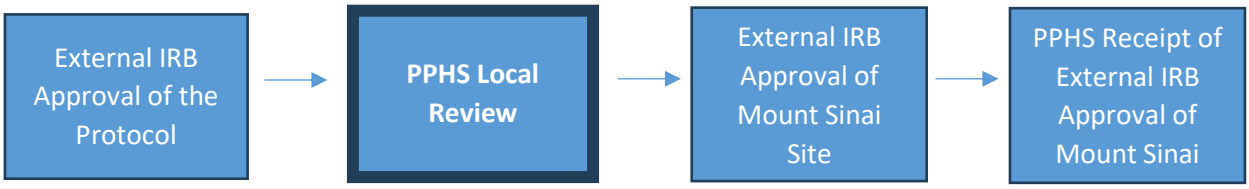
GUIDANCE: R2R Initial Submission Process in RUTH

Studies requesting to rely on an External IRB must obtain local review in RUTH by PPHS and relevant ancillary offices after the lead site has obtained IRB approval.

This local pre-review must be completed ***prior to the Reviewing IRB's review of the Mount Sinai site***. Follow this guide to prepare your Request to Rely (R2R) study application in RUTH.

Request to Rely (R2R) Submission Process Steps



The R2R submission process begins for the Mount Sinai study team at Step 2. Mount Sinai study teams should not submit in RUTH unless the External IRB has approved the protocol and consent form templates, often referred to as lead site approval.

Qualifications for Requesting to Rely on an External IRB

Only certain studies may be permitted to use an External IRB. Your study must meet at least one of the following criteria to use the R2R process:

- Research is an Industry-sponsored Multi-Center Clinical Trial where all must be true:
  - The Mount Sinai PI is not the overall PI of the Trial
  - The sponsor holds the IND/IDE
- Research is federally-funded and use of a single IRB is mandated as part of the grant
- Research is a Major Multi-Center Research Consortium Project
- Mount Sinai PI is a collaborator on Human Research primarily conducted at another organization and the Mount Sinai PI's role does not include interaction or intervention with subjects
- Mount Sinai is engaged in the human research solely because it is receiving federal funds

The following must also be true:

- Research is not a first-in-human study
- Research is not a registry
- Research is not planned emergency research
- Research does not involve the use of any Schedule 1 drugs

Step-by-Step Instructions for R2R RUTH Submission

GCO SUBMISSION AND TRIGGERING EVENT FORM

- Complete the following and include reference numbers in the RUTH Initial Submission:
  - Create a Triggering Event (TE) Form to disclose study personnel financial interests in eDMS
  - **Federally-funded studies:** Also create a GCO submission for the project in InfoEd.

Note: *Effective 1/1/2024, new industry sponsored clinical trials and related studies with no competitive review process and for which the agreement is negotiated by FACTS are no longer submitted to the GCO. This guidance and other guidance documents are available here.*

Links to those systems and more detailed directions for each may be found on the PPHS website: https://icahn.mssm.edu/research/pphs/researcher

CREATE NEW SUBMISSION IN RUTH

Click Create New Study on the RUTH Homepage.

Visit the PEAK portal to access PPHS videos demonstrating the R2R initial submission process. Type 'IRB' in the search bar to locate all IRB and R2R videos.

TRIGGERING EVENT (TE) FORM NUMBER

- Always CAPITALIZE the TE

BASIC STUDY INFORMATION

1. **Title of Study:** This title should match the title on the IRB approved protocol and approval letter
2. **Short Title:** The short title will be the visible title in the dashboard spaces
3. **Brief Description:** Include a concise summary of the overall study, preferably one paragraph.
4. **What Kind of Study is this:** Choose Multi-site
5. **Will an External IRB act as the IRB of record for this study:** Select 'Yes'
6. **Lead Principal Investigator:** Leave this answer blank, as RUTH only allows for Mount Sinai investigators to be pulled into this section. The reliance agreement will document

the Lead PI.

7. **Local Principal Investigator:** Select the Mount Sinai site PI
8. **Attach The Protocol:** Attach the IRB-approved protocol
9. **What identifiers will be accessed?**: Please list the identifiers that will be accessed for this study. See the Help (?) bubble for a list of identifiers.
10. **What health information will be accessed?**: Please list the health information that will be accessed for this study. If no health information will be accessed, indicate 'none.' If the External IRB is making HIPAA determinations, please also indicate that here.

