eIRB+ Tutorial: New Study Submission – External IRB Requiring a Signed Reliance Agreement

This is a step-by-step tutorial of how to submit a new study submission in eIRB+ for a study where a signed, study-specific reliance agreement is required for Northwestern University (NU) to cede review to an External IRB, as per HRP-092 - SOP External IRBs and HRP-801 - SOP Establishing Authorization Agreements. These instructions apply when using one of the following study-specific reliance mechanisms:

2. SMART IRB Letter of Authorization (LoA)
3. SMART IRB Online Reliance System (ORS)
4. IRB Reliance Exchange (IREx)
5. Master Agreement Acknowledgement Letter (used when ceding to Advarra or WCG).

Research activities may not commence at the Northwestern site until 1. A reliance agreement is in place 2. The IRB of Record has approved the Northwestern site, and 3. The Northwestern University IRB has provided acknowledgement for the xIRB submission. For additional information on the overall workflow of this process, please reference our Reliance Workflows.

For studies that will rely on an External IRB for which Northwestern has an established Master Reliance Agreement and that do not require the execution of reliance documents on a study-to-study basis (e.g., Lurie Children’s Hospital IRB, National Cancer Institute CIRB), please refer to the “New Study Submission - External IRB with a Master Reliance Agreement” tutorial.

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Step 1: eIRB+ Request for Reliance on an External IRB

To begin the process of executing reliance, the study team must first request for Northwestern to rely on an External IRB (i.e., create an external IRB submission in eIRB+) for a given study. In order to provide the necessary documents and information needed for the IRB Office to review a reliance request, follow the steps below.

1. Go to the eIRB+ main page and login.
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2. Once in the system you will be routed to your inbox.
3. On the left side of the page toward the top, select “Create New Study”.

4. You will then be routed to the “**Basic Information**” page of the New Study application. There are **8** questions in total to respond to, including a section to upload the overall study protocol.

   - **Question 1:** Please provide the title of the study as it is reflected on the overall protocol with “(xIRB)” at the beginning to reference that the study is being reviewed by an External IRB.
   - **Question 2:** Please provide the short title of the study with “(xIRB)” again at the beginning.
   - **Question 3:** Provide a “Brief Description” of the study. This should be a brief overview of the overall research objectives and activities.
   - **Question 4:** Select the review category appropriate to your research. Either Social-Behavioral or Biomedical.
   - **Question 5:** Principal Investigator (By system default the submission preparer is listed in this section. If this is not correct, then ensure the correct PI information is selected).
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- **Question 6:** Since this is a request to cede review to an External IRB, the response to this question should be “Yes”.
- **Question 7:** Select the study type appropriate for your protocol.
- **Question 8:** Provide the overall protocol approved by the External IRB or sponsor.

5. Once you have provided a response to all questions, select **Continue ➤** located at the top or bottom of the right side of the page.

6. The next page of the application is the “**External IRB**” page, on which there are 6 questions. Only numbers 1 and 6 are required at this stage.
   a. **Question 1:** Select the name of the External IRB (Please note: If the name of the External IRB is not available on the drop down list, email irbreliance@northwestern.edu and request for it to be added).
   b. **Question 6:** Provide rationale for why the study should be reviewed by the External IRB (For example: Per the Cooperative Research Requirement, the External IRB will serve as the IRB of Record for all study sites). This response must contain valid justification for Northwestern IRB to cede review to an External IRB for the reliance request to be approved. If utilizing an electronic reliance method like SMART IRB’s ORS or IREx state that here as well.

7. Once you have provided a response to the above questions, select **Continue ➤** located at the top or bottom of the right side of the page.

8. The next page of the application is the “**Sources of Funding and Other Support**” page, on which you will select the funding source for the study. Please ensure that, if any external funding is associated with the submission, you are linking that funding via the integrated “SR Chooser.” To do so, click the “add” button and a pop-up will appear.
   a. Carefully read and respond to Q#1. If you are receiving any funding from a source external to NU, and it has not been routed through LCH or SRALab, Q#1 should be answered “Yes.” If “No” is the correct response to Q#1, use of the SR chooser is not applicable, and you can skip steps b and c below. In the latter case, please manually provide as much information for the funding item as possible, including documentation of how the grant funding is routed.
   b. Next, in the “CERES ID” field that appeared, click the [...] button to the right of the input field. This will produce a pop-up that will automatically attempt to load all active funding records in the CERES system associated with the PI indicated in Step 4e, above. If listed, select the applicable funding item via the radio button to the left of the item. Click ‘OK’ to confirm your selection in the pop-up window.
   c. If you are not able to locate the correct funding item in the list, please be sure to browse all pages of entries and utilize the ‘Click here for more search options’ tool at the top of the page. If you are still not able to locate the correct funding item, please
verify that the funding is external and not being handled by an intermediary (e.g. LCH or SRALab). If funding is still unable to be linked, please fill in the rest of the questions manually, including as much information as possible.

