Category: CIRB, Regulatory
Title: Local Operating Procedures for NCI CIRB Trials
Department(s): CRO

1 Definitions

CIRB	NCI's Central Institutional Review Board
CRO	Clinical Research Organization
CTO	Clinical Trials Office
ICF	Informed Consent Form
IRB	Institutional Review Board
MCSF	Masters Submission Committee Form
MDG	Multi-disciplinary Group
NCI	National Cancer Institute
NCTN	National Clinical Trials Network
PI	Principal Investigator
PRC	Protocol Review Committee
PSU	Protocol Support Unit
SKCC	Sidney Kimmel Cancer Center
SKCN	Sidney Kimmel Cancer Network
TJU	Thomas Jefferson University
QIU	Quality Assurance & Process Improvement Unit

2 Introduction

2.1 Purpose

The purpose of this policy is to outline roles, responsibilities, and expectations related to the acceptance, study start-up, maintenance and closure processes of CIRB NCTN trials.

2.2 Policy Statement

The Sidney Kimmel Cancer Center is an NCI designated cancer center. The NCI requires that we evolve as a cancer center and make every effort to increase accrual in our clinical trials targeting cancer. As an NCI designated cancer center we are mandated to make appropriate clinical trials available to the community in which we serve. To ensure that our clinical trial portfolio fits our patient population and their needs, while supporting faculty research interests, a specific process must be followed to determine that pursuing a clinical trial is appropriate. This process is a two-fold one in which potential clinical trials are reviewed and vetted by the relevant MDG and then approved by the Director of Solid Tumor Oncology or the Director of Hematological Malignancies. As an NCI designated cancer center, we must also ensure that new trials are opened and activated in a timely manner. To do that, a streamlined process has been developed and implemented for NCI NCTN Trials for which TJU accepts CIRB review by an "independent review" process.

Responsibilities of the CIRB: The CIRB is the IRB of record and is responsible for both study review and review of local context considerations for enrolled Signatory Institutions. An Authorization Agreement and Division of Responsibilities document is signed by the Signatory Institution in the enrollment process. This document outlines the responsibilities performed by the CIRB and those performed by the local institution.

Responsibilities of Signatory Institution: The Signatory Institution complies with the responsibilities as identified in the Authorization Agreement and Division of Responsibilities document. This agreement covers only NCI-sponsored studies reviewed by the CIRB and opened by the institution with the CIRB.

The responsibilities of the CIRB and the Signatory Institution are described in further detail in the NCI CIRB Handbook for Local Institutions.

2.3 Scope

This SOP describes the processes for the management of the CIRB independent model trials at TJU:

- Completion of CIRB worksheets
- Initiating a new CIRB-approved protocol
- Amendments both internal and external (NCTN)
- Continuing Reviews
- Submitting Potential Unanticipated Problems or Acts of Serious Noncompliance
- Study closure

This policy is applicable to the following studies:

- CIRB-approved NCTN Trials accepted by the TJU IRB through the independent review process as described in the IRB Authorization Agreement between TJU and the NCI CIRB.

3 Responsible Personnel

Principal Investigator: The Principal Investigator or designee shall be responsible for the submission of the protocol for MDG review, final completion of the MCSF for PRC review, and compliance with CIRB Manager website requirements (e.g. worksheets, CTEP registration, etc), as well as overall responsibility for all study activity throughout the life of the trial

Multi-disciplinary Groups (MDGs): MDGs are responsible for vetting each trial for feasibility, coordination, data management, and regulatory resource capability and to ensure that the current docket does not contain open competing trials. The MDG leaders will approve the study to move forward by signing the MCSF.

Protocol Support Unit (PSU): Regulatory Coordinators are responsible for the completion of the MSCF in conjunction with the PI, submission of protocol and MCSF for PRC review, submission of relevant worksheets through CIRB Manager site for CIRB review, processing all amendments, continuing reviews, and study closures at the local level, as well as overseeing all other regulatory items or maintenance throughout the life of the trial.

Protocol Review Committee (PRC): PRC is responsible for reviewing protocol on the basis of scientific merit. NCTN protocols receive expedited administrative review.

