Northwestern

Navigating Continuing Reviews, Submission Guidelines & Key Considerations

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What is a continuing review?

- A federally mandated re-evaluation of an approved study
- Required to be conducted at least annually
- To reassess the totality of a study and assure that risks are minimized, and still reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may be expected to result.

When should I submit my CR?

- **When to Submit:**
  - Submit Continuing Review info **no sooner than 60 days** and **no later than 30 days** before study expiration date.
  - Ensure adequate time for IRB processing.
  - Expiration date is listed on the study's main page in eIRB+.
- **Reminder Notices:**
  - eIRB+ automatically generates continuing review reminders.
  - Principal Investigator and Primary Contact will receive these notices.
- **Internal Reminders:**
  - Investigators should set up additional reminders to track submission deadlines.
- **Suggestions:**
  - Use electronic calendar reminders.
  - Hold frequent meetings with study staff to review expiration dates.

What studies **do not** require Continuing Reviews?

- New non-exempt, minimal risk, and non-FDA regulated research projects do not require an annual continuing review.

- What studies **do** require Continuing Review?
  - Greater than minimal risk, FDA-regulated studies
  - Check your approval letter
  - Reminders of expiration date

Does My Continuing Review Require Panel Review or Can It Be Expedited?

- **Expedited Review**:
  - If the study was previously determined to be **no greater than minimal risk** and has an **expiration date**, it can typically qualify for expedited review, avoiding the need for a full board review.
- **Full Board Review:**
  - Studies determined to involve **greater than minimal risk** during initial review usually requires a full board review
  - However, some of these studies may still qualify for **expedited review** if they meet specific criteria outlined in categories **8a, 8b, or 8c**.

Expedited Review Under Categories 8a,8b and 8c

Continuing review of research previously approved by the convened IRB as follows:

8a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

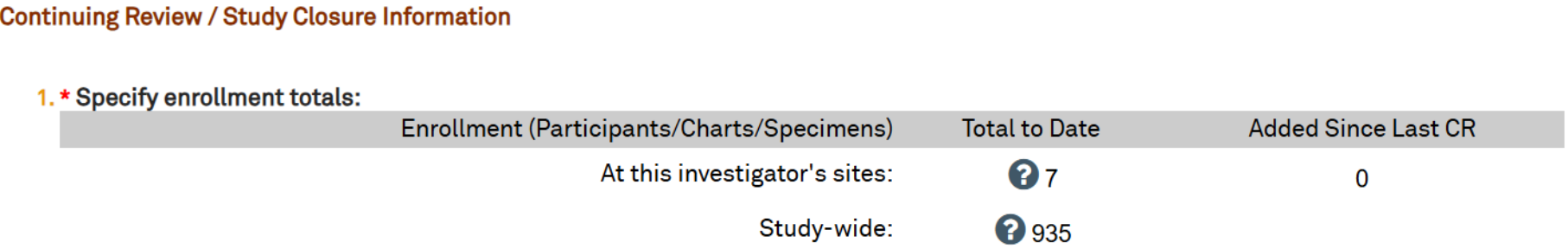
8b. where no subjects have been enrolled and no additional risks have been identified; or

8c. where the remaining research activities are limited to data analysis.

My study needs CR, where do I start?

- Go to eIRB+ page.
- Log in, select "My Studies," and filter by PI or Study Number.
- Choose the applicable study from the list.
- The study home page will appear. Click "Create Modification/CR" on the left.
- Select "Continuing Review" for CR of active study or study closure.
- For changes during review, select "Modifications and Continuing Review."
  - Submit team member changes in a separate modification. Team member changes (except PI/Co-I) are auto-approved.
- After clicking the appropriate button, the form will open. Complete all questions. Ensure all study personnel have completed **their annual COI disclosure and have up to date CITI training.**

Section 1 of Study Application Explained


Continuing Review / Study Closure Information

1. * Specify enrollment totals:

Enrollment (Participants/Charts/Specimens)	Total to Date	Added Since Last CR
At this investigator's sites:	7	0
Study-wide:	935	

- This section provides an overview of participants enrolled to date and in the last year
  - **Enrollment Numbers**: Reflect totals at the time of your submission. (This can be participants or charts reviewed)
  - **Added Since Last CR**: Indicate participants enrolled since the last CR, or since study start if it's the first CR.

