



12 STUDY-SPECIFIC PRE-IMPLEMENTATION ACTIVITIES

The steps for protocol development are outlined in Section 9A and must be completed before an IDCRC protocol can move into the implementation phase.

The Division of Microbiology and Infectious Diseases (DMID) Clinical Project Manager (CPM) (or other DMID representative for non-interventional protocols) and FHI 360 Protocol Specialist (PS) work closely with other protocol team members to identify and track all requirements that must be met to move into implementation; while some requirements apply to all studies, others may be study-specific. These requirements are described below as part of pre-implementation activities.

The PS also coordinates the site-specific study activation process for each study, which, as described in Section 12.10, should proceed in parallel with work toward study implementation. Sites may not begin enrollment in an IDCRC study until after they have received a site-specific study activation memo.

This MOP section describes requirements that must be met to move into the implementation phase.

12.1 Clinical Trials Agreement

A clinical trial agreement (CTA) is typically negotiated between a collaborating external organization or pharmaceutical company and NIAID/DMID to document the responsibilities and rights of each party for the clinical trial. The agreement typically includes, but is not limited to, Investigational New Drug (IND) application sponsorship (if applicable), provision of study products, safety and data monitoring, and access to data. In general, terms in the CTA covering access to data conform to NIAID/DMID policies.

When CTAs are required, the NIAID/DMID Office of Regulatory Affairs (ORA) leads negotiations with the company.

Site activation cannot proceed until the CTA and Non-Monetary Agreements (NMAs) are fully executed.

12.2 ClinicalTrials.gov Registration

[ClinicalTrials.gov](https://clinicaltrials.gov) is a US government-funded clinical trials registry. Specific types of studies (see [Final Rule for Clinical Trials Registration and Results Information Submission](#) [42 CFR Part 11] for clarification) must be registered and have summary results information submitted and posted in a timely manner (within one year after the Primary Completion Date, which is the date on which the last participant was examined or received an intervention to collect final data for the primary outcome measure[s]), whether subject to [FDAAA 801](#) or not. DMID will provide guidance on registration needs.

- For studies where the IND is held by DMID and the sponsor is DMID, the study is registered and maintained by DMID (or its regulatory contractor). Submission of IDCRC study results to clinicaltrials.gov (when required) is generally completed by the DMID CROMS contractor after

receipt of the results from The Emmes Company¹, or the Statistics and Data Sciences Unit (SDSU) when SCHARP², as appropriate. For studies where the IND is held by a different sponsor (e.g., external organization or pharmaceutical company) the study is registered and maintained by the sponsor (or its regulatory contractor).

- For non-IND studies when the IDCRC is the sponsor, the Clinical Operations Unit (COU) generally does not recommend registration of protocols with clinicaltrials.gov that do not meet the definition of a clinical trial³ due to workload of reporting and significant penalties for missed reporting requirements (e.g., site changes). However, the COU is aware that there may be compelling reasons to register with clinicaltrials.gov and will consider on an ad hoc basis. If a protocol is approved to be registered on clinicaltrials.gov, then Emory University will manage this process with clinicaltrials.gov. For non-IND trials approved to be registered on clinicaltrials.gov where Emmes serves as the SDCC, the study will be registered and maintained by DMID (or its regulatory contractor).

12.3 United States Food and Drug Administration Review

If an IDCRC protocol is submitted⁴ to the US Food and Drug Administration (FDA) under a new IND application, the FDA has 30 days to review. The FDA will review the protocol and notify the IND sponsor of any issues identified during this review. If the FDA is not able to complete its review within 30 days, the team may be informed that the timeline for the review has been extended; in this case, the study cannot proceed with implementation until approval from the FDA. IDCRC protocols will typically proceed with sIRB submission during this time although the IRB final approval is dependent on receiving the FDA determination.

If no communication is received from the FDA within 30 days of the submission, or if questions or comments are received in the absence of a Clinical Hold, the protocol may be considered “Safe to Proceed.”

If the FDA finds sufficient safety concerns, a Clinical Hold on the protocol may be issued. The FDA may require that the protocol be amended or that additional data be submitted to justify why an amendment is not required. The protocol team must coordinate with the DMID team (Clinical Project Manager [CPM], Medical Officer [MO] and DMID ORA) who leads the effort to respond to the FDA⁴ as soon as possible and within the timeframe specified by the FDA. There is no specified timeline for FDA to complete its review related to the Clinical Hold, and the study may not proceed with implementation until the FDA has given the approval to do so.

