# Continuing Review

## Background

IRBs are required to regularly review previously-approved research to ensure human subjects protections remain appropriate over the life of a study. This process is called "continuing review." Continuing review of non-exempt research is required at intervals appropriate to the degree of risk, but not less than annually, unless the research fits within one of the exceptions described below.

When required, continuing review must be substantive and meaningful, and it must address any new information or changes that relate to risk/discomfort, benefits, safeguards for participants, and informed consent to assure that all criteria for approval specified under 45 CFR 46.111 and 21 CFR 56.111 are satisfied. Informed consent forms(s) are reviewed to assess whether the information provided in the currently approved or proposed consent form is still accurate and complete, and whether any new information that may relate to the subject's willingness to continue participation should be included in the document.

## Continuing Review Submission Requirements

When continuing review is required, investigators must submit an amendment in IRBManager three to four weeks in advance of the approval expiration date. The application will request a progress report on activities conducted for the research during the review period, including the following:

- Summary of study progress;
- Accrual of study participants;
- Enrollment status of participants including the number of withdrawals;
- Summary of any new information that may be relevant to the research or participants' willingness to stay enrolled in the study;
- Summary of any modifications implemented since last IRB review; and
- Summary of any unreported adverse events, unanticipated problems, or subject complaints.
- Verification of the continued use and accuracy of informed consent form(s) and recruitment materials.

Supplemental information or materials should be provided when applicable, including the following:

- Description of any proposed modifications;
- An updated investigator's brochure, if available, for FDA regulated studies; and/or
- Any other significant information/documents, if applicable, such as reports from a Data Safety and Monitoring Board.

In some instances, the IRB may require verification from sources other than the investigators that no material changes have occurred since the prior IRB review and approval.

# Determining Frequency of Review

The convened IRB or expedited reviewer will determine the frequency at which continuing review is required at the time of approval. Normally, research is granted approval for one year. Certain types of research may be granted three-year approval (see Extended Approval Periods below).

In determining the frequency of continuing review, the IRB or expedited reviewer will consider the following factors, as appropriate to the context of the research study:

1. The risks posed by the project and degree of uncertainty regarding the risks;
2. The vulnerability of the subject population;
3. The experience and qualifications of the investigators related to the research procedures;
4. The IRB's prior experience with the investigators, such as compliance history, prior complaints, etc.); and
5. Whether the research involves novel interventions.

# Extended Approval Periods

Some research that requires continuing review (i.e., does not fall into one of the exceptions, or the IRB determines continuing review is necessary) may be granted an extended approval period of up to three years. The longer approval period eliminates the need for principal investigators (PIs) to submit continuing review applications on an annual basis.

To be eligible for extended approval, the research must present *no more than minimal risk* to human subjects (as determined by the ISU IRB via convened or expedited review), and it *must not include any of the following:*

- Federal funding, including federal training and program project grants, federal no-cost extensions, federal flow-through funding, etc.;
- FDA regulated components (i.e., food products or additives, dietary supplements, medical devices [including activity monitors], drugs, vaccines, biologics);
- Contractual obligations or restrictions that preclude eligibility for extended approval (i.e., a non-federal sponsor or funder requires annual IRB review);
- Prisoners as subjects, unless the study is eligible for exemption or review via expedited procedures;
- Any findings of serious or continuing noncompliance related to the study or the principal investigator within the past two years;
- Any incidents that meet the definition of an unanticipated problem involving risks to subjects or others within the past two years.

*The IRB (including the IRB Chairs/Co-Chairs), at its discretion, may make exceptions to this policy and require more frequent review.*

During the approval period, principal investigators are responsible for

- reporting to the IRB any changes in funding or sponsorship that involve federal sources; and

- obtaining approval for any change(s) to the IRB-approved protocol, *prior to implementation of the change(s)*, unless the change is necessary to eliminate apparent immediate hazards to participants;
- reporting any unanticipated problems or serious adverse events.

# Expiration/Lapse in IRB Approval

Investigators are responsible for seeking continued approval of ongoing projects prior to the expiration date. They must submit complete continuing review application materials with sufficient time to allow for meaningful IRB continuing review. Courtesy reminder notices of upcoming expiration are sent to principal investigators and any supervising investigators.