QIU Reviewer: The Quality Assurance & Process Improvement Unit (QIU) Reviewer is responsible for the ensuring that regulatory documents comply with both TJU and CIRB requirements.

TJU IRB Personnel: The TJU IRB is responsible for assigning IRB numbers to CIRB trials during study start up.

4 Procedures

4.1 Start-Up of CIRB Protocol (upon MDG approval)

Role	Step	Activity
PI, PSU, MDG	1.0	Once study is MDG approved, the trial is entered into JeffTrial. The protocol title format must read '(CIRB)' before the actual protocol title and end with the NCTN number. For example: (CIRB) A study to test drug X (E1234) Upon approval, MCSF will be completed by PSU in conjunction with the PI, meeting all signature requirements. *Note:* If MDG declines interest in the trial, the trial can still open for SKCN affiliates only. Proceed to step 1.1 below.
Regulatory Coordinator	1.1	Upon study assignment, complete the following simultaneously: 1. Retrieve most current protocol from CTSU website 2. Submit the current protocol and completed MCSF to PRC for expedited administrative review. 3. Submit the 'Study-Specific Worksheet About Local Context' xForm on the CIRB Manager website. Before this can be submitted, the PI must be registered with the NCI. If not, the PI will not appear in the Investigator drop down menu at the beginning of the xForm. 4. Notify the PI that the 'Study-Specific Worksheet About Local Context' has been submitted on their behalf. This is done via email using template language that includes instructions regarding their CTEP username and password. They will need a current CTEP username and password in order to complete their 'PI Intent to Comply' on the CIRB Manager website.

		***Please note that a PI's CTEP username is not the same as their NCI number. If a PI does not know their CTEP username, they need to contact CTEP. (It is possible to have an NCI number and not a CTEP username.)*
PI	1.2	Completes the 'PI Intent to Comply' on the CIRB Manager website.
PRC	1.3	Approves the trial via expedited administrative review.
Regulatory Coordinator	1.4	The following needs to be confirmed for the PI: o 'Annual PI Worksheet About Local Context' is on file with CIRB o CIRB roster o NCTN roster o CTEP username and password The following needs to be confirmed for Co-Is and key personnel: o NCI registration (for Co-Is) / CTEP ID (for key personnel) o NCTN roster *For CTO coordinated trials: Reach out to SKCN for any participating sites • The CIRB will review the xForm, and issue an approval letter via e-mail to the submitter.
Regulatory Coordinator	1.5	• Submit the MCSF to the TJU IRB via the IRB Portal. Electronic submission only (no paper copy will be submitted). ➢ When submitting to the IRB Portal, select 'CIRB' as Application Type • Once MCSF is submitted to the IRB Portal, email the appropriate IRB personnel notifying them of the submission. *Note:* The purpose of this submission is twofold: to trigger the assignment of IRB control # and to enter the study onto an IRB agenda.
TJU IRB Personnel	1.6	Receives MCSF from TJU IRB Portal and logs into JeffTrial to assign the IRB control number and place it in the management tab section in a timely manner **No TJU IRB approval letter is issued**
Regulatory Coordinator	1.7	• Merge current sponsor ICF with the local TJU OHR-8K. • Draft SKCN consent addendums for participating sites (if applicable) • Send the merged ICF and other applicable documents for internal QA:

		➢ Email the following to the QIU reviewer using the subject line: "CIRB QA Request – IRB # NCTN ID" - Sponsor template consent - Tracked OHR-8K - Clean OHR-8K - Current CIRB approval letter containing the expiration date (found on CTSU) - SKCN Addendums, if applicable *Note:* Subject materials **do NOT** require internal approval
Regulatory Coordinator	1.8	Request the Investigator Brochure(s), if applicable, from PMB. *Note:* This can be done via email to ibcoordinator@mail.nih.gov and you will need to include the PI's NCI number, the study's NCTN ID, and the drug
QIU reviewer	1.9	• Review the documents to ensure all NCTN and TJU language is included and that there were no alterations or omissions. ➢ If corrections are needed it will be returned to the Regulatory Coordinator, changed and resubmitted to the QIU reviewer. • Once accepted, mark approval date on pdf versions of finalized document(s) and email the regulatory coordinator within 3 business days. **Expiration dates are not recorded on approved ICFs** ***Note:*** ****You may NOT QA and approve documents that you created****
Regulatory Coordinator	1.10	• Upon receipt of the CIRB Approval of the Study-Specific Worksheet About Local Context, create transaction and release the study documents in JeffTrial: Under "Review Information": ▪ Review date: date CIRB reviewed ▪ Submit date: date CIRB reviewed ▪ Committee: NCI CIRB ▪ Review Reason: Initial ▪ Review Type: per CIRB letter ▪ Action: Approved ▪ Action date: current date ▪ Expiration Date: per CIRB approval letter Under "Details" upload and release the following documents: ▪ Protocol ▪ CIRB Approval of the Study-Specific Worksheet About Local Context ▪ Most current CIRB approval letter (contains current

