Reliance Process Overview:
Northwestern University IRB serving as the IRB of Record

Obtaining full IRB approval for projects where Northwestern is serving as the IRB of Record (i.e., approval of the overall protocol and approval of each participating site(s)) occurs in approximately three phases. This document outlines our standard process for executing reliance and onboarding participating sites. However, some flexibility exists in this process (e.g., what documents are included in which modifications, number of modifications necessary, etc.), so please reach out to your assigned analyst if you have any questions. Note: This document is intended for use by the Northwestern Study Team, and is separate from documents intended for sharing with participating sites (i.e. relying sites).

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Phase One – Initial Protocol Review

1. Submit your project in eIRB+.
    a. Review Northwestern's IRB webpage on initial submissions for guidance on submitting your project for initial review.
    b. This submission will look very similar to a normal single-site study.
    c. Include the following:
        i. Single IRB Letter of Support (sIRB LOS) (if applicable)
        ii. A thorough description of activities happening at each site within the "Multi-Site or Collaborative Research" section the protocol
    d. Do not include participating sites on the "Sites" page or the participating site responsible party on the "Study Team Members" page. You will add these later via a modification and reliance agreements will be submitted during that review.
        i. See **Phase Two** for more information.
2. After your project is submitted in eIRB+ for initial review your assigned Biomedical or Social Behavioral (SBR) Analyst will review the protocol and other study materials.
3. If the IRB Office determines it is appropriate to do so, you will be issued an initial approval letter.
    a. This letter indicates that the protocol and other study materials have been approved for use at Northwestern. This letter DOES NOT indicate that research activities may commence at external sites as Reliance Agreements and review of external sites are not typically executed in initial submissions.

b. To request IRB review of participating sites and execute Reliance Agreements, you will next create a modification for the project in eIRB+ as detailed in Phase Two.

Phase Two – Execute Reliance Agreement(s)

Consult with your participating sites regarding which Reliance pathway is most feasible and identify who will sign Reliance Agreement (i.e., who their Signatory Official is). If multiple external sites will rely on the Northwestern IRB, the same Reliance mechanism should be used for all sites. You may use the "Request to Rely on Northwestern" template to communicate expectations with participating sites.

1. Open a modification in eIRB+
    a. Indicate the reliance mechanism
        i. If using an IAA or SMART IRB LOA, include a draft version of the Reliance Agreement. This means you should fill out the portions relevant to the Northwestern site and study team (e.g., study title, PI names etc.). Additionally, with these types of agreements, one Reliance Agreement should be uploaded to eIRB+ per participating site. Participating sites can be added in any order, and at any time (i.e., they do not need to all be added in the same modification). Please note, it is our preference to review draft reliance agreements before signatures are added. If the reliance agreement has already been signed by a participating site still include it at this step.
        ii. If using SMART IRBs ORS or IREx, indicate as such in the modification summary and include an ID number from that platform. Please visit https://irb.northwestern.edu/reliance/smart-irb-irex.html for detailed instructions on executing reliance through these platforms.
        iii. If the reliance pathway has not yet been determined, please visit https://irb.northwestern.edu/reliance/nu-serving-as-the-irb-of-record.html for more information about the different reliance pathways.
    b. Add all participating sites to the "Sites" page and add the responsible party per Site (i.e., Site PIs) to "Study Team Members" page under External Study Team Members. Submit after you've ensured the rest of the submission is up to date.
2. After submitting your modification...
    a. Once your assigned Biomedical or SBR analyst has completed their pre-review, a Reliance Ancillary Review will be added. This allows the Reliance Team to review the reliance components of the submission. We will communicate any necessary changes or clarifications via eIRB+.
    b. When the draft reliance agreement (i.e., IAA, SMART IRB LOA) is ready, the Reliance Team will obtain Northwestern's signature on the agreement and

provide signed documents via eIRB+ comment. Please note, reliance agreements are *not* executed via email.