¹ For most IND studies under the IDCRC, The Emmes Company, DMID contractor, serves as Statistical and Data Coordinating Center (SDCC).

² The Statistical Center for HIV/AIDS Research and Prevention (SCHARP) at the Fred Hutchinson Cancer Research Center is the Statistics and Data Sciences Unit (SDSU) for the IDCRC. The SDSU also serves as the Statistics and Data Management Organization (SDMO) on non-IND studies under the IDCRC and some IND studies when requested by DMID.

³ Clinical trial is defined “as a type of clinical study in which participants are assigned to groups that receive one or more intervention/treatment (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study's protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.” <https://clinicaltrials.gov/ct2/about-studies/learn>

⁴ Submissions to the FDA are handled by DMID Regulatory Affairs Manager (RAM).

In addition to the above, FDA Review questions and comments may be received at any time during the lifecycle of a study. The protocol team must coordinate with the DMID team to address any such questions and comments within the timeframe specified by the FDA.

12.4 Laboratory Central Assay Plan

A Laboratory Central Assay Plan (CAP) is developed for most IDCRC studies as a detailed laboratory-related companion document to the protocol. This CAP provides detailed instructions for triggering specimen shipment to endpoint laboratories supporting IDCRC protocols and studies and describes the content of data reports for each endpoint assay. The CAP also lists relevant contact information for endpoint laboratories.

The IDCRC Laboratory Operations Unit (LOU) representative assigned to each protocol is primarily responsible for developing the CAP, consulting with the protocol team and endpoint laboratories as needed. The protocol team is responsible for reviewing the CAP and ensuring that it matches the protocol Schedule of Activities (SoA) and other relevant sections of the protocol. Review and approval are required from the protocol chair (PC), LOU representative, DMID study team member (e.g., Medical Officer [MO] or Scientific Lead [SL]), and PS. The CAP should be available to sites before site activation can proceed.

The LOU representative is responsible for finalizing and maintaining the CAP, requesting its posting to protocol team SharePoint site and distribution, and ensuring appropriate version control. The CAP is a living document and if the CAP requires updates during study implementation, the LOU rep will coordinate that process. Further details regarding the CAP may be found in IDCRC https://idcrc.org/includes/documents/idcrc-mop--17-specimen-management-v1.0_12oct2022.pdf

12.5 Data Collection Materials

Data collection instruments (e.g., data collection forms (DCFs) and electronic case report forms (eCRFs)) are used by study staff to record protocol-required information. Emmes or the SDSU/SCHARP are responsible for developing the data collection instruments and associated materials (e.g., forms submission schedules, eCRF completion instructions, memory aids) needed for each study. Standard data collection instruments are used preferentially, but study-specific instruments are developed as needed to meet the data collection needs of each study as efficiently as possible.

IDCRC data collection instruments are developed as follows:

- Development of the data collection instruments for a study typically begins when the protocol is in the final stages of development.
- The data management team drafts required data collection instruments based on protocol objectives, schedules of evaluations, and reporting needs. Scientific expertise is sought (from the protocol team, Expert Working Group (EWG) members), as appropriate.
- Draft data collection instruments are distributed to the protocol team for iterative review and comment. Data collection instruments go through a series of reviews:
 - Team review
 - Internal Data Management (DM) review, including Clinical Data Interchange Standards Consortium (CDISC) standards review, as needed
 - Site Study Coordinator(s) pilot of draft data collection instruments, if deemed necessary and appropriate by Team and/or DMID
 - 2nd DMID Quality Crosswalk review, if deemed necessary and appropriate by DMID

- Final team review
- If select data collection instruments require translation into local languages after they are finalized in English, the Emmes DM team will manage the submission, approval process for translation and back translation. The FHI PS will manage translations when the SDSU/SCHARP is acting as the data management organization; for single site studies, FHI 360 may coordinate translations directly with the local study team and their certification process as appropriate.
- Once the data collection instruments have been reviewed by the team and are ready to be finalized, they are provided to DMID for sign-off. The final data collection instruments are then posted to the DM website. The data manager will notify the protocol team and participating sites once the data collection instruments are available.
- Once the data collection instruments have been approved by DMID, internal DM processes are initiated for development and configuration of the clinical and specimen data systems. This process requires approximately six weeks. If the protocol to be implemented for participant enrollment is modified after data system development has been initiated, this timeline may be extended.