		expiration date) ▪ Approved local consent(s) ▪ Approved SKCN consent addendum(s) (if applicable) ▪ Subject Materials (as obtained directly from CTSU) ▪ IB(s) (if applicable) • Enter all staff into the 'Staff' list in JeffTrial, along with their corresponding role.
Regulatory Coordinator	1.11	Send internal notification email, directly followed by training email. Save evidence of training accordingly
Regulatory Coordinator	1.12	Activates trial as per CRO standard practice

4.2 Continuing Reviews

Regulatory Coordinator	2.0	CIRB study expirations will be tracked by the regulatory coordinator. Prior to a CIRB study meeting its expiration date, it will be processed internally by the regulatory coordinator as follows: • Retrieve the CIRB approval letter from the CTSU website and save in study folder on sharedrive
Regulatory Coordinator	2.1	Create a new transaction in JeffTrial: Under "Review Information": ▪ Review date: date CIRB reviewed ▪ Submit date: date CIRB reviewed ▪ Committee: NCI CIRB ▪ Review reason: Continuing Review ▪ Review type: per CIRB letter ▪ Action: per CIRB letter ▪ Action date: current date ▪ Expiration date: According to CIRB approval letter Under "Details", upload the following documents: ▪ CIRB Continuing Review Approval letter *Note:* CR will NOT be uploaded to the Portal
Regulatory Coordinator	2.2	Send internal notification email and file accordingly

4.3 Amendments (Internal)

Examples of internal amendments include: ▪ Investigator or key personnel changes ➢ If the PI changes, both the TJU IRB and the CIRB need to be notified. For detailed instructions on PI changes, please refer to the 'CIRB: Changing the PI' guidance document. ▪ Increasing/decreasing local accrual goal ▪ Closing to local accrual only (not per NCTN group) ▪ Consent QA ▪ Addition of SKCN site		
Regulatory Coordinator and QIU Reviewer	3.0	**<u>Addition/Removal of Co-Is and key personnel</u>:** • Receive the request to add or remove ➢ Note: For Co-Is, obtain PI approval of addition(s) (email is acceptable). File evidence of PI approval. • For additions only, verify credentials: ➢ For Co-Is: • NCI registration • NCTN roster • CV and ML on file • CITI training ➢ For key personnel: • CTEP ID • NCTN roster • CITI training **<u>For adding/removing Co-Is only</u>:** 1. **If the trial is open to accrual**, update consent and send to QIU Reviewer for QA/approval ➢ Send the following documents: - Current approved consent and/or SKCN addendum - Tracked consent and/or SKCN addendum - Clean consent and/or SKCN addendum - Current CIRB approval letter containing expiration date 2. Create new transaction in JeffTrial: Under "Review Information": ▪ Review date: current date ▪ Submit date: current date ▪ Committee: NCI CIRB ▪ Review reason: Amendment Review - Personnel Change