Section 2 of CR Application Explained

Research milestones: (select all that apply)

Note: The first four checkboxes are sequential and describe the milestones of the overall study. If the first four milestones have been met and are checked, then the study will be closed. If Northwestern University serves as the IRB of record, Research Milestone questions are for all sites relying on the Northwestern University IRB.

NEW: If your study is closed to enrollment, the IRB will not finalize your consent form(s) with a new expiration date. Please provide a justification in section 4 if you do need the consent form(s) finalized with a new expiration date.

- ☐ Study is permanently closed to enrollment OR was never open for enrollment (at the local and relying sites)
- ☐ All participants have completed all study-related interventions OR not applicable (e.g. study did not include interventions, no participants were enrolled at the local and relying sites)
- ☐ Collection of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- ☐ Analysis of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- ☐ Remaining study activities are limited to data analysis only (at the local and relying sites)
- ☐ Study remains active only for long-term follow-up of participants. * (at the local and relying sites)

Section 2 of CR Application Explained

- This section tracks key research milestones.
  - The first four milestones are sequential.
  - Once completed, the study will be closed.
  - For studies with Northwestern University as the IRB of record, milestones apply to all sites using their IRB.
  - If your study is closed to enrollment, the IRB will not finalize your consent form(s) with a new expiration date. Please provide a justification in section 4 if you do need the consent form(s) finalized with a new expiration date.

Section 2 of CR Application Explained

1. **Study is permanently closed to enrollment OR was never open for enrollment (at the local and relying sites)**
    - **Explanation**: This point indicates that the study is no longer accepting new participants at the local and relying sites, either because the enrollment phase has ended, or the study was never open for new enrollments at these locations.
2. **All participants have completed all study-related interventions OR not applicable (e.g., study did not include interventions, no participants were enrolled at the local and relying sites)**
    - **Explanation**: This point indicates that if the study included any interventions, all participants have now completed them. If no interventions were part of the study, or no participants were enrolled, this point is marked as "not applicable."
3. **Collection of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)**
    - **Explanation**: The study has completed the process of gathering all private, identifiable information from participants, or if no participants were enrolled, this point is marked as "not applicable." This ensures that any sensitive data collection has been finalized.

Section 2 of CR Application Explained

4. **Analysis of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)**
    - **Explanation**: This point confirms that any analysis involving private, identifiable information of participants has been concluded. If no participants were enrolled, the point is marked as "not applicable."

5. **Remaining study activities are limited to data analysis only (at the local and relying sites)**
    - **Explanation**: At this stage, the study has finished any participant-related activities and is solely focused on analyzing the collected data. This marks the transition to the final stages of the study, where data interpretation and reporting occur.

6. Study remains active only for long-term follow-up of participants. (at the local and relying sites)*
    - **Explanation**: The study may continue to be active for the purpose of long-term follow-up with participants, such as for post-study monitoring or outcome tracking. This point applies if participants need ongoing observation after study interventions have ended.

Example

- Study is approved to enroll 25 participants. No subjects have been enrolled in the study yet.

- Study is permanently closed to enrollment OR was never open for enrollment (at the local and relying sites)
- All participants have completed all study-related interventions OR not applicable (e.g. study did not include interventions, no participants were enrolled at the local and relying sites)
- Collection of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- Analysis of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- Remaining study activities are limited to data analysis only (at the local and relying sites)
- Study remains active only for long-term follow-up of participants.* (at the local and relying sites)

- None of the options should be checked if the study is open to enrollment

Section 2 Key Takeaways

- Check **all relevant** boxes to reflect the study's status.
- When the **first 4 boxes** are checked, it indicates the study is closing in eIRB+
- Multiple boxes **can be** checked at once to best represent progress at the time of your continuing review.
  - Review the study's current progress carefully to ensure that all relevant boxes are checked, giving an accurate picture of the study's status.

Example

1. * **Specify enrollment totals:**

Enrollment (Participants/Charts/Specimens)	Total to Date	Added Since Last CR
At this investigator's sites:	75	0
Study-wide:	0	

2. **Research milestones:** (select all that apply)
Note: The first four checkboxes are sequential and describe the milestones of the overall study. If the first four milestones have been met and are checked, then the study will be closed. If Northwestern University serves as the IRB of record, Research Milestone questions are for all sites relying on the Northwestern University IRB.
NEW: If your study is closed to enrollment, the IRB will not finalize your consent form(s) with a new expiration date. Please provide a justification in section 4 if you do need the consent form(s) finalized with a new expiration date.