The data manager informs the protocol team when all DM materials (i.e., data collection and participant enrollment materials) are ready for study opening. These materials must be available before a study can be implemented.

Final sign-off by DMID is required for data collection instruments.

12.6 Clinical Database Systems

Part 11-compliant data management and reporting systems will be used for all IND studies. Emmes will provide data management for most IND studies using the Advantage eClinical system. For some non-IND studies and for low risk/non-interventional studies, where SDSU/SCHARP is responsible for data management, Medidata Rave or REDCap data management systems may be used. Other data management systems may be used as appropriate. In addition to study eCRFs, both systems electronically capture, manage, and report screening, enrollment, and retention data for study subjects in IDCRC studies.

12.7 Study-Specific Manual of Procedures

A study-specific manual of procedures (MOP) serves as an operational resource for implementation of IDCRC studies. The purpose of a study-specific MOP is to supplement the protocol with further information to optimize adherence to study protocols and standardization of study procedures across sites.

Study-specific MOP development typically begins when the protocol is in the final stages of development. For IND studies, Emmes (DMID contractor) is typically responsible for coordinating the development, review, and finalization of all MOP sections. For studies where the SDSU/SCHARP is the SDMO, FHI 360 is responsible for development and finalization of the MOP. Both organizations will approach the work in a similarly collaborative way by working in close cooperation with the PC and other protocol team members, some of whom are typically assigned primary authorship responsibilities, as outlined in Table 12-1. Protocol Team Member Study-Specific MOP Responsibilities and Requirements. Regardless of primary authorship assignments, Emmes or FHI 360 (as appropriate) will coordinate the development and finalization of all sections, requesting and incorporating input from other protocol team members and site staff as needed prior to finalization.

The full protocol team is responsible for reviewing draft sections of the study-specific MOP when distributed. Once the MOP has been reviewed by the protocol team and has the required approvals per Table 12-1. Protocol Team Member Study-Specific MOP Responsibilities and Requirements, it is finalized as v1.0 (either by Emmes or FHI 360). The final MOP is then posted to the appropriate website and/or the protocol team SharePoint site, and/or distributed to participating sites (as appropriate).

The final study-specific MOP must be available before sites can be activated or the study can be implemented.

The MOP is considered a living document and will be updated as needed during study implementation to include additional details, procedures, or clarifications. When updates are required, Emmes or FHI 360 (as appropriate) will coordinate that process by drafting or incorporating revisions and then circulating for team review. Once completed, the draft will be circulated to DMID for final sign-off. Emmes or FHI 360 will maintain version control using file naming conventions and a version control log located at the front of the MOP section or in a separate document (e.g., Emmes' *Current Versions of Study Materials*). Depending on the complexity of the study-specific MOP, it may be versioned in its entirety or by section (this will be reflected in the version control log).

Emmes or FHI 360 (as appropriate) will notify the protocol team and participating sites of all study-specific MOP updates. It is the responsibility of the site investigators to ensure that the current version of the MOP is maintained on-site, in all relevant locations, and that updated MOP content is communicated to all applicable study staff in a timely manner. If further training is required due to MOP revisions, documentation of training will be collected by FHI 360.

Table 12-1. Protocol Team Member Study-Specific MOP Responsibilities and Requirements

Protocol Team Member	Responsibilities and Requirements
Protocol Chair and DMID Lead(s)	Responsible for review of all sections
DMID CPM	Responsible for review of all sections; approval of final version and any updates
Site Lead Study Coordinator(s)	Responsible for review of all sections; triage sections to site team as appropriate
Data Manager	Responsible for review of sections related to data collection and management
Laboratory Operations Unit (LOU) representative	Responsible for input and review of sections related to specimen collection, processing, testing, shipping, and other related sections
Protocol Team Site Investigators	Responsible for input and review of sections related to clinical or other specialized procedures and safety reporting
DMID Pharmacist (and Site Pharmacists as needed)	Responsible for input and review of sections related to study drug and study drug management
Emmes or FHI 360 Protocol Specialist (as appropriate)	Responsible for input and review of sections related to introduction, contact information, documentation requirements, accrual and retention, informed consent, study procedures, safety and clinical procedures, and any other sections related to study-specific requirements; responsible for tracking outstanding issues / questions to resolution