		▪ Review type: Administrative ▪ Action: Approved ▪ Action date: current date ▪ Expiration date: ***leave blank*** ▪ Summary: write who is being added or removed 'Addition of John Doe, MD' Under "Details" upload and release the following applicable document(s): ▪ New approved consent(s) ▪ New approved SKCN addendum(s) Enter 'CURRENT' in all caps in the description box for newly uploaded consent(s) and/or SKCN addendum(s) Un-release previous versions of consent(s) and/or SKCN addendum(s) within their transactions, deleting the word 'CURRENT' from their description boxes. 3. Update JeffTrial staff list with either start date or end date 4. Send notification email 5. For additions, send training email and file accordingly. 6. Update IRB submissions log ***If the trial is closed to accrual,** enter Co-I's end date in the JeffTrial staff list. No transaction needs to be created. Save a tracked version of the consent with Co-I(s) removed, and save with the file name including the words 'NEVER STAMPED'. **<u>For adding/removing key personnel</u>**: 1. Update JeffTrial staff list (for removals enter end date) 2. Send notification email for additions only 3. Send training email for additions only, and file accordingly ➢ **No transaction** needs to be created for addition/removal of key personnel.
Regulatory Coordinator and QIU Reviewer	3.1	**<u>Increasing/Decreasing Local Accrual Goal</u>**: 1. Receive the request to change local accrual goal 2. Obtain PI approval of accrual change (email is acceptable, file accordingly) 3. Update the consent and send the following documents to the QIU Reviewer for QA/approval: - Current approved consent - Tracked consent - Clean consent - Current CIRB approval letter containing expiration

		date 4. Create a transaction in JeffTrial Under "Review Information": ▪ Review date: current date ▪ Submit date: current date ▪ Committee: NCI CIRB ▪ Review reason: Other ▪ Review type: Administrative ▪ Action: Approved ▪ Action date: current date ▪ Expiration date: ***leave blank*** ▪ Summary: write accrual change details, for ex. 'Increase accrual to XX' Under "Details" upload the following documents(s): ▪ New approved consent(s) Enter 'CURRENT' in all caps in the description box for newly uploaded consent(s) Un-release previous versions of consent(s) within its transaction, deleting the word 'CURRENT' from their description boxes. 5. Update the JeffTrial to reflect this accrual change. 6. Send internal notification email *Notes:* - CIRB **does not** need to be notified of changes to internal accrual goals - OHR- 12Bs are not used in this process. The IRB can get staff information from JeffTrial Staff list.
Regulatory Coordinator	3.2	**Closing Accrual Locally:** Closing accrual doesn't change the consent, therefore: 1. File correspondence from the PI, PRC or department chair announcing closure 2. Update the status in JeffTrial 3. Send internal notification email Note: No transaction line in JeffTrial is created for internal accrual closures.
Regulatory Coordinator and QIU Reviewer	3.3	**Consent QA:** Local consents for CIRB studies must contain both TJU local OHR-8K language and current NCTN language. At any point during a study, a consent can be reviewed for compliance with this requirement.

		Regulatory coordinators will send the following to the QIU reviewer: - Current approved consent and/or SKCN addendum - Tracked consent and/or SKCN addendum - Clean consent and/or SKCN addendum - Current sponsor consent - Current CIRB approval letter containing expiration date The QIU Reviewer will then review and send approved documents to regulatory coordinator. The Regulatory coordinator will then proceed with releasing approved documents following normal procedure (JeffTrial, notification email, etc). Please note, within the JeffTrial transaction the Review Information will be the same as above scenarios, with exception of the summary.
Regulatory Coordinator and QIU Reviewer	3.4	**Adding SKCN sites** • Receive SKCN Request Form and confirm with RNO office the approval status of request • Create SKCN Addendum and send to QIU for review/approval • In JeffTrial: ➢ Add site to the Institutions ➢ Add site personnel to the Staff tab, including their start date (training date) The Regulatory coordinator will then proceed with releasing approved documents following normal procedure (JeffTrial, notification email, etc). Please note, within the JeffTrial transaction the Review Information will be the same as above scenarios, with exception of the summary.