i. If using SMART IRB's ORS or IREx, this signature will be executed within the appropriate platform. We will notify you via eIRB+ once complete.
ii. It is the responsibility of the study team to shuttle the reliance agreement to the participating sites to obtain their signature on the document if the document still requires.

c. The Reliance Team will help facilitate the inclusion of the Local Context Form(s) via eIRB+.
    i. At this stage, a Local Context Form (LCF) will need to be obtained for each participating site. The Reliance Team will provide either a completed site-specific LCF or a template LCF to be completed by the IRB Office or equivalent at the participating site(s).
    ii. The study team is expected to review the completed site-specific LCF, make any necessary adjustments to the study regarding local context requirements (e.g., consent form language), and upload the completed LCF to eIRB+.

3. At this stage, please utilize the "Request to Rely on Northwestern" email template to send all currently IRB approved study materials, the Northwestern-signed Reliance Agreement (or equivalent for SMART IRBs ORS or IREx), Local Context Form (if directed to do so by the Reliance Team), and Reliance Welcome Packet Cover Letter to your external participating sites.
    a. If applicable, within the draft site-specific Consent form and HIPPA authorization, instruct participating sites to locate and delete Northwestern's language related to subject injury, Conflict of Interest/Financial disclosure/compensation, and HIPPA language, and replace it with their local required language.
    b. At this point, if they haven't done so already, the participating sites will need to obtain the signature of their Signatory Official on the SMART LOA or IAA (if applicable), or they will need to instruct their IRB Office to execute reliance in SMART IRBs ORS or IREx.
    c. Remind your participating sites that they should be in communication with their local IRB, or executive leadership team, to ensure their local procedures relating to relying on an external IRB are followed.
4. Fully executed Reliance Agreements and Local Context Forms:
    a. If using an IAA/SMART IRB LOA, if not already in eIRB+, once signed by the participating site's Signatory Official, upload the fully executed Reliance Agreement to the eIRB+ modification submission.
    b. If using SMART IRB's ORS or IREx, please notify the Reliance Team via a comment in eIRB+.
    c. Ensure the completed LCF is uploaded to eIRB+.

Note that at this point, while Reliance has been fully executed, the Northwestern IRB Office has not reviewed or approved participating sites. Human research activities at participating sites cannot occur until reliance agreement(s) are fully executed, LCF(s) are completed and uploaded to eIRB+, and approval for the participating site(s) has been issued by the Northwestern IRB.

Phase Three – Review of Participating Site(s)

After reliance is fully executed, i.e., the reliance agreements are signed by both/all sites, Northwestern's IRB will need to review the human research activities proposed at the participating site(s). Note: It is preferred that participating site human research activities and related documents are submitted in the same modification in which reliance is executed.

1. Submit all site-specific documents in eIRB+. Include any documents received from the participating site(s).
    a. If the participating site(s) will be consenting research participants, then site-specific consent form(s) (with HIPAA authorization, if applicable) and recruitment materials which include their site's required local language and site PI contact information, should be included.
2. If there are no site-specific materials, local research activities will still need to be described in detail in the protocol for review and approval.
3. Participating site research activities will be reviewed by the appropriate IRB Analyst and/or IRB. The Northwestern IRB Office will then issue an approval letter which lists each external site.
    a. Once this step is reached, a participating site is often called a relying site.
    b. If it is not possible to provide participating site materials at this time (e.g., a site-specific consent form), it should be clear in the protocol and eIRB+ study record that related human research activities will not commence at participating sites until Northwestern IRB review and approval of these materials occurs in a subsequent modification.
4. Remind your participating sites that they should be in communication with their local IRB, or executive leadership team, to ensure their local procedures relating to relying on an external IRB are followed before research activities begin at each site.
5. Throughout the life of the project, while Northwestern is the IRB of Record, the Northwestern PI maintains the responsibility of retaining all reliance documentation, submitting continuing reviews, modifications, and submitting any Reportable New Information that comes from the Northwestern site or any other participating site(s).