    Please note that if PHI is used or accessed for research purposes, in most cases the External IRB will serve as the Privacy Board and make HIPAA determinations.
11. **Project Initiated by (select one):** Select 'investigator' or 'sponsor'
12. **Submission Department:** Select the PI's department
13. **Is this cancer-related research?:** Select 'Yes' if the project involves cancer-related research. Attach the PRMC review letter to 'Local Site Documents.'

BASIC LOCAL SITE INFORMATION

1. **Brief description of activities this site will perform:** Include a succinct description of all study activities that the Mount Sinai study team will perform to ensure that PPHS can conduct an effective review.

   Examples: The Mount Sinai study team will…
   - *Analyze identifiable data that will be collected from Institution A and Institution B as a part of this study.*
   - *Conduct all study procedures per the protocol, including recruiting and consenting, interventions, surveys, focus groups, follow-up data collection, etc.*
   - *Conduct data coordinating center activities, including…*
   - *Serve as the prime recipient of grant funding but otherwise access de-identified data only and never have access to the code to relink identifiers.*

Please note that insufficient information may delay completion of the local review process and, ultimately, IRB approval. PPHS must understand all study activities that will be conducted locally to effectively apply PPHS and institutional policies.

EXTERNAL IRB

1. **External IRB:** Choose the external IRB from the list
2. **External Study ID:** List the external study number, if known
3. **Specify The Reason (per PPHS guidance):** Explain why this study should be reviewed

by an External IRB according to the Guidance section of page 1 of this document (i.e., industry-sponsored multi-site clinical trial where Mount Sinai PI is not the lead PI, study is federally funded and a single IRB is required).

If there are additional details related to the proposal to use a particular External IRB, also include that rationale here.

4. **Date Submitted to External IRB:** This field should be left BLANK until the study is submitted to the External IRB. You can complete this field when the External IRB approval is submitted to PPHS for final review and acknowledgement.

STUDY FUNDING SOURCES

- Confirm that the sponsor pulled correctly from eDMS via the TE Form listed.
- **Important:** If the sponsor's name does not appear in the list and 'Other' populates, please submit a ticket to Research IT to add the sponsor to the system.
- **The sponsor name listed must be the entity from which Mount Sinai is directly receiving funding.**
  Example: If Mount Sinai is a sub-awardee to federal funding, and Institution A is the prime awardee/direct recipient of funding, list Institution A as the funding source.

LOCAL STUDY TEAM MEMBERS

- Confirm that all study team members were pulled correctly from eDMS
- All study team members must meet PPHS education requirements per the PPHS Training and Education webpage and current CVs must be provided.
- The PI's name will auto-populate in this section but it can be removed since they are already listed in "Basic Study Information.".
- Administrative Staff who are only responsible for managing RUTH submissions can be added, if not already pulled in from eDMS.
  - Their role should be listed as "Administrative Staff (non-FCOI)"
  - Non-FCOI individuals **cannot** conduct study activities

STUDY SCOPE

- Answer all questions.
- Complete the following external forms and attach completed forms to 'Local Site Documents.'
  - **REQUIRED:** Complete the Ancillary Review Form (link found on the Smartpage in RUTH).
  - **If Mount Sinai will make HIPAA determinations:** Complete the HIPAA Wizard if

PHI will be used or shared for research purposes *without first obtaining a signed HIPAA Authorization*.(link found on the Smartpage in RUTH). ***Please contact PPHS if you have questions related to HIPAA determination responsibilities.***

- A full HIPAA Waiver of Authorization is requested. You are not obtaining a signed consent form and HIPAA Authorization.
- PHI will be accessed prior to obtaining a signed consent form and HIPAA Authorization. i.e., screening/recruitment purposes
- A HIPAA Waiver or Alteration is requested for another reason

LOCAL RESEARCH LOCATIONS

- Add all Sinai locations where the research will be conducted

DEVICES, DRUGS, AND IMAGING

- Answer all questions.

STUDY-RELATED DOCUMENTS

- Provide the External IRB's initial approval letter.
- **Optional:** Provide consent form templates from the External IRB or sponsor.

Note: Providing the External IRB's consent form templates allows PPHS to verify that the site-specific version aligns with the External IRB's approved language, ensures that no substantive changes were introduced beyond permitted local edits, and supports regulatory compliance by providing a clear baseline for what was centrally approved.