4.4 Amendments (External)

Once amendment is released by NCTN group and approved by the CIRB, Regulatory Coordinator will process internally following the below steps. Please note, these instructions pertain to amendments as well as CIRB acknowledgements of study activities (ex. closing accrual nationally, patient materials, etc.).		
Regulatory Coordinator	4.0	Download all amendment materials from CTSU, including CIRB approval/acknowledgment letter

Regulatory Coordinator and QIU Reviewer	4.1	Process amendment as needed. If consent changes, send the following to QIU for review/approval: - Current approved consent - Tracked consent - Clean consent - Sponsor consent - CIRB approval letter of the amendment Approved consents will be returned within 3 business days.
Regulatory Coordinator	4.2	Create a transaction in JeffTrial: Under "Review Information": ▪ Review date: date CIRB reviewed ▪ Submit date: date CIRB reviewed ▪ Committee: NCI CIRB ▪ Review reason: Amendment Review ▪ Review type: per CIRB letter ▪ Action: per CIRB letter ▪ Action date: current date ▪ Expiration date: ***leave blank*** ▪ Summary: write what the amendment is, for ex. 'Amendment 4' or 'Closed to accrual nationally effective XX/XX/XXXX' Under "Details": ▪ Protocol --only if changed ▪ Subject materials --only if changed ▪ Approved Consent(s)-- only if changed ▪ IB- -only if changed ▪ CIRB Amendment Approval/Acknowledgment letter (stamped with the date you release) *Note:* These amendments **will NOT** be uploaded to the Portal
Regulatory Coordinator	4.3	• Send internal notification email and file accordingly • Send training email and file accordingly

4.5 Final Closure (External, per CIRB)

Regulatory Coordinator	5.0	Receives closure notification from NCTN group and downloads CIRB acknowledgment letter of final study closure

Regulatory Coordinator	5.1	Create transaction in JeffTrial: Under "Review Information": ▪ Review date: date CIRB reviewed ▪ Submit date: date CIRB reviewed ▪ Committee: NCI CIRB ▪ Review reason: Final ▪ Review type: per CIRB letter ▪ Action: per CIRB letter ▪ Action date: current date Under "Details": ▪ CIRB Final Closure Approval letter *Note:* Final Reports are NOT uploaded to the Portal
Regulatory Coordinator	5.2	• Send internal notification email and file accordingly • Update status in JeffTrial to reflect 'IRB Study Closure'

4.6 Final Closure (Internal- no subjects enrolled)

Regulatory Coordinator	6.0	Receives closure notification via email from PRC, department chair, etc. **Final Closure of CIRB studies can only occur when no subjects have been enrolled.** If any subjects were enrolled, regardless of their status (ie. all expired) the study must remain open until the NCTN group terminates the trial nationally. This is because queries can come in at any time on expired subjects. *Note: If the Lead Protocol Organization (ex. RTOG) has a specific early termination form, be sure to complete this form and receive approval to close prior to completing step 6.1
Regulatory Coordinator and CIRB	6.1	Log into CIRB Manager website and complete the Study Closure or Transfer of Study Review Resp. xForm CIRB will review the application and email you a final approval letter.
Regulatory Coordinator	6.2	Create a transaction in JeffTrial: Under "Review Information": ▪ Review date: date CIRB reviewed ▪ Submit date: date CIRB reviewed ▪ Committee: NCI CIRB

		▪ Review reason: Final ▪ Review type: per CIRB letter ▪ Action: per CIRB letter ▪ Action date: current date Under "Details": ▪ CIRB Final Closure Approval letter *Note:* Final Reports are NOT uploaded to the Portal
Regulatory Coordinator	6.3	• Send internal notification email and file accordingly • Update status in JeffTrial to reflect study 'IRB Study Closure'

5 References

CIRB NCTN Trials, version 3.0_April 16, 2014 (initial version of this SOP)

'CIRB: Changing the PI' guidance document

CIRB Standard Operating Procedures, version April 15, 2016

CIRB Handbook for Local Institutions, Version Date: May 26, 2015

CTSU website

6 Document History

Version	Effective Date	Description of Change
1.0	N/A	Draft
2.0	N/A	Draft
3.0	4/16/2014	Initial
4.0	3/17/2017	Comprehensive changes

8 Approval

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Date of Signature March 17, 2017

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Date of Signature March 17, 2017

Does this document require review and approval from the SKCC Associate Director of Clinical Research?

☐ **Yes** ☑ **No** **Initials** RO

SKCC Associate Director of Clinical Research Approval W. Kevin Kelly, DO
Date of Signature

Does this document require review and approval from the SKCC Director or Deputy Director?

☐ **Yes** ☐ **No** **Initials**

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