

# IRB Review: Continuing Review Submission Process

Dyna Wilston  
IRB Analyst

# Importance of Continuing Reviews

- Continuing Review is a federally mandated re-evaluation of an approved study that is required to be conducted at least once per year.
- Reassess risk to benefit ratio
- Ensure risk to subjects continue to be minimized
- Ensure subject safety

# Final Common Rule

- Effective Date: July 19, 2018 Enforcement Date: January 21 2019 (allowed for grace period and to implement burden reducing provisions early)
- Intended to better protect human subjects involved in research, while facilitating valuable research and reducing burden and delay for researchers.
- Relevant Burden Reducing Provision: The allowance of no continuing reviews for studies that fall under particular review categories
- [Does my human research study qualify for No Continuing Reviews?](#)
  - Non-FDA regulated, non-exempt minimal risk studies.
  - Non-FDA regulated, greater than minimal risk studies that are either limited to data analysis or limited to long-term follow up of participants.

\*Continuing Reviews may be required for non-FDA regulated, non-exempt minimal risk studies on case by case basis.

# Key IRB Considerations When Evaluating Research Undergoing Continuing Review

- Does the research study continue to meet the criteria for IRB approval?
  - [HRP-314 Criteria for Approval](#)
- Is there any new information that would alter the IRB's previously made determinations?
  - Subpart determinations, waiver determinations, drug/device determinations, risk level determinations etc.
- Is there any new information that would necessitate revisions to the protocol / informed consent document?
  - i.e. new risk information

# Questions Asked by IRB to Consider

- Enrollment & Study status
  - What is the study enrollment target and how has the study moved towards its enrollment goal? Have there been any withdrawals and if so, how many subjects (provide subject IDs) and what are the reasons? Are there any concerns?
  - Does the research milestone section of the CR application accurately reflect the current study status?
- New Information
  - Is there any new information that would 1) change the risk/benefit ratio 2) Impact the participant's willingness to continue on study.
- Changes to study over the year
  - Do the modifications made to the study over the past year collectively change the risk/benefit ratio of the study.

# Questions Asked by IRB to Consider

- Current Human Subjects Protection Training
  - Have all study team members completed the [required training](#)? Is this training documented in eIRB+. If not, has the study team provided adequate documentation?

\*Please note that the CITI Good Clinical Practice Training will not satisfy the NU IRB human subjects protection training requirement.

Training completed through an external institution should be submitted to [irbtraining@northwestern.edu](mailto:irbtraining@northwestern.edu) for verification.

- Conflict of Interest
  - Has the Conflict of Interest (COI) office completed COI Review? If so and if a conflict has been identified, has the management plan been implemented? If COI Review has not been completed, the IRB staff will notify the COI Office.
- Any Relevant Reports
  - DSMB/DMC/DSMC reports and recommendations, interim findings etc.

# Routes for Continuing Review

- Expedited IRB review:
  - Continuing Reviews for non-exempt minimal risk studies
  - Continuing Reviews for greater than minimal risk that are 1) Limited to data analysis 2) Limited to long-term follow-up or 3) There are no subjects enrolled to date.
  - Study Closure
- IRB Full Board Review:
  - Continuing Reviews for greater than minimal risk where the study is open to enrollment / undergoing study interventions.

*\*A minimal risk study may be reviewed by a Full Board as necessary*

# Minimal Risk IRB Review Process

- Typically Minimal risk studies do not require Continuing Review. Exceptions include:
  - *FDA regulated research or special IRB determinations*
- Once the CR application is submitted, it will be assigned and reviewed by an IRB Analyst in the order received. Typically the IRB analyst will re-evaluate the study and determine whether it continues to meet the criteria for approval.
- The Renewal may be delayed if the study is pending COI Review



# Greater than Minimal Risk IRB Review Process

- IRB Analyst will complete a pre-review and confirm:
  - Accurate enrollment, accurate reporting of study status, documentation for any un-checked statements in Section 3 of the CR application, study team training and COI Review.
  - If there are any updated study document, these must be uploaded into the study application via a modification. The PI must also confirm whether changes affects risk/benefit ratio, require changes to the study documents, affects alternatives available to study participants or represent new information that should be provided to participants. (for example: Investigator's Brochure or Package Insert)
- The CR is assigned to [Panel Q](#) for review.
- The panel's determination is communicated via eIRB+

# Research Milestones

## 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.

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

\* 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.

# Research Milestones

- Study is open to enrollment
  - None of the research milestone boxes should be selected
- Study is closed to enrollment and participants are on interventions
  - Select the ‘Study is closed to enrollment’ box
- Study is closed to enrollment and all participants have completed study interventions
  - Are participants in long-term follow-up? If so, select the following milestones:
    - Study is closed to enrollment
    - All participants have completed all study-related interventions
    - Study remains active only for long-term follow-up of participants
  - Is the study limited to data analysis?
    - Study is closed to enrollment
    - All participants have completed all study-related interventions
    - Collection of private identifiable information is complete
    - Remaining study activities are limited to data analysis only

# Research Milestones

- Study is completed and the study team would like to close the study:
  - Study is closed to enrollment
  - All participants have completed all study-related interventions
  - Collection of private identifiable information is complete
  - Analysis of Private Identifiable Information is complete