Protocol Statistician	Responsible for review of relevant sections. SDSU statistician as applicable will review related to statistical design and analysis and reporting requirements. Responsibilities may vary depending on the level of SDSU involvement.
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12.8 Study Oversight and Clinical Monitoring

Each IDCRC study protocol specifies how clinical monitoring will be performed throughout the course of the study. In general, clinical monitoring is required for interventional studies only; DMID will decide the level of monitoring – if any – needed for non-interventional protocols. For low resource, non-interventional studies, the COU develops a protocol-specific quality oversight plan. Additionally, sites conduct internal quality management and oversight as outlined in their Clinical Quality Management Plan (CQMP) or protocol-specific Clinical Quality Management Plan (psCQMP).

The PS will confirm that plans for oversight and monitoring are finalized prior to site activation.

12.8.1 External Contract Monitoring

For IND studies, DMID or its designee (e.g., ICON) is responsible for developing a clinical monitoring plan (CMP) that details the study data to be monitored; the type, frequency, and content of monitoring reports that will be generated; and responsibilities for generating, receiving, and reviewing monitoring reports. The content of the CMP must be consistent with relevant sections of the study protocol (e.g., safety related roles and responsibilities, monitoring). DMID sign-off is required prior to finalizing the CMP. DMID will ask for protocol team input as appropriate.

For non-IND interventional studies, DMID and the IDCRC LG, as the sponsors, may have shared responsibilities for developing CMPs.

12.8.2 Clinical Quality Management Plan (CQMP)

Each VTEU currently has a CQMP in place that meets the requirements per DMID CQM [policy](#). The COU has responsibility for ensuring that the CQMPs are maintained on an annual basis. Early in pre-implementation phase for a particular protocol, FHI 360 will verify that there is a current CQMP on file for each site; for some VTEUs, FHI will confirm their plan to create a protocol-specific CQMP.

For low resource and/or non-interventional studies, DMID may determine that formal external monitoring will not be required. For these protocols, quality oversight will be conducted by FHI 360 in consultation with the COU, as described in a protocol specific Quality Oversight plan (QOP). During pre-implementation, FHI 360 will work with the COU, and PC(s) as needed to develop the QOP and submit for review and approval by DMID prior to study implementation.

To address protocol-specific sites and sub sites that do not have a current, DMID-approved CQMP, the COU will work with PCs to customize the DMID protocol-specific CQMP (psCQMP) template as needed and route as appropriate to DMID, LG and/or VTEU PIs for review and approvals. For more details, see IDCRC SOP on CQMPs and protocol-specific CQMPs.

12.9 Site Assessment Visit (SAV) and Site Initiation Visit (SIV)

An SAV is completed by the DMID monitoring contractor as requested by DMID (typically required for sites that have not been previously assessed by DMID or have not been monitored by DMID monitoring contractor in 12 months or more). The purpose of the assessment visit is to verify adequacy of the facilities, equipment, personnel, personnel training, clinical operations, ability to enroll and conduct protocol-specific functions. In addition, the Monitor verifies compliance with ICH/GCP, overriding Federal regulations, DMID-specific guidelines, and protocol-specific requirements, as applicable. The SAV may be combined with the SIV.

A Site Initiation Visit (SIV) is conducted by the DMID monitoring contractor before any site is authorized by DMID to begin any study-related activities. The purpose of the SIV is to prepare the site to conduct the study and confirm site readiness.

