Yale *Human Research Protection Program*

Continuing Reviews & Study Closures

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Jennifer Reese **Carrie McDaniel**

Sharishma Pinnamaraju

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Learning Objectives

- Learning Objective #1
  - Review IRES IRB system requirements for submission of Continuing Reviews and Closures
- Learning Objective #2
  - Discuss the IRB review of the submissions to determine approvability
- Learning Objective #3
  - Offer best practices to ensure seamless review process

Training Agenda

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Continuing Reviews	5-16
Continuing Reviews for Yale sIRB studies	17-20
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General Comments

- The presentation will reflect Yale IRB review – studies under external IRB purview must follow policies and procedures of the reviewing IRB;

- The discussion will focus on non-exempt research (research that was approved by the IRB via expedited or convened board review procedures);

HOT TIPS:

- Only the Principal Investigator or assigned PI Proxy can submit actions in IRES IRB system;
- None of the documents are re-watermarked after approval of a Continuing Review.

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Continuing Reviews

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Purpose of the Continuing Review

- The purpose of the continuing review – to determine whether the study continues to meet approval criteria and all other applicable local requirements related to human subjects research (e.g., compliance with training);

- The IRB will consider any relevant information received since the date of the last IRB review and approval (e.g., Data Safety Monitoring Board recommendations, relevant publications, etc.);

- The IRB will review to assess whether or not the study's risk/benefit ratio is still favorable;

- The IRB will also review subject enrollment to ensure that the study is likely to achieve the research goals (if enrollment is not proceeding as planned, the IRB may question whether it is ethical to expose additional participants to risks if the research is unlikely to yield meaningful results).

Continuing Review Requirements

- Minimal risk studies not subject to FDA or DOJ oversight
  - Approval can be granted without the requirement for continuing review.
  - For minimal risk studies, the IRB reserves the right to request an annual review with a rationale for doing so.

- Greater than minimal risk studies or studies subject to FDA or DOJ oversight
  - The IRB will conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year.

Expiration Dates

- The expiration date is based on the most recent approval of the study – either initial approval or the most recent continuing review;

- Each year's expiration date may be different – Yale IRB does not maintain the same anniversary date of the approval;

- As a courtesy, IRES IRB sends reminders to the investigator prior to the study's expiration date, notifying them that the study is due for a continuing review. Although courtesy reminders are sent, it is still the responsibility of the study team to submit the continuing review on time.

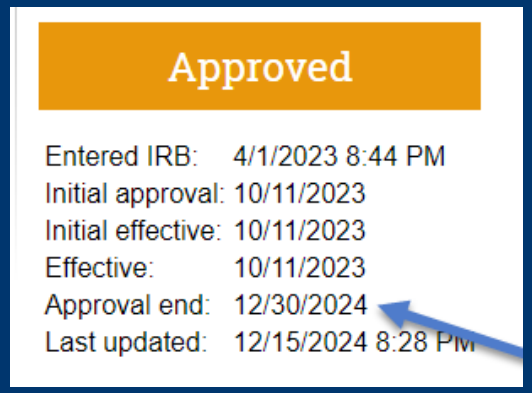
Continuing Review Requirements

- Research that is approved for a specified approval period cannot continue past the expiration date.

- If the protocol expires, **all human research procedures must cease**, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information; All research and fund expenditures also must stop.

- To extend the approval period, create and submit a continuing review request in IRES IRB **60 days** prior to the study's expiration to ensure adequate time for IRB review.

- The expiration date of the protocol can be found in the main study record or in the latest IRB approval letter.



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Submitting CRs in IRES IRB

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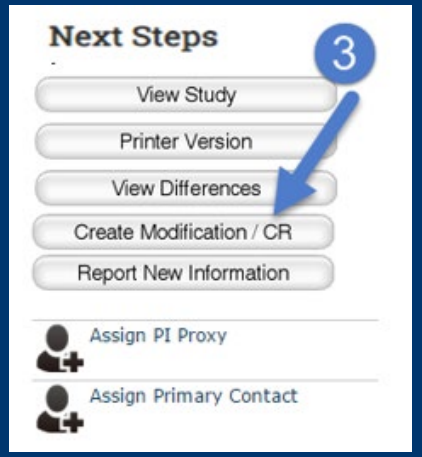
Submitting Continuing Reviews in IRES IRB

- A continuing review submission request is created from the main study workspace, as part of the Continuing Review action *(#3 below)*.
- If the continuing review also involves modifications to previously approved research, you can create a combined continuing review/modification submission.



Submitting Continuing Reviews in IRES IRB

- **Report enrollment totals as follows:**
  - For the Yale site, since the initial approval,
  - For the Yale site since the last approval (excluding MOD approvals and RNI acknowledgments),
  - Enrollment totals for a multisite study.

  ➢ **HOT TIP!** If the study enrolls only at the Yale site, then answers to questions 1 and 3 should align (shown on next slide).