- [x] Study is permanently closed to enrollment OR was never open for enrollment (at the local and relying sites)
- [x] All participants have completed all study-related interventions OR not applicable (e.g. study did not include interventions, no participants were enrolled at the local and relying sites)
- [x] Collection of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- [x] Analysis of private identifiable information is complete OR not applicable (no participants were enrolled at the local and relying sites)
- [ ] Remaining study activities are limited to data analysis only (at the local and relying sites)
- [ ] Study remains active only for long-term follow-up of participants.* (at the local and relying sites)

* Note: Long term follow up includes research interactions that involve no more than minimal risk to subjects (e.g., quality of life surveys); and collection of follow-up data from procedures or interventions that would have been done as part of routine clinical practice to monitor a participant for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research protocol. Long term follow-up excludes research interventions that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.

* **I acknowledge that this study will be closed:** [x]

Section 3 of CR Application Explained

3. **Check the items that are true since the last IRB continuing review for all sites involved in the study. For each item left unchecked, include a corresponding explanation or supporti**

- [x] NO subjects experienced unexpected harm (that wasn't previously reported to the IRB).
- [x] Anticipated adverse events have NOT taken place with greater frequency or severity than expected.
- [x] NO subjects have withdrawn (discontinued participation) from the study since the last IRB approval (initial or continuing review).*
- [x] There have been NO unreported unanticipated problems involving risks to subjects or others.
- [x] There have been NO complaints about the study.
- [x] There have been NO publications in the literature relevant to risks or potential benefits that would indicate a need to modify any part of the study.
- [x] There have been NO interim findings.
- [x] There have been NO multi-center trial reports.
- [ ] There have been NO data safety monitoring reports.
- [x] There have been NO regulatory actions that could affect safety and risk assessments (e.g. FDA drug recall).
- [x] There has been NO other relevant information regarding this study, especially information about Biomedical risks including box warnings or ANY updated package inserts, IBs
- [x] In the opinion of the Principal Investigator, the risks and potential benefits are unchanged.
- [x] There have been NO modifications to the study that have not been submitted to or approved by the IRB.
- [x] All problems that require prompt reporting to the IRB have been submitted.
- [x] Study enrollment/recruitment is proceeding as planned. (If you have not enrolled anyone in the last year, please uncheck this box and provide an explanation by uploading a s

* Note: Only participants who discontinue study participation following enrollment are considered withdrawn (does not include participants who consent to study participation b
Document the reasons for withdrawal, which may include but are not limited to the following: personal reasons, lost to follow-up, dissatisfaction, investigator terminates subject

What should I attach in Section 4?

- **Section 3 Instructions State:** Check the items that are true since the last IRB continuing review for all sites involved in the study. For each item left unchecked, include a corresponding explanation or supporting document in section 4 below:

- *Therefore, anything left unchecked should have a supporting document in Section 4*

What should I attach in Section 4? Examples

- DSMB report
  - These are submitted at the time of CR, not with a modification
- Interim Finding
- Multi-center trial reports
- Participant withdrawal (discontinuation from the study and reasons for withdrawal
- Enrollment Chart
  - Optional Element that provides a more detailed visual of enrollment numbers than that provided in Section 1

Enrollment Chart Tool

Study Title:
PI Name:
Date:

Patient Status - Please make sure that this section includes all sites that are within Northwestern IRB and any other site that is using our IRB as the IRB of record.	**#Number of participant(s) enrolled at NU (Site1)**	**#Number of participant(s) enrolled at NU control/other group** ***(If applicable)***	**#Number of participants enrolled at all sites.**	**Check the box below if the participant(s) withdrawal was study related**	**Reason or clarification for participant(s) withdrawal. Must include Participant(s) ID/Reason for**	**Additional Comments**
Number of **participants** consented to the research: (If consent is not required, how many participants were included in the research?)						
Number of participants who are currently in screening (i.e. consented but not registered or screenfail): (if there is no screening period, enter n/a)						
Number of participants who failed screening:						
Number of participants who enrolled to the research:						
Withdrawals: Number of participants who decided to stop taking part in the research or were removed by the study team before reaching a study endpoint (Document the reasons for withdrawal, which may include but are not limited to the following: personal reasons, lost to follow-up, dissatisfaction, investigator terminates subject participation, etc.)				☐		
Number of participants who completed the research: ("Completed" means the subject is no longer participating in the research and has completed all research procedures, or reached a study endpoint. This includes patient death as well as patient transfer to a research site not covered by NU IRB.)						
Participants who remain on active study or treatment:						
Of the participants who remain on study, number who are in long-term follow-up: (Long-term follow-up includes research interactions that involve no more than minimal risk to participants (e.g., quality of life surveys); and collection of follow-up data from procedures or interventions that would have been done as part of routine clinical practice to monitor a participant for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research protocol. Long term follow-up excludes research interventions that would not have been performed for clinical purposes (e.g. research blood draw), even if the research interventions involve no more than minimal risk. Ask the Coordinator and COM for help on this.)						
Attach document title(s) submitted with this continuing review submission *						