During the SIV, the following topics are typically reviewed:

- Investigator and staff qualifications
- Site personnel responsibilities
- Study population and accrual goals
- Informed consent process
- Protocol and study design NOTE: IDCRC COU recommends having the study protocol chair(s) perform this portion of the SIV content.
- Remote monitoring procedures
- Site facilities and equipment, if not completed during the SAV, or if there were changes in the interim
- Procedures for dispensation, transport, accountability, and administration of study product as well as any blinding considerations
- Discussion of regulatory documents and logs including site's process for Specimen Retention documentation and records per the protocol
- Source documentation and CRF procedures and Data Management responsibilities
- Serious Adverse Event (SAE) and Adverse Event (AE) reporting requirements
- Site management procedures, including but not limited to: Regulatory, Communications, Supervision, and Quality Management
- IRB/IEC and regulatory requirements
- GCP
- DMID policies, procedures, and standards for conduct of clinical trials
- Training of site personnel (including Protocol-Specific and Non-Protocol-Specific trainings)
- Confirmation of the QA checklist
- Clinical emergency support

12.10 Site-Specific Study Activation

During protocol development, the PS compiles a study-specific listing of regulatory, operational, and other applicable requirements that must be met for participating sites to initiate study implementation. This is referred to as the "IDCRC Site Activation Checklist." Sites are encouraged to complete all study activation requirements in a timely manner, with the overall goal of completing the activation process as soon as possible after the protocol is finalized as Version 1.0.

Additional study-specific requirements may be specified and tailored to the needs of the study as determined by the protocol team to ensure site readiness for study implementation. These may include

the following:

- Availability of specialized personnel
- Availability and confirmed operability of specialized equipment or supplies on site
- Availability of translated study implementation materials
- On-site review of study-specific documentation (e.g., study product investigator's brochure or package insert, study-specific MOP)

International study site(s) considerations may include the following:

- Study product import permit(s)
- Study product waiver(s)
- In country regulatory approval(s)
- Study specimen export permit(s)

The PS is responsible for adapting the template site activation checklist for each study site in close cooperation with the CPM. The PS will track progress and confirm elements of activation have been completed with the appropriate protocol team members (e.g., the participating site, data manager, LOU representative, LOC representative on study agreements, etc.). As described in the site activation checklist, the PS will also reach out to DMID staff and IDCRC LOC to confirm various milestones have been met such as:

- SIV/SAV completed and no outstanding issues from the SIV/SAV (OCRA Nurse consultant or other DMID contact for non-interventional studies).
- CTA has been executed (CPM).
- Site funding is in place (DMID Program Officer)
- IDCRC study agreement(s) with external partners have been executed (LOC); refer to Section 12.10.9

Once all site activation requirements have been met, the PS will email the checklist to the CPM to request review and approval. With CPM approval, the PS will issue a site-specific DMID Site Activation Memo indicating that the site may initiate study implementation.

Sites may not conduct any study-specific screening or enrollment (on-study) procedures prior to receipt of their site-specific DMID Site Activation Memo.

12.10.1 IRB/EC and Other Regulatory Approvals

Consistent with 45 CFR 46 (and 21 CFR 56 for IND studies), all sites must obtain IRB/EC approval of IDCRC study protocols. When a VTEU site is providing oversight for a sub-site or protocol-specific site, the VTEU will need IRB/EC approval.

For multi-site studies in the US, sites rely upon approval by a single IRB (sIRB) for cooperative research. For IDCRC protocols, the IDCRC has set up agreements with the sIRBs at Advarra and other academic sIRBs. All primary VTEU sites have a current reliance agreement with these sIRBs. The IDCRC and DMID may decide to contract with a commercial sIRB such as Advarra or WIRB Copernicus Group for fast-track protocols or as needed.

The FHI 360 PS will manage the study level submission with the sIRB, which includes completing the protocol application and submission of protocol v1.0, ICFs, memory aid, study level recruitment

materials, and any other subject facing materials. As part of this process, the PS will enter names and contact information of site investigators at participating study sites into the sIRB database. Once study level approval is obtained, sites will be prompted to complete required information (i.e., a survey re: their local HRPP), and upload their site-specific documents (or send them to the PS). Each site should complete study-specific submissions to local IRBs/ECs, IBCs, and other regulatory entities as soon as possible after v1.0 of the protocol and prior to their site level sIRB review. Once site level information is submitted, the sIRB reviews and approves each participating site's informed consent and assent forms (if applicable) and any site-specific materials.

For international locations, the protocol will need to be submitted to the in country institutional ethics and scientific review committee for review and approval. Additionally, the sponsor or PI will typically need to register their protocol and obtain clinical trial authorization from the in country regulatory body (such as the Pharmacy Board) responsible for approval, oversight, and inspections of clinical trials prior to trial commencement. Additionally, the VTEU with oversight of the international site will need to submit the study for IRB approval; local IRB for single site study and sIRB approval for multi-site study. This step should be completed prior to in country submissions to reduce the potential for required changes requested by the domestic IRB.