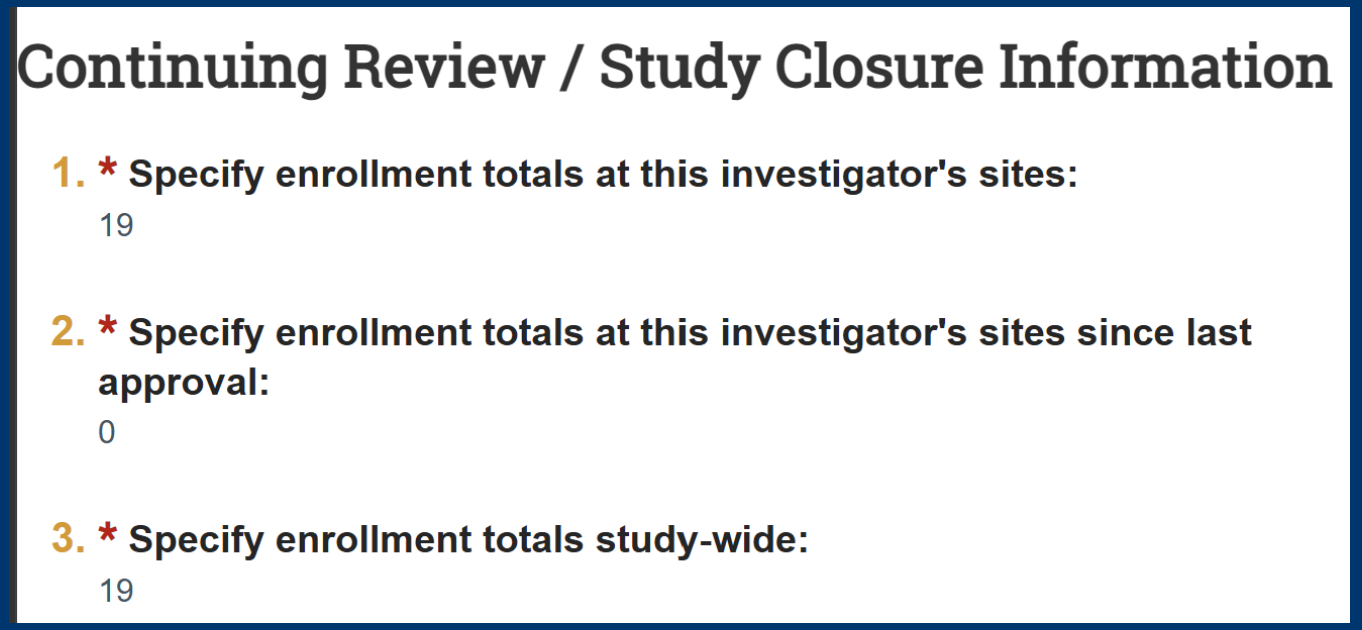
- *Please click on "?" for further Information.

- **NEW! As of May 2026, a Progress Report is now required with each continuing review.**

Submitting Continuing Reviews in IRES IRB

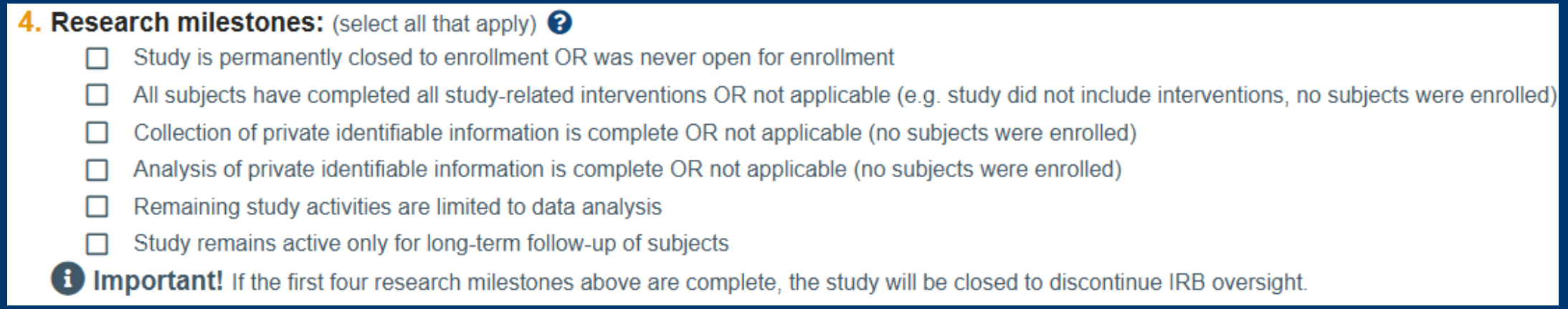
HOT TIP:

- Provide a breakdown of enrollment in your Progress Report if you are enrolling more than one subject cohort.



Submitting Continuing Reviews in IRES IRB

- Read the statements under the Research Milestones question. Check off all the true statements.


4. **Research milestones:** (select all that apply)

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

Important! If the first four research milestones above are complete, the study will be closed to discontinue IRB oversight.