9. Then select located at the top or bottom of the right side of the page.

10. The next page of the application is the “Study Scope” page, on which there are 2 questions where you will indicate if drug or device is being used as a part of the study.

11. Select located at the top or bottom of the right side of the page.

12. If the study does not involve a drug or device, skip to step 15 below.

13. If the study involves a drug or device, the application will direct you to an additional page to provide information and documentation regarding the drug or device.
   - For each drug or agent listed under Q#1 of the ‘Drugs’ page, a package insert, investigator’s brochure, or product labeling document should be attached to the row item.
   - For each device listed under Q#1 of the ‘Devices’ page, an investigator brochure, product labeling document, or device instructions should be attached to the row item.

14. Once you’ve entered all the study drug or device information and uploaded drug or device documents, select located at the top or bottom of the right side of the page.
15. The next page of the application is the “Study-Related Documents for non-NU Research Sites” page, on which there are three questions. Only Question 1 requires a response at this stage.

- **Question 1 “Consent Forms”**: Upload any template/master consent form(s) provided by the sponsor or approved by the External IRB. These documents do not need to contain Northwestern site-specific language at this stage.

16. Select Continue located at the top or bottom of the right side of the page.

17. Next is the final page of the application. Select “Finish” to continue. Please note: the final page will also include an RSS (Research Supplemental Submission) if applicable to your study. IRB Office Staff & Reviewers cannot access the RSS, but it must be completed before the system will allow the PI to submit the application.
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18. You will then be directed to the main page of the “Study” application. There will be a red script indicating that there is an unsubmitted “Site” record, which will need to be completed to proceed.

19. There will be two links to the “Site” record, both links will take you to the same “Site” application page. Select one of them to continue.

OR

20. You will then be directed to the main page of the “Site” application. Select “edit site” to update the application.
21. You will then be routed to the “Basic Information” page where the information from the “Study” application should be pre-generated for the 4 questions.

   **Basic Information**
   
   1. **Title of site:**
      
      Site for (xIRB) Test Study
      
   2. **Short title:**
      
      Site for (xIRB) Test Study
      
   3. **Brief description of local study activities:**
      
      Site for (xIRB) Test Study
      
   4. **Principal investigator:**
      
      SC1 Test Account

22. For **Question 3**, add to or edit the study description to describe the research activities that will occur at the Northwestern site and/or be conducted by Northwestern personnel.

23. Verify that the rest of the pre-generated information is correct, then select **Continue** located at the top or bottom of the right side of the page.

24. The next page of the application is the “Sources of Funding and Other Support” page. You will need to again select the funding source for the study. The funding items entered here should match the funding source selected in the “Study” application.
Step 1: eIRB+ Request for Reliance on an External IRB – **IRBSITE Submission**

Please ensure that you are linking all funding from external (non-NU) sources via the “SR Chooser,” as described above.

25. Select **Continue** located at the top or bottom of the right side of the page.

26. The next page of the application is the “**Study Team Members**” page, on which you will need to identify each additional person, not including the PI, who will be involved in conducting the research. Importantly, no external study team members (e.g., the PI or Co-I’s from non-Northwestern affiliated institutions) should be listed on this page. (If any study team members are affiliated with Northwestern, but not available to be selected on the drop-down menu, they will need to register for eIRB+ using their Northwestern University NetID).

27. Once you’ve added all study team members, select **Continue** located at the top or bottom of the right side of the page.

28. The next page of the application is the “**Site-Specific Documents**” page. There are **three** questions. Only **Question 3** requires a response at this stage.
   - **Question 1 “Consent Forms”:** We do not expect to see Northwestern-specific Consent forms at this stage.
     i. Our process is to review consent forms for use at/by Northwestern after they are approved by the external IRB. The external IRB will review the Northwestern site and our documents after reliance agreements are fully executed. The Northwestern consent form(s) must include Northwestern
local template language from our Biomedical or Social Behavioral
Consent Template (as applicable). This includes but is not limited to -
financial disclosures, costs to subjects, subject injury, and HIPAA
authorization.