12.10.2 Collection, Review, and Approval of Essential Documents

During pre-implementation, FHI 360 PS will reach out to sites to request a list of essential documents (EDs) in preparation for site activation, following guidance from the DMID Essential Document Review Worksheet and DMID Regulatory File Document [Guidelines](#). Upon receipt of EDs, the PS reviews the documents for completeness, errors, and compliance. The PS will follow up with site staff until all documents are collected and confirmed as accurate and complete. Once complete, the PS will upload the documents to DMID's SERD database.

12.10.3 Study-Specific Personnel Signature and Responsibility Log (PSRL)

DMID requires clinical research sites to maintain study-specific DMID Study Personnel Signature and Responsibility Log (PSRL). The PS will customize the DMID template for the study to include relevant delegated tasks and then will share that with the team and work with specified site staff to ensure the log is correctly completed. This is a living document that will be updated and maintained by study site staff and shared with PS when revised, until a final version is signed and dated by the site PI after study site closure.

12.10.4 Financial Disclosures

For studies conducted under an IND, all individuals listed on Form FDA 1572 must complete a study-specific financial disclosure form to fulfill 21 CFR 54 requirements. The DMID Financial Disclosure Form (FDF) and instructions are available on the [DMID CROMS website](#). The PS will provide sites with the current DMID FDF form to be used for a given study.

To meet study activation requirements, financial disclosure forms must be completed by all individuals listed on the Form FDA 1572. The completed forms are submitted to FHI 360 for review and upload to the DMID SERD system. Completed forms must be available on site for review by site monitors and other sponsor, IDCRC, FDA and other regulatory entity representatives.

12.10.5 Study Product Acquisition and Shipment to Sites

Before study products can be provided to a study site, all required essential documents in Tier 1 per DMID Essential Document Review [Worksheet](#) such as the completed FDA Form 1572, Principal Investigator (PI) CV, single IRB (sIRB) (for multi-site studies only) and/or local IRB approvals must be uploaded to DMID Site Essential and Regulatory Document (SERD) database.

Study product must be available for ordering with the Product Support Team (PST) before a study can be opened to accrual. Questions regarding study product acquisition and shipment should be directed to the DMID protocol pharmacist for the study.

For international locations, the Site Investigator and Protocol Pharmacist or delegate are responsible for understanding the local requirements and obtaining the necessary approvals, including those that may provide waivers of import fees. When DMID is sponsor, sites should communicate with the DMID Clinical Project Manager (CPM) and the Clinical Material Services (CMS) repository to address actions related to importation of Investigational Product (IP). The PST may also provide assistance to a CPM and the CMS. As per the DMID Guidelines for Clinical Study Product Management, customs agents may also be engaged to assist in these matters. See [DMID Guidelines for Clinical Study Product Management](#) for more details. For non-IND trials, the IDCRC may grant a waiver to allow study product to be shipped to sites prior to when a site activation notice is issued. Following guidance from the DMID Essential Document Review Worksheet and [DMID Regulatory File Document Guidelines](#), all required essential documents in Tier 1 must be completed, including local regulatory approvals. The IDCRC will also require certain activities and documents be completed for a site to be eligible to request shipment of the study product prior to receipt of a site activation memo.

For studies involving drugs or biologics that are not conducted under an IND, export approval from the US FDA may also be required before study product can be shipped to certain countries. This approval may be sought by either the product manufacturer or the local drug authority and can take a long time to obtain; therefore, the process to obtain approval should be initiated as early as possible in the pre-implementation phase of the study.

12.10.6 NIH/DMID Required Trainings

As part of the essential document collection, the FHI 360 PS requests training documentation from the sites for study staff. All site staff assigned to a protocol are required to provide training certificates (required every 3 years per NIH) for International Council for Harmonization (ICH) Good Clinical Practice (GCP) E6(R2) and Protecting Human Subjects (45 CFR 46). Additionally, per DMID Clinical Site Training policy and as excerpted here, documentation of completion of DMID CROMS training modules is also required prior to site activation. See Table 12.2 for list of required DMID CROMS Training Modules by role/responsibility for IDCRC protocols as per DMID Project Officer guidance. NOTE: DMID policy takes precedence over the below table in the case of discrepancies.