HOT TIPS:

- Read each option carefully, because some of the options contain two different statements.

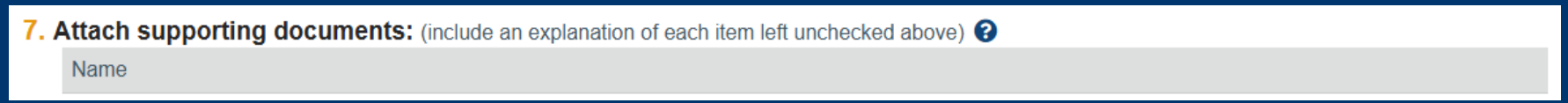
- Study-related interventions are research interventions/procedures during the active enrollment and research procedures such as CT scans during follow-up.
- Long-term follow-up usually means record review, phone call, or survival follow-up.
- Provide the follow-up procedures that are ongoing if this box is checked

Submitting Continuing Reviews in IRES IRB


6. **Check the items that are true since the last IRB approval for all sites involved in the study:**

- [x] NO subjects experienced unexpected harm
- [x] Anticipated adverse events have NOT taken place with greater frequency or severity than expected
- [x] NO subjects withdrew from the study
- [x] NO unanticipated problems involving risks to subjects or others
- [x] NO complaints about the study
- [x] NO publications in the literature relevant to risks or potential benefits
- [x] NO interim findings
- [x] NO multi-center trial reports
- [x] NO data safety monitoring reports
- [x] NO regulatory actions that could affect safety and risk assessments
- [x] NO other relevant information regarding this study, especially information about risks
- [x] In the opinion of the PI, the risks and potential benefits are unchanged
- [x] All modifications to the protocol have been submitted to the IRB
- [x] All problems that require prompt reporting to the IRB have been submitted

- Under Question 7, attach any supporting documents. This includes an explanation of each item left unchecked above. These can also be addressed in the Progress Report.


7. **Attach supporting documents:** (include an explanation of each item left unchecked above)

Name

- See the Research Guide: Submitting Continuing Review (page 5) for any statements that cannot be checked off as true in Question 6.

Progress Report

The Yale IRB Progress Report form is found in the IRES IRB Library (Other Forms) and consists of the following topics:

- Assessment of Enrollment and Overall Progress of the Study;
- Assessment of Recruitment Efforts;
- Description of any challenges faced during research and/or any changes to the duration of the study;
- Additional Information.

1.	**IRES IRB#:**
2.	**Assessment of Enrollment and Overall Progress of the Study** Include: • Progress in each study arm/cohort (# of enrolled participants, completers, status of the arm, etc.) • Progress of the study since the last report e.g., milestones reached • For studies in long term follow-up, describe the ongoing research procedures, e.g., telephone follow-up phone calls vs. CT scans or biopsies
2.	**Assessment of Recruitment Efforts** Include: • Description whether the actual rate of enrollment aligns with the previously anticipated rate • Any anticipated changes in timelines for completion of the study based on the rate and total number of enrolled participants
3.	**Description of any challenges faced during the research** Include: • Description of any issues that may affect conduct of the research e.g., delays with setting up the central data management system, etc.
4.	**Additional Information** Include: • Explanation for any item left unchecked in question #6 in the IRES IRB Continuing Review • Description of any additional relevant information related to this project that may affect the IRB determinations related to risk assessment and monitoring or adequacy of the process for obtaining informed consent • Description of any investigator or institutional issues that may affect the acceptability of the research e.g., shift in departmental resources devoted to research, changes in the investigator's licenses or research team qualifications, etc.

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CRs for Yale sIRB Studies

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Continuing Review Process for Yale sIRB Studies

- Continuing Review is approved for the entire study, inclusive of all participating sites;

- There will be only one IRB approval letter for the study; the letter will reference the names of the sites that participate in the study;

- You can combine the continuing review request with modifications but if site specific documents are affected by the change, a site modification will need to be separately submitted to each site;

Continuing Review Process for Yale sIRB Studies

There are two steps to submitting the continuing review report to the IRB:

1. Obtaining information from sites for the continuing review report.
    - You will need the following information from each of the sites:
        - Total enrollment # at the site,
        - Total enrollment # since the last approval (initial approval or last continuing review, whichever happened last),
        - Verification of whether certain statements are true for the site (Question #6 in the CR),
        - Any supporting information e.g., explanation of the progress,
        - Any additional comments about the study.

- To obtain the information from the site, you can copy the table found in in Section 14.6 of the Investigator Manual and email it to the sites with a request to complete it.

Continuing Review Process for Yale sIRB Studies

2. Once you obtain the continuing review information from the sites, you will need to submit the report in IRES IRB.

- Report Continuing Review Data for the sites
  - In each site workspace, under Next Steps, click on Report Continuing Review Data. Transfer the information you received from the site. You can also upload any relevant documents received from the site.