- **Question 2 “Recruitment Materials”:** This question is optional at this stage.
- **Question 3 ”Supporting Documents”:** This question is required at this stage.
  
  i. If utilizing a PDF reliance mechanism such as an IRB Authorization
     Agreement (IAA), SMART IRB Letter of Support (LOS), or a Master
     Agreement Acknowledgement Letter (i.e., Advarra, WCG), then upload a
draft version of that PDF here. Specifically, the reliance mechanism
should contain important information regarding the study (e.g., study
name) and External IRB (e.g., their name, FWA, etc.). It is not expected
that this document has relevant signatures at this time. **The reliance
team will facilitate obtaining the NU signatory official’s signature, if it is
appropriate to execute the reliance agreement.**

  ii. **It is highly preferred that the proposed reliance agreement aligns with
Northwestern’s standard terms for reliance.** Please reference the
Northwestern IAA or SMART IRB LOA template available on our website:
https://irb.northwestern.edu/reliance/nu-relying-on-an-external-irb.html
Note: Using an agreement that varies from our standard terms or that
includes indemnification language will result in additional time required
for review.

  iii. **If the study involves federal funding,** this is the location that your single
IRB Letter of Support must be uploaded. If your study involves federal
funding and you have not yet completed the **single IRB consultation
intake process,** please do so at the earliest time point possible. A letter of
support is **required** before we can execute reliance for studies involving
federal funding. Please see **our single IRB planning webpage** for more
details.

  iv. If applicable, also upload a completed local protocol addendum in this
section. The IRB Office may request this document on a case-by-case
basis.
Step 1: eIRB+ Request for Reliance on an External IRB – IRBSITE Submission

Site-Specific Documents

1. Consent forms: [Add]
   - Document
   - Category
   - Date Modified
   - Document History
   - There are no items to display

2. Recruitment materials: (add all material to be seen or heard by potential participants, including ads) [Add]
   - Document
   - Category
   - Date Modified
   - Document History
   - There are no items to display

3. Supporting Documents: (any study-related documents not attached elsewhere) [Add]
   - Document
   - Category
   - Date Modified
   - Document History
   - There are no items to display

29. Select Continue located at the top or bottom of the right side of the page.

30. The next page of the application is the “Sites” page, on which you will need to select the study site information. Responses are only required for Question 1 “Please specify Northwestern and Northwestern Affiliate study site(s)”. Note: Other research sites do not generally need to be listed under Q#2 of the “Sites” page for external IRB submissions. This is because other sites will be under the purview of the IRB of Record, not NU.

31. Once the site information has been provided, select Continue located at the top or bottom of the right side of the page.
32. You will be taken to the Final Page of the “Site” application. Select Finish and you will be taken to the main page of the “Site” application. The “Study” (STU) and “Site” (IRBSITE) applications are ready to submit. Please note submit functionality only occurs on the “Site” page and submitting from the “Site” page will also submit the “Study” application.

33. Once on the main page for the “Site” application, you can then submit the application (if you have appropriate permissions in eIRB+ to do so) or notify the PI to submit. Please note: Notifications to PI’s to submit the study are sent via email from the eIRB+ system. (If applicable and if you receive an error message, make sure that the RSS indicates “Completed” before notifying the PI to submit)

The application process to request Northwestern IRB to cede review to an External IRB is complete. Upon submission, the “Site” and “Study” application will be routed to the Northwestern IRB for reliance review to determine if the study is appropriate to cede review to an External IRB. Proceed to the next section of the tutorial for further instructions.
Step 2: Execution of Reliance & NU Site Review by IRB of Record

During the initial reliance review in eIRB+, the NU IRB may ask for additional information or updates to the “Study” and/or “Site” applications. If warranted, the request(s) will come in the form of a “Clarification Requested” within the “Site” application only. Once the clarifications are addressed and the “Site” application is re-submitted, the Northwestern IRB will then determine whether it is appropriate to cede review to an External IRB.

If the request is deemed not appropriate to cede review to an External IRB, the rationale and instructions for next steps will be provided within the “Site” history tab.

If the request to cede review is accepted, the Northwestern portion of the reliance agreement will be executed (i.e., signed) by the Northwestern IRB Executive Director and provided via a “Clarification Requested” within the “Site” application. If an electronic system for reliance will be utilized, then further guidance will be provided via a “Clarification Requested” within the “Site” application.