Submitting a Continuing Review with Modification

- The eIRB+ system allows for the submission of a Modification during the processing of a Continuing Review. Access to eIRB+ is available via this site's eIRB+ page.
  - After logging in, choose “My Studies” and filter by PI or Study Number to find the applicable study.
  - Choose the applicable study from the resulting list.
  - In the left-hand side of the study workspace, in the "home screen" you will select "Create Modification/CR" to make any changes to your study at continuing review.
  - The appropriate form will open. You must complete all questions. You can make edits by clicking the "View Periodic Review" button.
  - When you have reached the final page of the application, click "Finish" or "Exit". *Neither of these activities actually submits the continuing review form to the IRB Office.*
  - To submit the Modification/CR to the IRB, the PI or PI proxy must click "Submit."

Examples of MOD/CR's

Usual modifications submitted with a continuing review	**Modifications that should be submitted separately from a continuing review.**
Minor administrative changes or changes to the protocol, consent forms, recruitment materials, inclusion/exclusion, procedures or data collection materials.	It is recommended that you submit study team member changes in a separate modification and not combine it with a CR. The reason why we suggest submitting these changes separately is because Study team member (Not PI' or Co-I's) modifications are approved automatically by the eIRB+ system.

When to Close a Study in eIRB+

- If all research-related interventions or interactions with participants have been completed and collection and analysis of identifiable private data (as described in the IRB-approved protocol) are finished, the study should be closed with the IRB.

How To Close A Study in eIRB+?

- **To Close a Study:**
  - PI must complete a Continuing Review submission.
  - Select and confirm the first 4 statements in the Research Milestones section.
  - Selecting these 4 statements will close the study.
- **IRB Review:**
  - The IRB may request additional information to confirm the study is in good standing.
  - Once approved, the study is closed and archived.

Post-Closure Information

- **Resuming Research:**
  - To resume research after closure, a new study submission is required.
- **Industry-Sponsored Studies:**
  - Closure fees apply to industry-sponsored studies submitted on/after September 1, 2021.
  - See the IRB Fees webpage for more details.
- **Data Retention:**
  - Investigators may retain data (including identifiable, private data) if consistent with the IRB-approved protocol.
  - Investigators must continue confidentiality protections and honor commitments made to participants.

Study Closure Guide

What happens if the study expires?

- **If IRB Approval Expires:**
  - Investigator must stop all research activities related to the study until continuing review and approval occur.
- **Exception:** If the investigator judges it to be in the best interest of current participants to continue.
  - In such cases, the investigator must notify the assigned IRB analyst promptly via email.
- If the IRB Board determines it is not in the best interest of participants to continue:
  - All research activities must stop.
  - This includes:
    - Intervening/interacting with subjects.
    - Obtaining or analyzing identifiable private information about participants.

How To Resume Study and Time Limits

- **How to Resume the Study:**
  - Investigator may resume research activities once continuing review is approved by the IRB.
- **Time Limits:**
  - Investigators have up to 60 days after study expiration to obtain approval.
  - After 60 days, the IRB will permanently close the study.
  - A new study must be submitted for review if approval is not obtained within 60 days.

Resources

- How do I submit a continuing review? NU Link
- FDA Guidance for IRBs, Clinical Investigators, and Sponsors
- SOP: Determining and Processing When Continuing Review is Required (HRP-033)
- Study Closure Guide
- Expedited Categories
- 45 CFR 46

References

- chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.fda.gov/media/83121/download
- https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.103
- https://irb.northwestern.edu/submitting-to-the-irb/continuing-review-closure.html

Questions?