- Create and submit Continuing Review for the study
  - Once the site information has been submitted, return to study workspace and create study Continuing Review as described earlier.
  - **Note:** Questions #1 and #2 apply only to Yale sites. Questions #3 and #4 apply to the overall study.

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Continuing Reviews with Modifications

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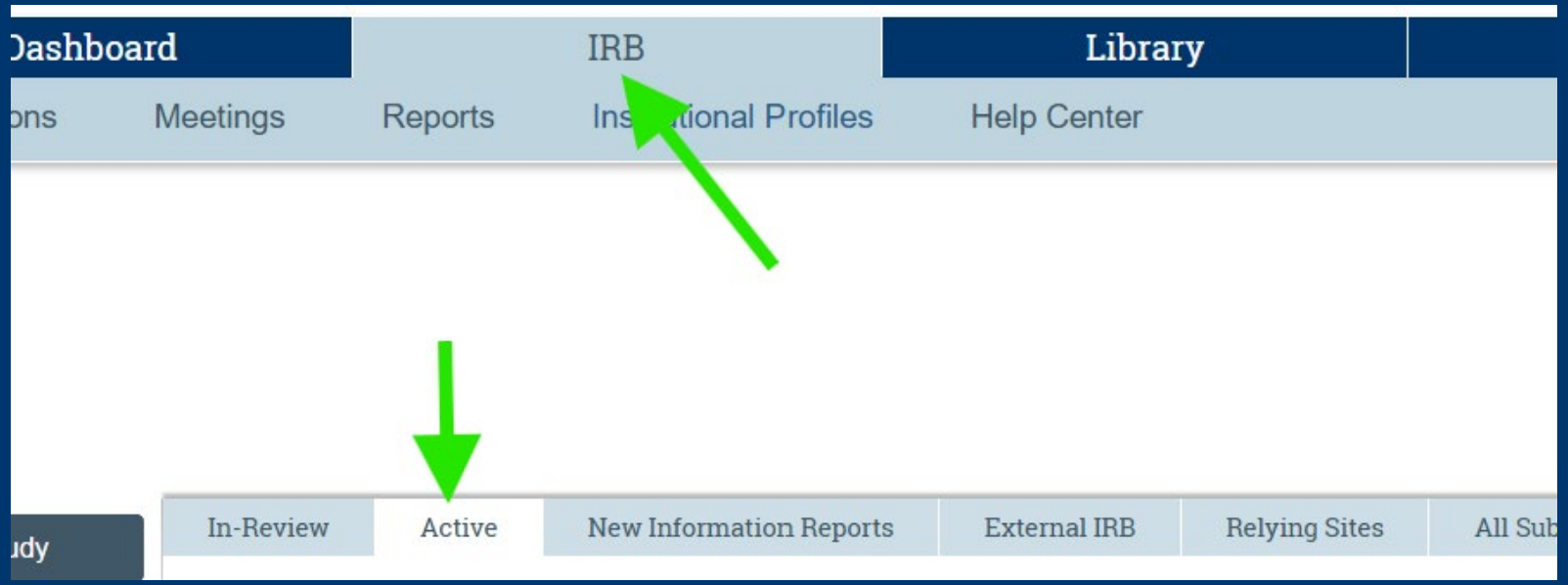
IRB review of MODCRs

- Changes to approved protocols must receive IRB approval before their implementation
  - **Exception:** changes to eliminate an apparent immediate hazard to participants (e.g., immediately stopping study treatment in a participant experiencing a serious side effect) must be promptly reported to the IRB via a Report of New Information (RNI).

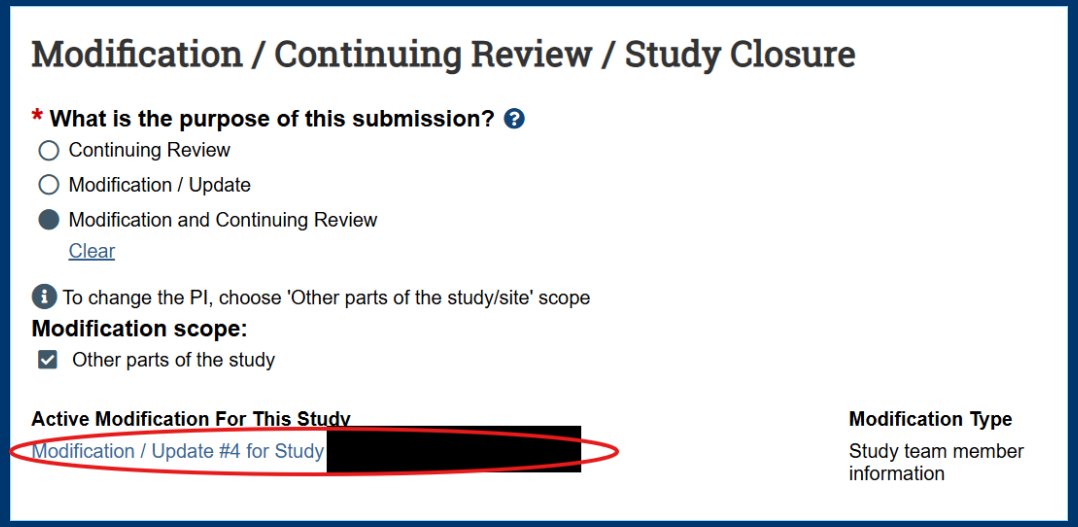
- The IRB reviews proposed changes to determine whether the revised protocol continues to meet approval criteria and other regulatory and local requirements for human subjects research e.g., state statues, local policies, etc.

