SOP#: PM-7	**Clinical Research Study Initiation**
Version #: 6.0	**Next Review Date: 03/2025**
Approved Date: 03/2023	**Review Interval Period: Biennial**
NCI Clinical Director Signature/ Effective Date:	James Gulley Digitally signed by James Gulley Date: 2023.03.03 13:13:38 -05'00'

POLICY

All applicable protocol initiation activities must be completed before the clinical research study opens to participant recruitment. This requirement applies all research studies, including observational (screening, tissue acquisition, natural history) studies.

Note: Institutional Review Board (IRB) approval does not automatically signify that a clinical research study may be opened for participant recruitment.

PURPOSE

To clarify the study initiation activities that are required to be completed prior to opening the study for participant recruitment. While the PI is responsible for ensuring that all of these activities are completed prior to participant recruitment, assistance is provided by the office or group identified with the activity.

RESOURCES

- Center for Cancer Research Standard Operating Procedures
- CCR Office of Sponsor and Regulatory Oversight (OSRO) website
- CCR Office of the Director
- CC-DCRI Protocol Order Sets
- Clinical Center Pharmacy Department
- NCI Technology Transfer Center
- NIH Intramural Institutional Review Board Office (IRBO) – includes the NIH Office of Human Subjects Research Protections (OHSRP)
- NIH Office of Science Policy
- NIH Office of Technology Transfer
- 2023 Data Management and Sharing Policy

PROCEDURES

STEP 1: Review Study Initiation Activities

The Principal Investigator (PI), Study Coordinator (SC) and Protocol Support Office (PSO) Manager will review the study initiation activities listed below to determine which activities are applicable to the study. The PSO Manager will typically start the checklist in Appendix A. Most of these activities are relevant to most treatment research studies and must be completed prior to the study being opened for participant recruitment. See Appendix B for types of studies and the associated study initiation activities.

REQUIRED STUDY INITIATION ACTIVITIES

1. All contracts and funding agreements fully executed and/or approved

   The NCI Technology Transfer Center (TTC) will assist with any contracts/agreements [e.g., Clinical Trial Agreement (CTA), Cooperative Research and Development Agreement (CRADAs), Material Transfer Agreement (MTA)] with industry sponsors, manufacturers or other external collaborators. TTC will also assist with patents and licensing if required. TTC should be contacted early in the concept/study process.

   Some studies will need funding for equipment, special lab supplies, and study medication not supplied by the manufacturer. The PI should work with their branch chief and administrative officers in the CCR Office of the Director (not Office of the *Clinical* Director) to determine if a Resource Request System (RRS) form is required for the study.

2. Clinical Center Protocol Resources Impact Assessment (PRIA) approval

   Clinical Center PRIA approval is required when using CC resources (e.g., participants being seen in the clinic/departments or using expertise of departments for review of pathology specimens, images, etc.). PRIA for CCR studies should be submitted at time of SRC submission in PROTRAK (exception: CTEP Letter of Intent (LOI) are not submitted in PRIA until the LOI is approved by CTEP and a draft protocol is available); approval could occur after IRB approval.

3. Reliance agreements with any outside investigators/collaborators fully executed, as applicable

   If the study involves a non-NIH site or investigator who is involved in the research but not located at the Clinical Center, a reliance (authorization) agreement may need to be executed. The Office of Human Subjects Research Protections (OHSRP) and CCR PSO Manager will assist with this agreement(s).

   Note: If the site/investigator is involved in drug manufacturing or real-time sample processing, for instance, this reliance agreement(s) may be needed before the study may be initiated/opened to recruitment. Otherwise, the reliance agreement for a participating site(s) or investigator(s) is only needed prior to initiation of activities at each site/by that investigator.

4. Data Management and Sharing (DMS) Plan, including Genomic Data Sharing (GDS) Plan elements (if applicable), is approved.

   All research studies are required to have an NIH Data Management and Sharing (DMS) Plan that incorporates GDS Plan elements (i.e., the latter if the protocol generates genomic data that meet a reporting threshold), approved prior to study initiation.

5. Institutional Certification (IC) Memo approved by CCR Scientific Director, if applicable

   All research studies that generate genomic data and meet the GDS policy requirements are required to have an Institutional Certification Memo completed and approved. Refer to CCR SOP RPS-21.

   NOTE: For multi-site studies for which the CCR is the coordinating center and will be sharing study data, each participating sites must have a GDS Institutional Certification Memo.

6. IRB approval

   The PSO Manager will assist with required submissions to oversight committees. The IRB will communicate its decisions to the PI and PSO Manager via email.