The study team may then proceed with obtaining External IRB approval of the Northwestern study site. It is the responsibility of the Northwestern PI and study team to shuttle documents and information to the study team at the IRB lead site or the IRB of Record directly, in order to facilitate the IRB of Record’s review of the Northwestern site.

Please note: If participants will be enrolled at the Northwestern site, the External IRB’s consent form may be used in lieu of the Northwestern IRB consent form template. However, the External IRB consent form approved for use at the Northwestern site must contain the required Northwestern site-specific language, per HRP-092 - SOP External IRBs. This includes but is not limited to financial disclosures, costs to participants, subject injury, and HIPAA authorization.
Step 3: IRB of Record Approval Returned & Obtaining Northwestern IRB Acknowledgement

Once the Northwestern study site is approved by the External IRB, a copy of the fully-executed reliance agreement, documentation of IRB approval, and all documents approved for use at the Northwestern site must be returned via the open eIRB+ submission. Additionally, any instructions logged in the eIRB+ clarification request should be addressed.

Review of all returned materials is necessary in order to obtain the Northwestern IRB’s acknowledgement, indicating that all local and institutional requirements have been met. As a reminder, research activities at the NU Site cannot begin until the Northwestern University IRB has provided acknowledgement for the xIRB submission.

In order to provide the necessary documents and information needed for the Northwestern IRB to issue an acknowledgment, follow the steps below.

1. Go to the eIRB+ main page and login.

2. Once in the system you will be routed to your inbox.
3. Locate the study in your inbox, which will be identified by the IRBSITE number. Click on link associated with the Short Name of the study.
4. You will then be routed to the “Site” application.
5. First, take a moment to review the clarification request that was returned when NU executed its portion of the reliance agreement. Note any items that need to be corrected or addressed as you work through your return submission.
6. You will need to edit both the “Study” and “Site” applications. Click on the link to the “Study” application in the top right corner of the screen.
Step 3: IRB of Record Approval Returned & Obtaining Northwestern IRB Acknowledgement – **STU Submission**

7. You will then be routed to the “Study” application. Select “edit study” on the left side of the page to update the application.

![Image of the “Edit Study” button on the “External IRB” page.]

8. You will then be routed to the “**Basic Information**” page of the “Study” Application. Review all 8 questions to ensure they are still accurate and update if needed. Specifically, ensure that the protocol document uploaded to **Question 8** is the same version listed on the External IRB Northwestern site approval letter. If the protocol version has been updated, since the initial reliance request, select “update” and upload the current protocol approved by the External IRB.

9. Once you have confirmed responses are current for all questions, select located at the top or bottom of the right side of the page.

10. The next page of the application is the **“External IRB”** page, on which there are 6 questions. Provide responses to numbers 2 - 5 as applicable.

   a. **Question 2:** If there is a study ID number provided by the External IRB, please provide that number.

   b. **Question 3:** Select “Upload” and provide the External IRB approval letter for the Northwestern site. If you previously uploaded an initial approval letter from the External IRB, then all subsequent approval letters should be uploaded to the “Site” submission under “Supporting Documents”.

   ![Image of the “Upload” button for approval letters.]

   c. **Question 4:** Select the initial approval date as provided by the External IRB.

   d. **Question 5:** If applicable, select the last day of approval (expiration date) as provided by the External IRB. Note: For most non-exempt, minimal risk, and non-FDA regulated research projects, there will be no expiration date.

11. Once you have provided a response to the above questions, select located at the top or bottom of the right side of the page.
12. The next page of the application is the “Sources of Funding and Other Support” page, which was previously completed. Review to ensure information is still accurate and that external funding has been correctly linked via the SR chooser. Update if needed, then select located at the top or bottom of the right side of the page.

13. The next page of the application is the “Study Scope” page, which was previously completed. Review to ensure information is still accurate and update if needed, then select located at the top or bottom of the right side of the page.

14. If the study does not involve a drug or device, skip to step #17 below.

15. If the study involves a drug or device, the application will direct you to an additional page for the drug or device. Review all previously entered responses and documents to ensure they are still accurate and update if needed. Specifically, ensure that any drug or device document uploaded the row items under Question 1 is the same version listed on the External IRB Northwestern site approval letter. If the document version has been updated since the initial reliance request, select “update” and upload the current drug or device document approved by the External IRB.