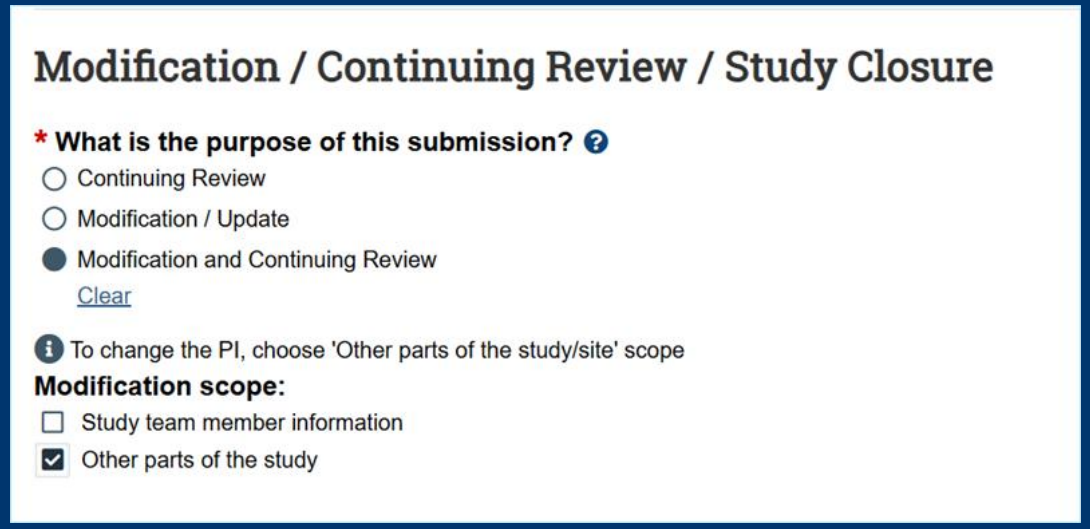
Steps in IRES-IRB for a MODCR submission

- Locate approved research project in Active tab, IRB section of IRES IRB
- Click on Create Modification/CR in the study workspace



Submission of a MODCR



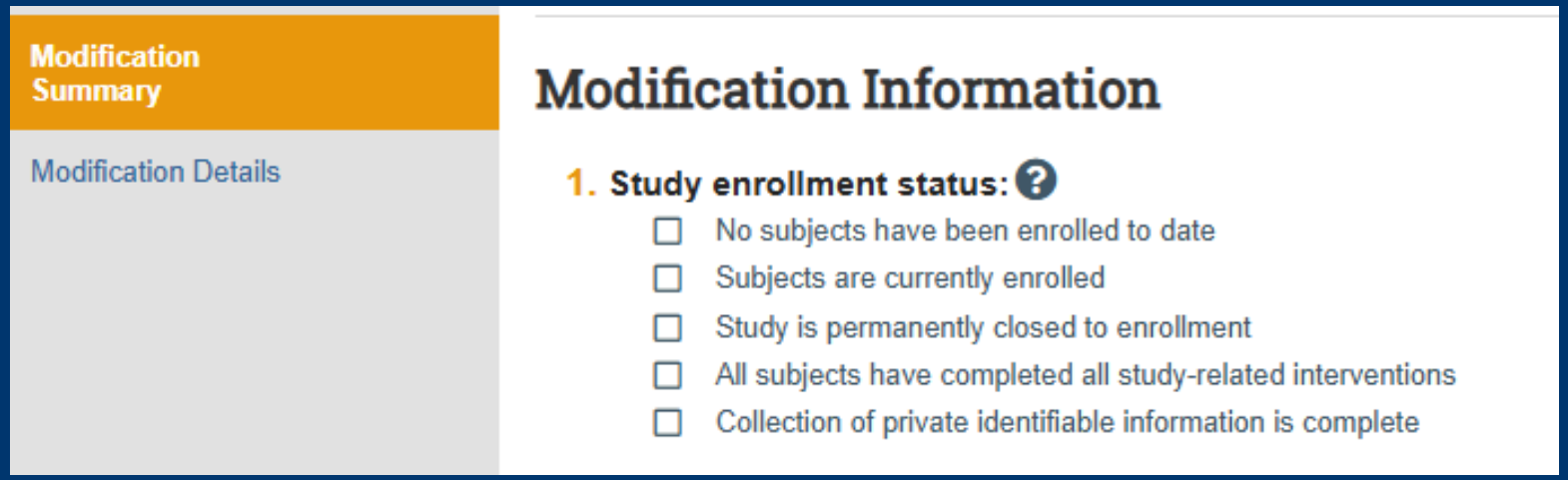


- After you select the submission purpose and continue to the next form, you cannot change the submission purpose or scope.