   For Network studies (i.e., ETCTN, NCTN), approval of Local Context Worksheet is also required – this will come from the NCI Central IRB.

   Note: For more information about required activities prior to IRB approval, please see CCR SOP RPS-5 "NIH IRB Submission and Response: New Protocol."

The following activities occur after IRB approval:

7. Site initiation visit (SIV) completed for IND/IDE studies

   All industry-sponsored studies will have SIVs coordinated by the sponsor and communicated to the CCR via the QA Mailbox.

   All CCR-sponsored IND/IDE studies will have SIVs coordinated by the CCR Office of Sponsor and Regulatory Oversight (OSRO). If the study includes multiple institutions, OSRO will coordinate SIVs for each site. See OSRO's website for documents/activities required prior the SIV.

   CTEP does not perform SIVs for their sponsored studies. Therefore, CCR Office of Education and Compliance will conduct the visit prior to the study being open to recruitment. Please contact CCR Office of Education and Compliance (OEC) to schedule the SIV.

8. Study start-up meeting completed for non-IND/IDE intervention studies

   Contact the CCR OEC to schedule the meeting

9. Study start-up meeting completed for CCR coordinated, multi-site observational studies

   All multi-institutional observational studies for which CCR is the Coordinating Center are required to have a site initiation visit completed prior to opening the study for recruitment at any site. This will ensure that CCR research staff are aware of responsibilities associated with coordinating a multi-site study. Each participating site will also need to have a SIV prior to enrolling participants at that site. Contact the CCR OEC to schedule the meeting.

10. Communication received from CC Department of Transfusion Medicine (CC DTM) that cell processing facility is ready to process cells, if protocol requires cell processing

    The research team must confirm from CC DTM personnel indicating that the cell processing facility is ready to process cells.

11. Communication with research lab performing research sample processing, shipping and/or storage that the research lab is ready to accept specimens and lab tracking database is completed and ready for data entry.

    If the protocol is going to utilize a research lab (e.g., Dr. Figg's lab) for research sample processing, shipping, and/or storage, the research team must confirm with lab personnel within each lab to confirm readiness to start.

12. All CCR study database(s) built

    For studies using a CCR electronic data capture system (e.g., Medidata Rave, Labmatrix), all study-specific database(s) must be completed and ready for data entry.

13. CRIS protocol order sets submitted to the Department of Clinical Research Informatics (DCRI)

    The Study Coordinator should work with DCRI to create protocol-specific order sets in CRIS. Finalized order sets must be signed off by the PI per MAS policy.

14. Written notification from study sponsor that study may be activated at site, if applicable

    For CCR-sponsored INDs, notification will come from OSRO.

15. CCR Safety Monitoring Committee (SMC) and/or Data Safety Monitoring Board (DSMB) prepared to provide oversight

    The CCR SMC and/or DSMB should be notified that the study is ready to initiate recruitment and the committee(s) representative will acknowledge intent to provide oversight. The SMC Chair/Executive Secretary should be reached via the PSO Director and the Head of CCR Biostatistics and Data Management should be contacted for DSMB.

    Note: A separate notification for OSRO safety oversight activities for CCR-held IND/IDE studies is not required for study initiation.

16. Manufacturer notified that investigational product can be shipped

    Once required agreements/contracts are fully executed and the pharmacy has indicated that it is ready to accept the investigational product, the PI must notify the drug manufacturer that study drug can be shipped.

17. Communication received from pharmacy that all investigational products and other drugs/biologics used in the study are available in the pharmacy and the pharmacy is ready to dispense.

    The research team must request an email from pharmacy personnel indicating that investigational products and other protocol-specified drugs/biologics are available in the pharmacy and that the pharmacy is ready to dispense investigational products and study drugs/biologics. This email is required to be maintained with the completed Study Initiation Activities Checklist.

    Note: If the protocol does not allow for "starter supplies" (e.g., CTEP sponsored studies) or if the study drugs are ordered as needed, please note that on the checklist.

18. Confirmation required indicating that the study is registered and posted on www.clinicaltrials.gov (i.e., the NCT number is available).

    Note: For CCR-sponsored studies and/or where NIH is the Responsible Party for Food and Drug Administration Amendments Act (FDAAA) requirements, this posting is done by the Office of Protocol Services (OPS) after IRB approval with confirmation sent to PSO.

19. For industry-sponsored studies, the following additional activities must also be completed:
    - Study team training on sponsor electronic data capture system.
    - Required supplies (e.g., blood collection kits, shipping materials) and documents (e.g., study Manual of Procedures, sponsor SOPs) received on site.

    Note: There may be other sponsor-specific activities that are required prior to study initiation.