Table 12.2 DMID CROMS Training Modules for IDCRC protocols

DMID CROMS Training Module	Applicable for:
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AE/SAE	PI, Sub-Is (who will assess AEs)
Essential Regulatory Documents	PI, Quality Manager (QM), and Regulatory contact
FDA Site Inspections and Audit Preparedness (interventional studies only)	PI and Regulatory contact; and others as needed to prepare for audit (if audit is scheduled)
Investigator Responsibilities	PI, person(s) delegated investigator responsibility
Regulatory Document File Guidelines	PI, QM, person responsible for essential docs OR person responsible for ethics filings (if different)
Source Documentation Standards	PI, QM, study staff who record data on source documents or transcribe data from source documents
Study Product Management (Interventional studies only)	PI, Pharmacists, anyone delegated responsibility for activities regarding study product (including ordering, receipt, handling, preparation, administration, and accountability).
Clinical Quality Management (CQM)	PI, QM

12.10.7 Pharmacy Requirements / Study Product Management Plan (SPMP)

All sites must have a DMID-approved Study Product Management Plan (SPMP). As part of the site activation checklist, FHI 360 will confirm that each site has a current, DMID approved SPMP that will be followed for the specific protocol. Other pharmacy requirements may include availability of required pharmacy infrastructure or equipment, availability of supplies for study drug administration on site, and completion of specialized pharmacist training, when applicable. Additionally, as part of Essential Document review, the PS will confirm that the pharmacy address matches the information listed on the 1572. The PS will also confirm with the CPM that the address is associated with the correct MI code⁵.

Study product is not shipped to sites until after the site activation notice is issued.

12.10.8 Data Management Requirements

Completion of data management activation requirements is generally confirmed by the protocol data manager, who notifies the PS when requirements have been met. The protocol team may require translation and back-translation of study-specific data collection instruments as an activation requirement. If so, translated instruments must be independently back translated into English for review and approval by the Emmes or SDSU/SCHARP, as appropriate. Other data management requirements for activation may include completion of database training, specimen tracking system (e.g., GlobalTrace (Emmes) or LDMS (SCHARP)), Direct Data Entry (DDE) training (if applicable), and availability of relevant materials and equipment on site for study implementation.

12.10.9 Laboratory Requirements

⁵ An MI code is a unique identifier for sites (issued by DMID) which DMID references for a variety of internal resources such as clinical monitoring, pharmacy/product shipments, regulatory document submission, etc. It is critical that sites have a valid MI code associated with their facility address to ensure proper identification across various DMID resources.

Receipt of relevant local laboratory credentials/certifications and study-specific laboratory reference ranges by FHI 360 is required prior to activation. (The PS will share with the data management group (e.g., Emmes or SCHARP) for database range setting). Initiation or completion of specimen or material transfer agreements may also be required prior to activation to ensure that samples may be shipped in a timely manner as applicable for the study.

Completion of other laboratory-related activation requirements is generally confirmed by the protocol LOU representative, who notifies the PS when requirements have been met (see [https://idcrc.org/ includes/documents/idcrc-mop--17-specimen-management-v1.0_12oct2022.pdf](https://idcrc.org/includes/documents/idcrc-mop--17-specimen-management-v1.0_12oct2022.pdf)).

12.10.10 Study-Specific Operations Overview

Study-specific operations overview conducted by FHI 360 takes place at the discretion of the protocol team and DMID. At a minimum, a site should have initial site level IRB approvals, all essential and regulatory documentation submitted to FHI 360 and noted as acceptable, and a draft MOP in place for the overview to be scheduled. The PS will conduct the session with input from all relevant sources (PC, CPM, LOU, data managers from Emmes or SDSU/SCHARP, Lab Managers, Clinicians, etc.) generally during a 1-2 hour webinar, as appropriate. Determining the mode and timing of the session should be discussed with the PC and CPM.

Sites will be required to complete “pre-training” activities/documentation prior to their scheduled training. Pre-training activities will be sent to sites as early as possible, and sites must return confirmation of completion prior to the scheduled site session.