# Continuing Review Section 3 & 4

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 supporting document in section 4 below:

- NO subjects experienced unexpected harm (that wasn't previously reported to the IRB).
- Anticipated adverse events have NOT taken place with greater frequency or severity than expected.
- NO subjects have withdrawn from the study after initial screening procedures, if any.
- There have been NO unreported unanticipated problems involving risks to subjects or others.
- There have been NO complaints about the study.
- 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.
- There have been NO interim findings.
- There have been NO multi-center trial reports.
- There have been NO data safety monitoring reports.
- There have been NO regulatory actions that could affect safety and risk assessments (e.g. FDA drug recall).
- There has been NO other relevant information regarding this study, especially information about Biomedical risks including box warnings or ANY updated package inserts, IBs, or device reports.
- In the opinion of the Principal Investigator, the risks and potential benefits are unchanged.
- There have been NO modifications to the study that have not been submitted to or approved by the IRB.
- All problems that require prompt reporting to the IRB have been submitted.

4. **Attach supporting documents:** (For each item left unchecked, include an explanation or document. You may upload supporting documents explaining other situations even if all boxes are checked, such as a reason why there have not been any DSMB reports.) ?

Name

There are no items to display

# IRB Determinations and Definition

- Approved
  - The IRB found that the study continues to meet the criteria for approval ([45 CFR 46.111](#) and / or [21 CFR 56.111](#))
  - Approval Period is determined by the Panel
  - Approval letter may be held if study is pending COI Review
    - \*Check COI Status under the COI Tab of the study in eIRB+
- Modifications Required to Secure Approval
  - The study will continue to meet the criteria for approval, once minor stipulations have been addressed (i.e. updated training, specific lay language edits etc.)
  - Once the requested changes are completed, IRB Staff will issue the renewal letter.

# IRB Determinations and Definition

- Deferred
  - Additional information is required before the IRB can evaluate if the study continues to meet the criteria for approval (i.e. new information / reports indicate new risk information that must be included in the protocol and consent form document.)
  - A deferral response must be reviewed by the same panel
- Disapprove
  - The study did not meet the criteria for approval as set forth in the regulations and the IRB cannot describe modifications that might make the research approvable. The PI will be given an opportunity to respond to the IRB.
- Tabled
  - The Panel was unable to review the CR submission. It will be reviewed at a future meeting date.

# Lapse in IRB Approval

- No research activities can take place until the study secures IRB approval
  - except when the investigator judges it to be in the best interest of current participants to continue.
  - When the investigator makes this judgment, s/he must notify the IRB promptly. When the IRB reviews the investigator's decision, the Board will determine if it is in the best interest of participants currently enrolled in the study to continue to participate in the research. The Board will make this determination for participants either one at a time or as a group.



# Lapse in IRB Approval

- If you believe that current subjects are at risk of harm by stopping research procedures:
  - Prepare a written, coded list of subjects who will be harmed
  - Identify the research procedures that need to continue
  - Describe the reasons why these procedures need to continue.
  - Immediately provide the IRB Office with this information.

# Things to Keep In Mind

- Continuing Review submissions should be submitted no sooner than 60 days but no later than 30 days before the study's expiration date.
- The IRB does not stamp consent forms once the study is closed to enrollment. If the study team would like the consent forms stamped with the new approval period, a strong justification must be provided with the submission for consideration.
- If the protocol document indicates that there is a DSMB/DSMC/IDMC that will review the study data, please upload the reports from within the past year. If the sponsor confirms that there is no available reports, please inform us of this.
- During the review process, there may be questions that will need to be addressed. After responding to any clarification requests, **please submit the response back to the IRB**

# Things to Keep In Mind

- Minimal Risk studies that no longer require Continuing Reviews will still require any changes / updates to be reviewed and approved by the IRB before implementation. Any new information that meets the [NU IRB reporting criteria](#) must be reported via a RNI submission. Once the study is completed, a continuing review must be submitted to close the study.
- For studies that undergo full board review, the IRB reviewer may have questions prior to the panel meeting date. Keep an eye out on your submission in case the IRB Analyst communicates these questions via eIRB+. Addressing the reviewer's questions could potentially influence the Panel's determination.

# Take Away

- The takeaway from the CR form should be:
  - Be proactive
    - If you think we may ask, provide it proactively
      - No such thing as too much information
    - If you have a question, call us before you submit
  - Reread the protocol before you submit
    - Make sure that your enrollment/follow-up match what is happening in real life along with the protocol
    - DSMB/DSMC/IDMC information
      - Make sure that if you are supposed to have a report that it is submitted.
      - It's okay to say you have no received the report yet

## Contact Information

- Chicago

Biomedical Research  
Panels A, B, C, D, Q  
Arthur Rubloff Building,  
7th Floor  
750 N. Lake Shore Dr.  
Chicago, IL 60611  
Phone: (312) 503-9338  
[irb@northwestern.edu](mailto:irb@northwestern.edu)

- Evanston

Social and Behavioral  
Research  
Panel E

Chambers Hall, 2nd Floor  
600 Foster St.  
Evanston, IL 60208  
Phone: (847) 467-1723  
[sbsirb@northwestern.edu](mailto:sbsirb@northwestern.edu)

# QUESTIONS?