STEP 2: Complete Study Initiation Activities Checklist

The Study Initiation Activities Checklist in Appendix A must be completed with the date each applicable study initiation activity was completed. If an activity is not applicable, note "N/A" for that activity. The PI must sign and date the completed checklist and send to PSO Manager. The PI may use an electronic signature (PV card) to sign the completed checklist.

Important: Inpatient and/or Day Hospital nursing unit and outpatient clinic protocol-specific education must be completed prior to the first participant receiving treatment. A sign-in sheet should be completed for each in-service provided. A scanned copy of the sign-in sheet and any presentation materials should be maintained in the protocol's regulatory file.

STEP 3: Change Study Accrual Status in Clinical Center PROTRAK Query System (PQS)

Once the completed, signed checklist is received by the PSO Manager, the PSO Manager will ensure that the change to the study accrual status in PQS is updated to reflect that the protocol is recruiting and save the checklist and related documentation in the protocol's electronic regulatory folder.

Appendix A

Study Initiation Activities Checklist

Protocol – Abbreviated Title: _____

Protocol #: _____ PI: _____

Study Initiation Activity (see SOP for specifics)	**Date Completed** (mark N/A if not applicable)
All contracts and funding agreements fully executed and/or approved	
Clinical Center Protocol Resources Impact Assessment (PRIA) approval	
Reliance Agreement for outside investigators/collaborators fully executed, as applicable	
Data Management and Sharing (DMS) Plan approved	
Institutional Certification (IC) Memo approved, if applicable	
IRB approval, including approval of Local Context Worksheet, if applicable	
Site initiation visit (or Study Start-Up Meeting) complete	
Communication from CC DTM that cells can be processed, if applicable	
Communication from research lab that specimens can be processed, etc.	
All CCR study databases built	
CRIS protocol order sets submitted to DCRI	
Notification from study sponsor that study may be activated at site	
CCR SMC and/or DSMB acknowledges ability to assume oversight of the trial	
Manufacturer notified that investigational product can be shipped	
Communication from pharmacy that protocol agents are available and ready to dispense	
Confirmation that study is registered and posted on www.clinicaltrials.gov (NCT # available)	
The below activities are for industry-sponsored studies:	
• Research Team training on sponsor's electronic data capture system	
• Study-specific supplies and documents received	

_____ _____

PI Signature Date

Appendix B

List of Activities	Observational (including specimen collection and natural history)	Interventional: non-IND/IDE	Interventional: CCR-sponsored IND/IDE	Interventional: industry-sponsored IND/IDE
Contracts and funding agreements fully executed and/or approved	Possibly	Possibly	Required	Required
CC Protocol Resources Impact Assessment (PRIA) approval	Possibly	Required	Required	Required
Reliance Agreement for outside investigators/ collaborators fully executed, as applicable	Possibly	Possibly	Possibly	Possibly
Data Management and Sharing (DMS) Plan approved	Required	Required	Required	Required
Institutional Certification (IC) Memo approved, as applicable	Possibly	Possibly	Possibly	Possibly
IRB approval, including approval of Local Context	Required	Required	Required	Required
Site initiation visit complete for IND/IDE studies, including CTEP	N/A	N/A	Required	Required
Study start-up meeting for non-IND/IDE intervention studies	N/A	Required	N/A	N/A
Study start-up meeting for multi-site observational study	If multi-site	N/A	N/A	N/A
Communication from CC DTM that cells can be processed	N/A	N/A	Possibly	N/A
Communication from research lab that specimens can be processed, etc., including that lab tracking database is ready	Possibly	Possibly	Possibly	Possibly
All required CCR database(s) built	Possibly	Required	Required	Possibly
CRIS protocol order sets submitted to DCRI	Possibly	Required	Required	Required
Notification from sponsor that site can be activated	N/A	Possibly	Required	Possibly
SMC and/or DSMB acknowledges oversight of the trial	N/A	Possibly	Possibly	Possibly
Manufacturer notified investigational product can be shipped	N/A	Possibly	Required	Required
Communication from pharmacy that protocol agents are available and ready to dispense	N/A	Possibly	Required	Required
Confirmation that study is registered and posted on www.clinicaltrials.gov (NCT # available)	Required	Required	Required	Required

List of Activities	Observational (including specimen collection and natural history)	Interventional: non-IND/IDE	Interventional: CCR-sponsored IND/IDE	Interventional: industry-sponsored IND/IDE
Research Team training on sponsor's EDC	N/A	N/A	N/A	Required
Industry-sponsor study-specific supplies and documents received	N/A	N/A	N/A	Required