**If IRB approval lapses, all human subjects research activity must stop**, unless it is determined to be in the interest of already enrolled subjects to continue participating (e.g., the research intervention may directly benefit subjects, or withholding the interventions poses risk to enrolled subjects). No new enrollment may occur after expiration of approval. Investigators may make an initial assessment of whether it is in the best interest of subjects to continue, but must submit a request for concurrence by the IRB as soon as possible (requests may be submitted via email to IRB@iastate.edu). Requests for concurrence will be shared with the IRB Co-Chair who will consult with the IRB Chair and/or Vice Chair to determine if the final determination should be made by the convened IRB.

When continuing review does not occur by the expiration date, IRB approval expires automatically. If a continuing review application has not been submitted by the expiration date, the principal investigator and supervising investigator receive notification that their project is administratively closed and all human subjects research activities must stop. If a continuing review application has been submitted, but with insufficient time for IRB review, the principal investigator and supervising investigator are notified that all human subjects research activities must stop on the expiration date and until IRB approval is re-established.

If IRB approval has been expired for an extended period of time, the investigator may be required to submit a new application for approval. The IRB ID will normally remain the same in order to have consolidated documentation of the study. The IRB or IRB Chair(s) have the discretion to require a new application form in order to ensure that adequate updated information is provided to allow the IRB to determine that all criteria for approval are satisfied.

# Exceptions to the Continuing Review Requirement

Continuing review is generally not required for research that falls into one of the three exceptions listed below. However, for any research, the IRB or IRB reviewer may determine that continuing review is required for research that would not otherwise require it. Typically, this will be to assure protection of human subjects or to address compliance concerns. In these instances, the IRB or IRB reviewer must document the rationale for requiring continuing review.

**Note**: *These exceptions **DO NOT APPLY** to FDA-regulated research (e.g., studies of medical devices, drugs, vaccines, food additives, etc.). FDA-regulated research must undergo annual continuing review until the research no longer requires IRB oversight (see Study Closure for details).*

## Exception 1

Non-exempt research approved on or after January 21, 2019 that falls into one of the following:

a. New research protocols approved via expedited review procedures; or

b. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved protocol:

   i. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

   ii. Accessing follow-up clinical data from procedures subjects would undergo as part of clinical care.

## Exception 2:

Non-exempt research approved before January 21, 2019 ("ongoing research"), but is formally transitioned *by the IRB or IRB reviewer* to comply with the 2018 Common Rule, when one of the following applies:

a. The research is approved via expedited review procedures, or

b. The research has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved protocol:

   i. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

   ii. Accessing follow-up clinical data from procedures subjects would undergo for clinical care.

**Note**: *Continuing review is required for non-exempt research approved before January 21, 2019 until it is formally transitioned to comply with the new 2018 Common Rule.* Upon submission of an application for modification or continuing review, ongoing research protocols will be assessed on a case-by-case basis by the IRB or IRB reviewer to determine whether transitioning the study to comply with the 2018 Common Rule is appropriate. Transitioning to the 2018 Common Rule may require modifications to the study (e.g., revisions to the informed consent document, etc.).

## Exception 3

Research reviewed by the convened IRB may be excluded from continuing review requirements when all of the following are true:

a. The research has no federal funding, is not regulated by the Food and Drug Administration, and is not subject to contractual obligations that require annual review;

b. The convened IRB determines that the study presents only minimal risk to participants; and

c. The convened IRB determines that continuing review is not a necessary measure to ensure protection of human subjects or determines that the study is eligible for expedited review.

# Status Check in lieu of Continuing Review

ISU is responsible for continued oversight of all human subjects research, even when formal continuing review is not required. Toward this end, the IRB has implemented a brief "status check" process to ascertain the status of each protocol and verify that no unapproved changes or unreported problems have occurred.

The status check occurs at rolling three-year intervals. The first three-year period is established at the time of initial approval. A new three-year period is established upon approval of any subsequent modifications to the project. To facilitate the rolling three-year intervals, study status verification questions are included in all modification applications.

Researchers receive notification of an upcoming status check electronically via IRBManager in advance of the three-year period end-date.

To complete the status check, researchers provide the following information via a brief form in IRBManager:

1. Whether data collection has begun, is ongoing, or has ended.
2. Verification, via simple yes/no questions, that there is/are no
    a. New information relevant to risks or that may impact participants' willingness to continue participating,
    b. Unreported serious adverse events or unanticipated problems.
    c. New federal funding sources, or
    d. Unapproved changes to the protocol.

The status-check form directs researchers to complete additional actions when needed based on responses (e.g., submission of a modification application, reporting an adverse event, etc.).

If no additional actions are needed, another three-year period is established.

Document History

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