REVISION HISTORY:

Version number	Approval Date DD MMM YYYY	Summary of Changes
2.0	28 AUG 2024	<ul style="list-style-type: none"> Administrative changes to utilize section cross references and correct typos.
		<ul style="list-style-type: none"> Section 12.2: Updated to read clearly and provided examples of sponsor besides DMID and/or IDCRC. Added in content regarding non-IND trials approved to be registered on clinicaltrials.gov where Emmes serves as the SDCC, the study will be registered and maintained by DMID (or its regulatory contractor).
		<ul style="list-style-type: none"> Section 12.3: Clarified DMID team leads effort to respond to FDA clinical hold.
		<ul style="list-style-type: none"> Section 12.4: Use of Schedule of Activities, SoA, vs. Schedule of Evaluations. Replaced “Sign-off” with “Review and approval” from specified study team members on CAP. Removed V1.0 requirement of CAP on activation as LOU uses version dates instead. CAP versions to be posted on study SharePoint site. Added reference to MOP Section 17.
		<ul style="list-style-type: none"> Section 12.5: Removal of qualifier on when Emmes or SDSU is utilized. Replaced data coordinating center with data management organization. Clarified that if the protocol to be

		<p>implemented for participant enrollment is modified after data system development has been initiated, the timeline may be extended.</p> <ul style="list-style-type: none"> • Section 12.6: For some non-IND studies and for low risk/non-interventional studies, where SDSU/SCHARP is responsible for data management, Medidata Rave or REDCap data management systems may be used. • Section 12.7: Refer to SCHARP/SDSU as the Statistics and Data Management Organization (SDMO) instead of SDCC, as done in the LOU MOP sections and included references to Table 1. Updated Table 12-1. Protocol Team Member Study-Specific MOP Responsibilities and Requirements, Protocol Statistician entry, to clarify responsibilities for SDSU statistician as responsibilities may vary depending on level of their involvement. • Section 12.8: Added clarifying term of “Clinical” monitoring to separate from safety monitoring. • Section 12.8.1: For non-IND interventional studies, DMID and the IDCRC LG, as the sponsors, may have shared responsibilities for developing CMPs. • Section 12.8.2 on Protocol Specific Quality Oversight Plan was deleted and move underneath Clinical Quality Management Plan (CQMP). • Section 12.9 SAV/SIV: Regarding protocol and study design, added in NOTE: IDCRC COU recommends having the study protocol chair(s) perform this portion of the SIV content. • Section 12.10: Addition of language for international study site(s) considerations. Added language to ensure LOC representative on study agreement(s) have been consulted as a part of the site activation checklist process. • Section 12.10.1: Added content to clarify when a VTEU site is providing oversight for a sub-site or protocol-specific site, the VTEU will need IRB/EC approval. Removed direct reference to IDCRC approved academic sIRBs of VUMC and JHU. For international sites, added content regarding VTEU oversight of the international site will need to submit the study for IRB approval; local IRB for single site study and sIRB approval for multi-site study. This step should be completed prior to in country submissions to reduce the potential for required changes requested by the domestic IRB. • Section 12.10.3: Added a sentence to explain that the PSRL is a living document until a final version is signed and dated by the site PI after study site closure. • Section 12.10.4: Removed reference to IDCRC MOP Section 8 as does not contain details regarding DMID FDFs. • Section 12.10.5: Adding language to address ability for IDCRC on non-IND trials to grant a waiver to allow study product shipment to a site prior to receipt of a site activation memo
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		<p>under specific criterion being met by the site.</p>
		<ul style="list-style-type: none">• Section 12.10.6: Added "...per DMID Clinical Site Training policy and as excerpted here," to existing sentence regarding documentation of completion of DMID CROMS training modules required prior to site activation. Included a Note to clarify DMID policy takes precedence over Table 12.2 in case of discrepancy.
		<ul style="list-style-type: none">• Table 12.2: Updated for Study Product Management module Applicable for column to align with DMID provided updated policy language.
		<ul style="list-style-type: none">• Section 12.10.8: Added Direct Data Entry training if applicable.
		<ul style="list-style-type: none">• Section 12.10.9: Added link for MOP Section 16 reference.
		<ul style="list-style-type: none">• Section 12.10.10: Renamed header to align with FHI 360 terminology, Study-Specific Operations Overview, not Training.