- It's best practice to submit personnel changes separately from other types of modifications - they are faster to review.

MODCR cont.

When submitting modifications for IRB review, you need to provide the study enrollment status to determine if the changes are applicable to the Yale site. Choose all applicable options from the list in Question 1.



Note: "All subjects have completed all study-related interventions" AND "Collection of private identifiable information" should only be checked if the study is also permanently closed to enrollment.

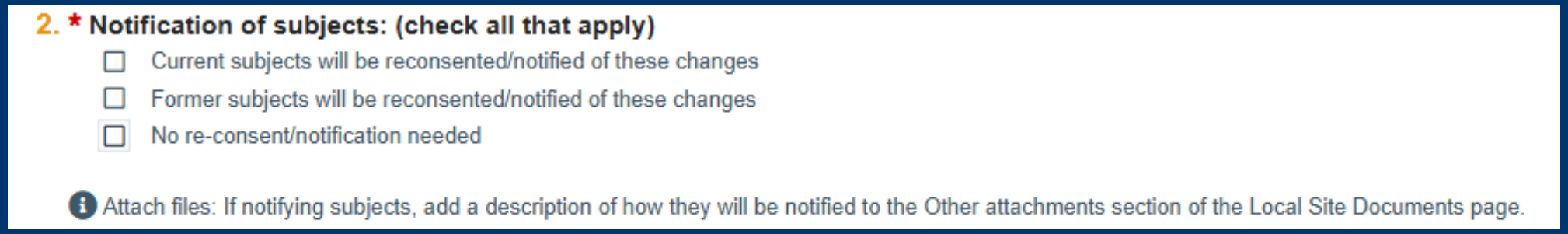
Notification of participants (question #2)

- Certain changes may require notifications to participants;

- Regulations do not include a term '***reconsent'*** but they require that participants are notified about any significant new information that could impact their willingness to continue in the study;

- Think about whether the new information is significant, and if so, who could be impacted by it – answer question #2 and provide a more detailed plan in question #3

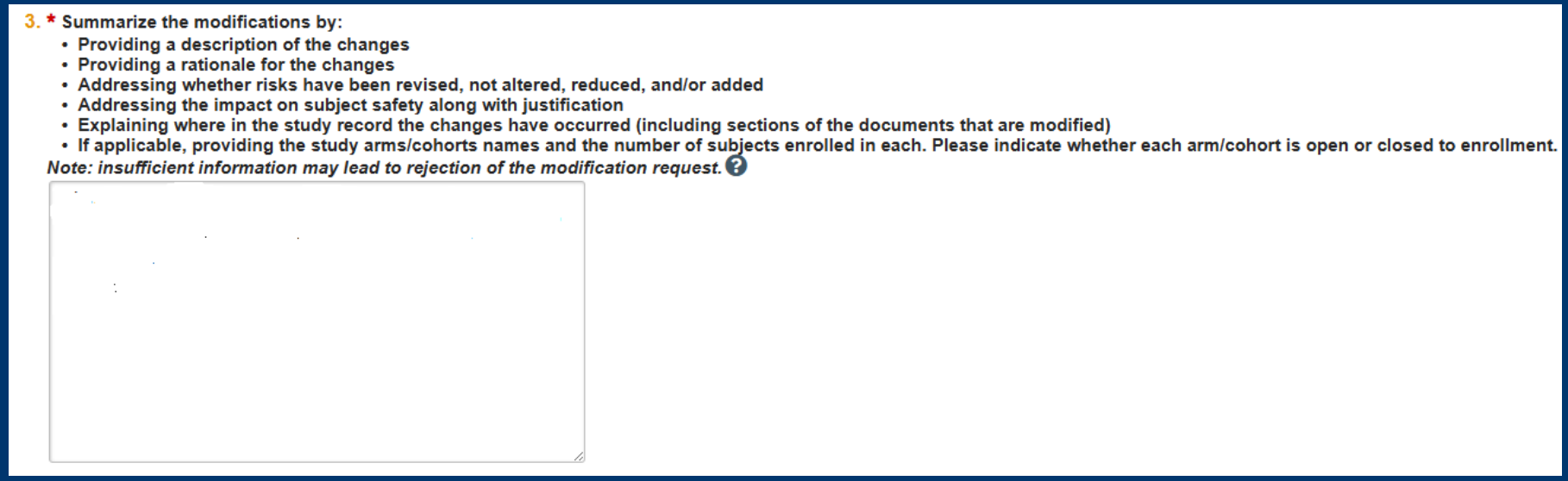
- The IRB will evaluate whether or not reconsent is required.



MODCR cont.

