form:

A brief description of the Clinical Site Certification Form is described in the table above. This section provides a more thorough description of this form, it's purpose, and when and how it is submitted.

Purpose of the Clinical Site Certification Form

A template Clinical Site Certification Form is provided as Corresponding Document B to this PPM document. This template form is intended to be used as a starting-point for developing the Clinical Site Certification Form for a given METRC Study. The MCC Study team updates this form prior to initial study trainings and posts the form to the relevant Study Materials section of the METRC website.

The Clinical Site Certification Form, once made study-specific and completed by a site seeking certification approval, is intended to serve as an official summary record of critical information regarding the participating site including: administrative and approval information, expectations for screening and enrollment, plans for implementing for critical or logistically complex components of the study protocol, the site's listing of study team members, etc.

Completing the Clinical Site Certification Form

The questions included on the Clinical Site Certification form are representative of the components of the protocol that are expected to be complex or logistically challenging. Most of the questions will only be answerable after the site research team has invested significant time and energy into discussing and thoroughly planning for study implementation. The MCC study team is available to help sites work though the study logistics. The MCC study team can also help facilitate correspondence with the Overall PI for the study, should his or her expertise or opinion be needed during the process of making implementation plans.

Submitting the Clinical Site Certification Form to the MCC

Once it is completed, the Clinical Site Certification Form should be submitted by the site seeking certification approval to the MCC Study team. The minimum requirements for this submission are as follows:

- A member of the study team should submit the form to the MCC Study Manager as an attachment to an email.

- It should be made clear in the body of the email that the site is submitting the form in support of its request for certification approval, i.e., that the form is complete and ready for review by the MCC.

- The study team member should carbon copy the Site PI on the email.

- In lieu of having a wet-ink or electronic signature on the completed Clinical Site Certification Form, the Site PI may instead *Reply All* and indicate that s/he agrees with all the information included on the form and that it represents the site's expectations and plans to best of his or her current knowledge. The MCC Study Team will not commence its review of the form until the Study PI sends this acknowledgement and electronic sign-off on the form that was submitted.

- If the Site PI is the one to submit the form to the MCC Study Manager in the first place, s/he may simply indicate his or her approval and agreement with the information included on the form, i.e., the additional step is not required.

IV. Optional Certification Activities and/or Documentation Requirements

For some studies, the Overall PI and the MCC Study Team may decide that additional documentation or additional activities are needed to ensure that sites are adequately prepared for study implementation. Examples of these additional activities include but are not limited to the following:

- Pre-Certification site visits: These visits would involve one or more members of the MCC Study Team traveling to the site to meet with the study team and to verify critical study logistics, institutional resources, etc.

- Certification phone calls: These phone calls would involve one or more members of the MCC Study Team and would be intended to discuss critical or potentially confusing components of the study protocol, etc. These calls may or may not include the Overall PI for the study and the

Site PI. The surgeon participation is particularly helpful if there is a need to discuss or clarify components of the protocol pertaining to injury classification, surgical procedures, etc.

- Development of local study-specific SOPs: For studies where there are logistically complex components of the protocol, it may be helpful to have the site develop a local SOP wherein they thoroughly describe how they will address the study components in question. For example, if a study requires that blood samples be taken within 3 hours of admission to the ER or Trauma Center, the study team will need to plan for how and by whom this patient identification will occur, how and by whom the samples will be taken, how and by whom the samples will be processed and/or stored, etc.

- Issuance of Provisional Certification: The Overall PI and MCC Study Team may wish to issue a *Provisional Certification* to sites prior to full certification approval. This provisional certification approval would allow the site to proceed with enrollment and initial data collection for a pre-specified number of patients (e.g., 3 patients). The MCC Study Team will review the provisionally certified sites' initial patients and will document issues or concerns if necessary. If the site has demonstrated the capacity to meet data collection and data quality requirements during the provisional certification period, the MCC will proceed with issuing full certification approval.

All certification requirements for the given study will be made clear to the sites at an appropriate time and within an appropriate forum, e.g., during study kick-off trainings, on the Clinical Site Certification Documentation Checklist, etc.

V. Certification Approval Procedures

When Certification Approval is Issued

The certification activity and documentation requirements are described in detail in earlier sections of this PPM document. Once a site has met all the requirements, the MCC initiates the formal certification approval process; this occurs within 5 business days of the site and the MCC Study Team verifying that all requirements have been met.

How Certification Approval is Issued

The MCC Study Team sends the Clinical Site Certification Approval Email; a template for this email message is included as Corresponding Document C. The following parameters apply:

- The email is sent to the Site PI of the site receiving Clinical Site Certification Approval
- All other clinical site study team members who are being certified, the Overall PI of the study, all members of the MCC Study Team including the MCC PI, and the MCC REDCap User Administrator are carbon copied on the message
- The subject line of the message makes clear that the email is an official Certification Approval
- The email message specifies which study team members are being certified to conduct which study activities based on their study role and on the documentation submitted in support of certification.
- The email message specifies which members of the study team should be given access to the REDCap database; the MCC REDCap Administrator issues REDCap access per the Certification Approval email (s/he is carbon copied on the message).

Documentation of Approval Dates and Information

Upon issuing certification approval to a given site, the MCC Study Team documents the date of certification approval in the site's study-status record within the MCC Administrative Database. This approval date may be used, thereafter, for calculating some study management and performance indices such as *Time to First Patient Screened, Time to First Patient Enrolled, etc.*

VI. Changes or Updates to Certified Study Personnel

Sites are required to notify the MCC as soon as possible when changes are made to the site's study team. These changes include departures of previously certified individuals, changes in a certified person's responsibilities on the study, or addition of new study team members.

New Study Team Members

New study team members must be certified by the MCC prior to initiating study activities. The site notifies the MCC that there is a new study team member requiring certification approval. The site submits all required certification materials for the new individual along with the notice to the MCC.

After verifying all required documentation for the new study team member(s), the MCC issues a *Reply All* message to the most recent certification approval message and includes a new table listing the newly certified individuals. The certification approval date for the new study team members is the date that the *Reply All* message is sent.

This process is repeated any time there are new study team members to certify; each time the most recently sent certification-approval-related message is the starting point. This allows for a complete history of all certification approval activity (initial approval and new study team member approvals) to be maintained in one email chain.

Please note: Newly added study team members must also be approved by the local or single IRB if that is the policy of the IRB of record. For DoD sponsored studies, the DoD HRPO may be notified of new study team members at the time of Continuing Review, except in the instance that there is a change of Site PI in which case HRPO must be notified as soon as the local or single IRB approves the PI change. Certification approvals for new study team members will not be issued until after IRB and, if applicable DoD HRPO, approval requirements are met.

Changes in a Certified Study Team Members Study Responsibilities

The site notifies the MCC as soon as possible if a member of the study team's scope of responsibilities for the given study have changed. For example, if a junior Research Assistant (RA) is promoted and will newly be involved in consent and enrollment activities that s/he was previously not involved in nor certified for, the RA will need to be re-certified by the MCC. The MCC will issue a re-certification for the given study team member(s). This re-certification process will mirror the certification approval process for newly added study team members (described in the paragraphs above).

Study Team Member Departures

When a study team member is leaving the clinical site or remaining at the site but discontinuing his or her work on the METRC study, the site notifies the MCC as soon as possible. The MCC acknowledges the departure and ensures that the individual's access to the REDCap database is discontinued and, if

applicable, that the individual is made inactive in the MCC Directory and removed from the MCC listservs.

If the policy of the IRB of record is to submit amendment upon departure of previously approved study team member, the site will submit documentation that such an amendment was filed.

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