LOCAL SITE DOCUMENTS

Attach the following:

- **All IRB-approved documents** that will be utilized by the local Mount Sinai study team that will impact Mount Sinai local context review. This includes but is not limited to:
  - Initial IRB approval letter from the External IRB
  - Protocol
  - Consent/assent forms
  - Study materials
  - Recruitment materials
  - Investigator brochures or device manuals

Note: If the External IRB has approved modifications to these documents, please provide IRB approval letters from the External IRB verifying the current version to be used at Mount Sinai is IRB-approved.

- **Reliance forms** that document the study-specific reliance arrangement between the

External IRB and Mount Sinai IRB.

- These may include the SMART IRB Letter of Acknowledgement (LOA) and the SMART IRB Implementation Checklist. **Obtain these from the External IRB or lead study team.**

- **Local context forms** that the External IRB may choose to use to collect local information from PPHS.
  - These forms will document how Mount Sinai will conduct the study locally, respecting New York state law, institutional requirements, PPHS policies, and the outcome of ancillary reviews. **Obtain these from the External IRB or lead study team.**
- The completed HRP-232R Request to Rely Form from PPHS. **This form is available on the PPHS R2R webpage.**
- Click FINISH to access the Submission Workspace. ***You must click Submit on the following screen to send the form to PPHS for local review.***

SUBMISSION WORKSPACE

Once the application form is populated and the Submission Workspace populates with the Pre-Submission status, complete the following:

- **Assign Primary Contact:** Primary contacts receive all RUTH notifications and can create and editComplete this step by using the “Assign Primary Contact” button.
- **Assign PI Proxies:** If desired, complete this step by using the “assign PI Proxy” button *This can only be done by the PI.*

Confirm that study team members have current CITI training via the TRAINING TAB (please visit the “Trainings and Education” page of the PPHS website for additional information regarding required trainings - PPHS Training and Education | Icahn School of Medicine).

- **Manage Ancillary Reviews:** Assign all Ancillary Reviews that are indicated in the completed Ancillary Review Form by clicking the ‘Manage Ancillary Reviews’ button.

  To assign an ancillary review, click “Manage Ancillary Reviews”, then click ‘Add.’
  - **Item 1**: Select the appropriate ancillary office for ‘Organization’ (click the three dots on the right to see a list of all ancillary organizations), and leave ‘Person’ blank.
  - **Item 2:** Select the same ancillary office from the dropdown menu.
  - **Item 3:** Select ‘Yes’ to indicate that a response is required.

- **Item 4:** This section may be left blank, or if necessary a comment may be left for the reviewing ancillary office.
- Click 'OK' at the bottom of the page.

Note: Once the ancillary review has been added, **do not** click the "Update" button. Do not re-assign an ancillary review before it has been completed, as this will delay the review process.

- **Click SUBMIT button in the left menu to send the R2R Initial Submission to PPHS for local review.**

PPHS CONDUCTS INITIAL REVIEW

- If additional information is needed for PPHS to complete the local review, the submission will be returned for CLARIFICATIONS REQUESTED. Resubmit to PPHS when all requested changes are made and all ancillary offices complete their reviews.

Response Time Exceeded Messages: *When PPHS sends the submission back to the Mount Sinai study team, the RUTH system tracks the length of time the submission is with the study team. After 16 days, an automated email reminder is sent to the PI, PI proxies, and Primary Contacts. Please add a comment to the submission after receiving a response time exceeded message to update PPHS on the status so PPHS can provide support.*

- When PPHS initial local review is complete:
  - The submission will move to 'Pending sIRB Review' in the Workflow Map.
  - The executed reliance agreement and completed local context forms will be attached to the "Reliance Confirmed" comment in the History Tab.
  - Revised HRP-232R and comments from Ancillary Reviewers will be available in the History Tab.
  - Instructions will direct the Mount Sinai study team to submit all local documents to the External IRB for IRB-approval of the Mount Sinai site.