When submitting modifications for IRB review:

- Provide a summary and rationale for the changes;
- Address how the change affects the risks and subject safety;
- Explain where in the study record the changes have occurred (including sections of the documents that are modified);
- If changes affect only certain cohorts, provide the names of the study arms/cohorts and indicate their status e.g., closed to enrollment, etc.


3. * Summarize the modifications by:
- Providing a description of the changes
- Providing a rationale for the changes
- Addressing whether risks have been revised, not altered, reduced, and/or added
- Addressing the impact on subject safety along with justification
- Explaining where in the study record the changes have occurred (including sections of the documents that are modified)
- If applicable, providing the study arms/cohorts names and the number of subjects enrolled in each. Please indicate whether each arm/cohort is open or closed to enrollment.

Note: insufficient information may lead to rejection of the modification request.

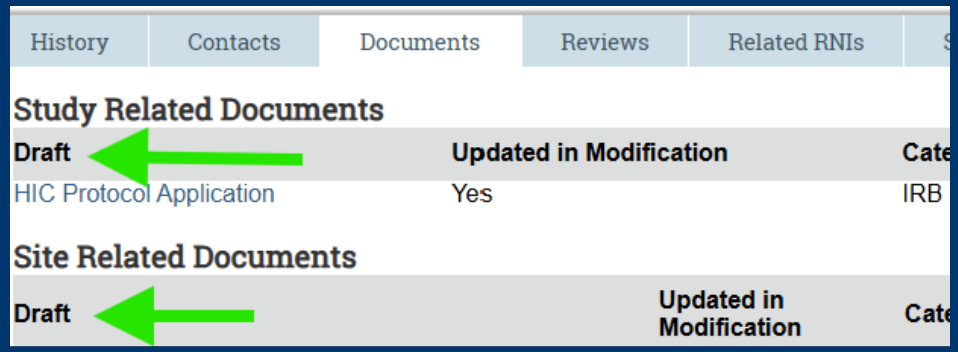
MODCR Best Practices

- Ensure that the proposed revision is reflected in all applicable documents and the IRES IRB record. The PI is responsible for reviewing the final revisions prior to IRB submission.

- Revisions to documents must be tracked using 'track changes' function – **do not upload clean versions.**
  - Highlights or using a different color font will not be accepted.
  - Maintain electronic copies of all information submitted to the IRB in case revisions are required.

MODCR Best Practices cont.

- Download the WORD version of the approved documents from DRAFT column in Documents tab in the Study Workspace. Accept previous changes but don't stop tracking new changes. Make the proposed changes into the document and save it as a new version.

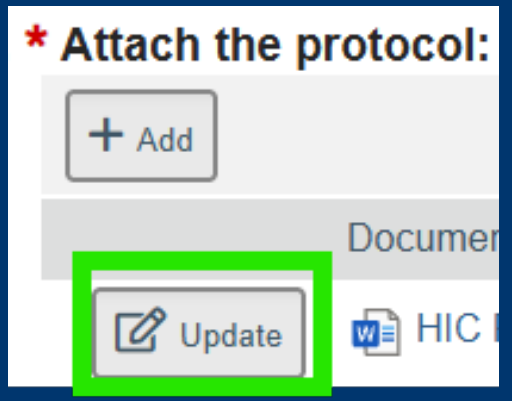


- Follow a reliable method of version control of your documents – use whatever method works for you as long as it is consistent.

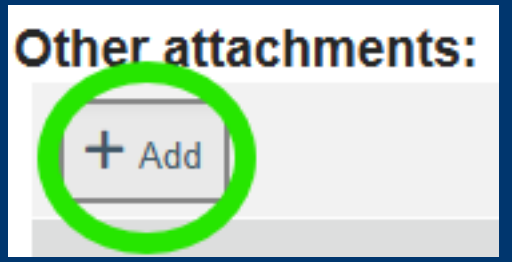
MODCR Best Practices cont.

Uploading revised documents:

- Choose "Update" to upload tracked versions of previously approved documents



- Choose "Add" if the document is new and there are no previous versions of this document in the study record.