16. Once you’ve confirmed the drug or device information is accurate, select located at the top or bottom of the right side of the page.

17. The next page of the application is the “Study-Related Documents for non-NU Research Sites” page, in which there are 3 questions.
   a. Question 1 “Consent forms”: The consent form template(s) provided by the sponsor or approved by the External IRB that were previously uploaded may remain. These documents only serve as records of templates provided for the initial reliance request. Northwestern-specific consent forms should not be uploaded here. They will be uploaded to the “Site” submission in a later step.
   b. Question 2 “Recruitment materials”: Upload all recruitment-related materials listed on the External IRB approval letter that are not specific to Northwestern. (For example, sponsor-run central recruitment campaign materials.)
   c. Question 3 “Supporting documents”: Upload all other study documents listed on the External IRB approval letter that are not specific to Northwestern. (For example, questionnaires utilized by all study sites should be uploaded into this section).
18. Select located at the top or bottom of the right side of the page.

19. You will be taken to the final page of the application, on which you will select “Finish” to continue. Please note: the final page will also include an RSS (Research Supplemental Submission) if applicable to your study. Review the RSS to ensure it is accurate, and update if needed.
Step 3: IRB of Record Approval Returned & Obtaining Northwestern IRB Acknowledgement – IRBSITE Submission

20. You will then be directed to the main page of the “Study” application.
21. There will be two links to the “Site” record, both links will take you to the same “Site” application page. Select one of them to continue.

22. You will then be directed to the main page of the “Site” application. Select “edit site” to update the Site application.

23. You will then be routed to be “Basic Information” page, which was previously completed. Review to ensure all information is still accurate and update if needed, then select located at the top or bottom of the right side of the page.
24. The next page of the application is the “Sources of Funding and Other Support” page, which was previously completed. Review to ensure all information is still accurate and that external funding is correctly linked via the SR chooser. Update if needed, then select located at the top or bottom of the right side of the page.
25. The next page of the application is the “Study Team Members” page, which was previously completed. Review to ensure information is still accurate and update if needed. Then select [Continue] located at the top or bottom of the right side of the page.

26. The next page of the application is the “Site-Specific Documents” page, on which there are 3 questions to complete.
   a. **Question 1 “Consent forms”:** Upload the External IRB approved and watermarked consent form(s) containing Northwestern site-specific language if participants will be enrolled at the Northwestern site.
   b. **Question 2 “Recruitment materials”:** Upload all recruitment-related materials listed on the External IRB approval letter that will be used specifically at NU.
   c. **Question 3 “Supporting documents”:**
      i. Delete the unsigned version of the reliance mechanism that was previously uploaded for the initial reliance request.
      ii. Upload the **fully executed** reliance mechanism that has all appropriate signatures.
      iii. Upload all other study documents listed on the External IRB approval letter that will be used specifically at Northwestern.
      iv. Upload all subsequent External IRB approval letters and any other associated approval documents. (For example, if an External IRB modification was also approved at the time of initial External IRB approval.)

27. Select [Continue] located at the top or bottom of the right side of the page.

28. The next page of the application is the “Sites” page, which was previously completed. Review to ensure information is still accurate and update if needed.

29. Once the site information has been reviewed and updated, select [Continue] located at the top or bottom of the right side of the page.
30. You will be taken to the Final Page of the “Site” application and then select Finish and you will be taken to the main page of the application.

31. Please note all documents listed on the External IRB approval letter should at this point be uploaded somewhere into the “Site” or “Study” applications in the corresponding sections. If any documents are listed on the External IRB approval letter that are not uploaded at this point, please review the “Study” and “Site” applications and upload any missing documents into the most appropriate corresponding section. Please reference our “Where to Upload Documents” table for guidance.

32. Once on the main page for the “Site” application, you can then submit the application (if you have appropriate permissions in eIRB+ to do so) or “notify the PI to submit”. Please note: Notifications to PI’s to submit the study are sent via email. (If applicable and if you receive an error message, make sure that the RSS indicates “Completed” before notifying the PI to submit)

33. Upon submission, the “Site” and “Study” application will be routed to the Northwestern IRB for administrative review and, if all local and institutional requirements are met, acknowledgment.

34. Once acknowledged, the Northwestern IRB acknowledgment letter will be posted within the “Site” application history tab.

35. Once the NU PI and study team has received approval from the IRB of Record, acknowledgement from the NU IRB, and no other holds are in place from the IRB of Record or Sponsor, research activities may commence at the NU site.