On managing turnaround times: *Please note that the single IRB reliance process includes the External IRB and PPHS as the Relying Institution – both signatories to the reliance agreement. Once PPHS confirms reliance and releases local documents for IRB approval, the expectation is that the Reviewing IRB will then receive these materials for IRB review. Providing documents to the CRO or Sponsor for review adds additional steps to the process and may create delays in IRB approval.*

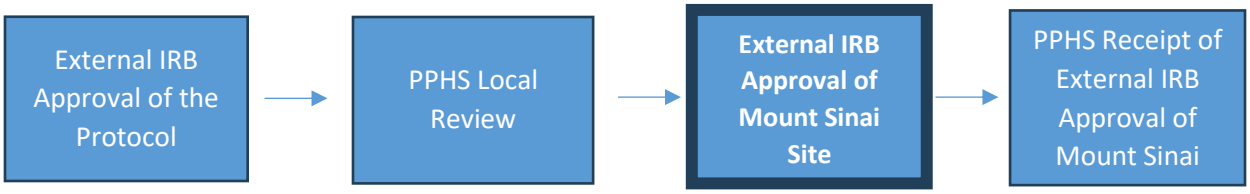
SUBMIT TO THE EXTERNAL IRB FOR REVIEW

The Mount Sinai study team will submit all local documents to the External IRB for review by providing these documents to the lead study team to submit on their behalf or by logging into the External IRB's portal and submitting these documents themselves.

PPHS encourages study teams to submit these local materials instead of designating this responsibility to the CRO or sponsor to reduce submission delays and enhance compliance with the reliance agreement and IRB-approved protocol.

If you experience delays after submitting to the External IRB for review, please add a comment in the RUTH submission to update PPHS on the status. PPHS will support, where necessary.

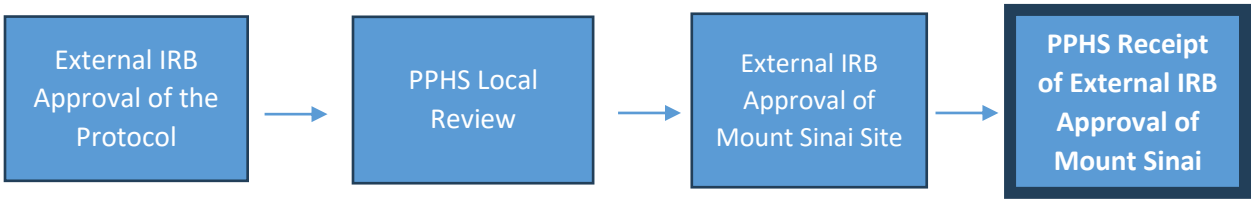
Request to Rely (R2R) Submission Process Steps



The Mount Sinai study team is now at Step 3. ***If the External IRB requests changes to Mount Sinai local documents prior to IRB approval, please connect with the IRB analyst to verify that amended documents do not require an additional PPHS local review.***

WHEN THE MOUNT SINAI STUDY TEAM OBTAINS EXTERNAL IRB APPROVAL

Request to Rely (R2R) Submission Process Steps



The Mount Sinai study team is now at Step 4. PPHS requires receipt of the External IRB approval letter to confirm that Mount Sinai is IRB-approved to conduct study activities. PPHS will use the expiration date in this letter to determine when a local continuing review is due in RUTH.

Return to the RUTH R2R Initial Submission and complete the following:

- Open study from EXTERNAL IRB TAB
- Click EDIT STUDY
- Click LOCAL SITE DOCUMENTS from the menu on the left-hand side of the screen
- Attach IRB-approved ICFs to the LOCAL SITE DOCUMENTS - CONSENT

FORMS Section

Important: ***Click "Update" to replace draft copies without adding or deleting***

- Attach additional IRB-approved local documents to OTHER ATTACHMENTS
- Attach Approval Letter from the External IRB to LOCAL SITE DOCUMENTS - OTHER ATTACHMENTS
- Click EXIT
- Click ADD COMMENT
    - #1 COMMENT: In this text box write "External IRB approval documents attached."
    - #3 Who should receive an email notification? >> Check the box for "IRB Coordinator."
- The local study team may begin study activities per the IRB-approved protocol once all required agreements and contracts are executed.

WHEN ALL LOCAL REVIEWS ARE FINALIZED

- The study will be moved to Active in RUTH
- PI, PI Proxy(s) and Primary Contact will be notified that PPHS has completed all local reviews and acknowledged the initial submission.
- Log into RUTH to access documents via the DOCUMENTS TAB.
- **Note:** The PPHS acknowledgement letter will be sent even if the FACTS CTA is pending. ***However, it is the responsibility of the Mount Sinai study team to ensure that CTA and other agreements are fully executed prior to beginning any research-related activities.***