- **!!! DO NOT delete any study documents!!!**

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Study Closures

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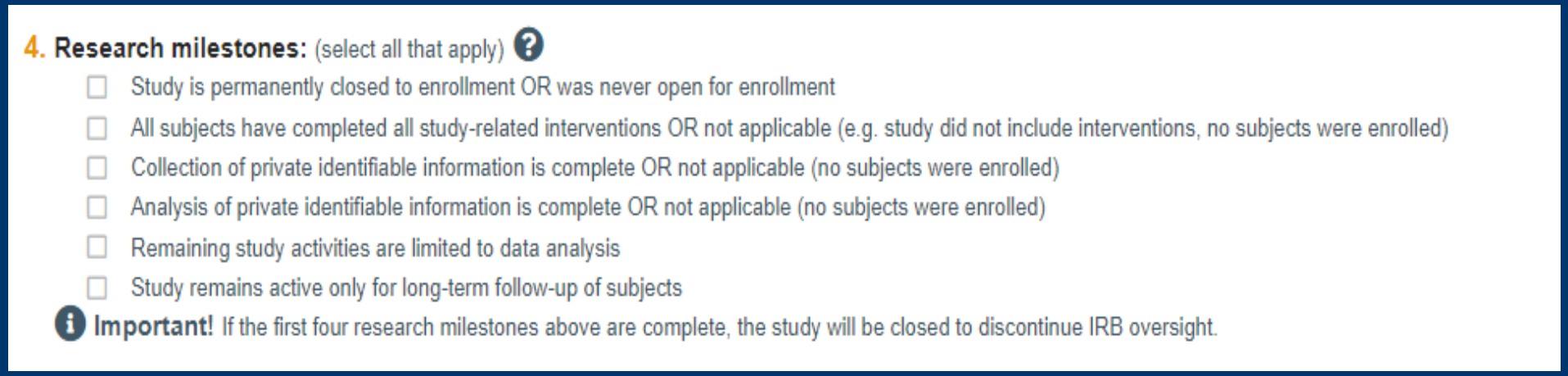
Study Closures

Research studies can be closed if **all** of the following criteria apply:

- The study is permanently closed to enrollment or was never open for enrollment;
- All subjects have completed all study-related interventions, including follow-up procedures (if applicable to the study);
- Collection of private identifiable information is complete (if any); and
- Analysis of private identifiable information is complete (if any).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- ☐ Study is permanently closed to enrollment OR was never open for enrollment
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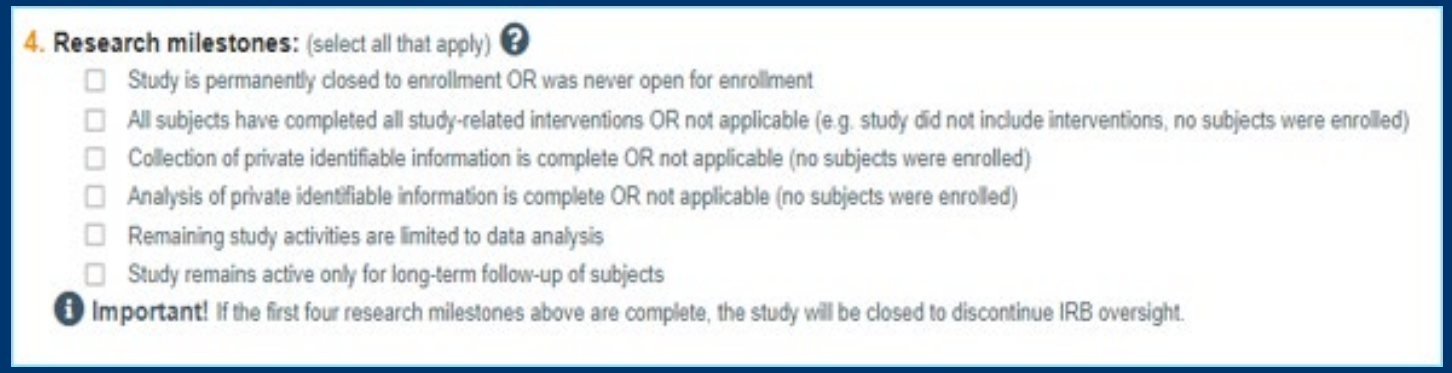
- ☐ Collection of private identifiable information is complete OR not applicable (no subjects were enrolled)
- ☐ Analysis of private identifiable information is complete OR not applicable (no subjects were enrolled)
- ☐ Remaining study activities are limited to data analysis
- ☐ Study remains active only for long-term follow-up of subjects

Important! If the first four research milestones above are complete, the study will be closed to discontinue IRB oversight.

Submitting Closures

- Create Continuing Review - if the first 4 statements are selected, you will be asked to acknowledge that the study will be closed by the IRB as it no longer requires IRB oversight



Note: once the study is closed, it cannot be reopened. It would need to be submitted as a new initial application.

Additional Resources

- **HRPP Website**

- **HRPP Policy and SOP Manual:** This document serves as the Yale HRPP Policy and Standard Operating Procedure Manual which serves as a guide for all components of the Human Research Protection Program, including the Institutional Review Board, Investigators and their Research Teams, and other members of the Research Community.

- **Investigator Manual:** The HRPP Investigator Manual provides detailed information on research preparation, IRB submission, and study team responsibilities.

- Quick Guides: step -by-step instructions for all system actions in IRES IRB Help Center.
- Researcher Guide: Submitting Continuing Review

- CR Progress Report

Additional Resources

- Training on IRES IRB System (Yale IRBs)

- Training on IRES IRB System (external IRBs)

Description: This on-line training session is designed for current and future PIs and coordinators of research studies under the purview of Yale IRBs. By the end of the session, the audience will gain an understanding of: - how to navigate the system; - how to submit protocols for initial and continuing reviews, - how to submit modifications and reportable new information, - where to find help.

Questions?

Questions? Contact HRPP@yale.edu
Yale HRPP Website

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