Federal regulations 14CFR1230.109a(e), 21CFR56.109(f), and 45CFR46.109(e) require that the NASA IRB periodically review research activities at intervals appropriate to the degree of risk, but not less than once per year*, except as described in §1230.109(f) and §46.109(f).

The purpose of HRP-440 is to identify the requirements for investigators and NASA IRB for the substantive and meaningful conduct of continuing review of human subjects research in accordance with the regulations and NASA IRB’s policies and procedures.

2018 Revised Common Rule: For research reviewed and approved by Expedited Review procedures on or after January 21, 2019, unless an Expedited Review determines otherwise, continuing review of research will be replaced with the requirement of a recertification every 5 years.

*Note: Research reviewed and approved prior to January 21, 2019 will follow the Continuing Review schedule (Expiration Date) indicated on the last approval. NASA IRB will transition applicable studies to the new Continuing Review schedule, per the Revised Common Rule, and issue a study memo indicating the transition along with any additional requirements.

Specifically, this SOP will:

1.1 Describe when CR of NASA IRB Approved Research IS required.
1.2 Describe when Continuing Review (CR) of NASA IRB Approved Research is NOT required.
1.3 Establish the process for making, documenting, and communicating the determination of when a CR is, or is not, required.
1.4 The CR process begins at the time of Initial Review when the determination regarding the CR requirement is made, continues through the lifecycle of a study [because modifications, Reportable Events (a.k.a. Reports of New Information (RNI)) and the changing status of a study (reported in a CR) may affect the initial determination], and ends when the approved research is closed with NASA IRB using the designated study closure process (See HRP – 240 – SOP Study Closure).
1. **Research Subject to the 2018 requirements.** The 2018 requirements shall apply to the following research:
   a. Research initially approved by NASA IRB on or after January 21, 2019;
   b. Research for which continuing NASA IRB review is waived pursuant to Expedited Review Categories in accordance with 14CFR1230.110, 45CFR46.110 and HRP-430 – SOP Expedited Review on or after January 21, 2019;
   c. Research for which NASA IRB determines that the research is exempt on or after January 21, 2019.
2. The NASA IRB Office has the discretion to make the final determination on when a CR will go to Full Committee, Expedited Review, or if the study qualifies for no CR.
3. The NASA IRB shall conduct continuing review (CR) of research requiring review by the convened NASA IRB at intervals appropriate to the degree of risk, not less than one year*, except as described below.
   a. *NASA IRB may require more frequent review depending on the level of risk.
4. NASA IRB requires continuing review at one of two levels:
   a. **Full Committee Review:**
      i. Human subject research which does not meet the criteria for expedited review exemption from IRB review must be reviewed by the Full Committee at a convened meeting.
      ii. Non-exempt studies subject to FDA regulations. Until such time as the FDA harmonizes the Continuing Review requirements with the revised Common Rule, minimal risk research under FDA jurisdiction will require annual (at a minimum) continuing review.
      iii. Greater than minimal risk studies which initially required Full Committee review will be reviewed by the convened Board at Continuing Review unless:
         1. the study meets the requirements for expedited review under federally defined DHHS Expedited Review Categories 8b or 9 [14CFR1230.109(f)(iii); 45CFR46.109, 21CFR56.110]; or
         2. changes to the protocol are included with the CR application such that the entire study now meets the criteria for expedited review, and the Convened Board determines that future reviews of the study may be reviewed using expedited review procedures;
   b. **Expedited Review:** Research that meets the criteria for expedited Continuing review will be addressed as specified in HRP – 430 – SOP: NASA IRB Review Level - Expedited Review.
      i. In summary: An Expedited Continuing Review may be performed by the NASA IRB Chair and/or by an experienced NASA IRB member designated by the
Chair, based on the member’s area of expertise. The Expedited review should, whenever possible and not conflicted, be the NASA Center representative [e.g. Ames, Langley, KSC].

ii. Research protocols that previously met the criteria for expedited review will require Full Committee review if changes to the protocol are proposed which: (1) present more than minimal risk to human subjects or (2) involve procedures which do not meet the criteria for expedited review.

c. NASA IRB may require renewal for research on a case-by-case basis as it deems appropriate. NASA IRB may determine that the requirement should be maintained for any of the following reasons:
   i. The study involves additional regulatory oversight (e.g. a conflict of interest management plan)
   ii. The study will be conducted internationally or at non-NASA facilities and the NASA IRB determines an annual (or more frequent) review is appropriate
   iii. A modification or incident report (RNI) of a Reportable Event reveals new information that requires additional oversight
   iv. The investigator, research personnel, and/or study site has previous serious noncompliance or a pattern of continuing noncompliance that is of concern
   v. Research involves an astronaut and the NASA IRB or IRB Chair determines the research requires continuing oversight
   vi. If Continuing Review is required for research that otherwise would not qualify, the NASA IRB must document the rationale for such requirements and communicate the requirement to the investigator in the NASA IRB determination letter.

5. Unless the NASA IRB determines otherwise, NASA IRB does **NOT require continuing review** of approved research for studies that meet the following criteria:
   a. Research granted Exemption, including exempt research requiring limited IRB review procedures [See NASA SOP 420]
   b. Research that is not subject to FDA regulations and is eligible for Expedited Review in accordance with NASA 14CFR1230.110, 45CFR46.110, and HRP-430-SOP: NASA IRB Review Level – Expedited Review.
   c. Research that is not subject to FDA regulations and requires review by the convened IRB, but has progressed to the point that involves only one or both of the following, which are part of the IRB approved study:
      i. Remaining study activities are limited to data analysis, including analysis of identifiable private information or identifiable bio-specimens (Expedited Category 8c; 14CFR1230.109(f)(iii)(A); 45CFR46.109(f)(iii)(A)); and/or
      ii. Remaining study activities are limited to long-term follow-up of participants where the research is accessing follow-up clinical data only from procedures the participants would undergo as part of routine clinical care and any research interactions involve no more than minimal risk to participants (e.g. quality of life surveys) (Expedited Category 8a; 14CFR1230.109(f)(iii)(B); 45CFR46.109(f)(iii)(B)).
Responsibilities

1. PI Responsibilities:
   a. For multi-year research, the PI is responsible for submitting a continuing review application through eIRB with sufficient time prior to the expiration of the current IRB approval so that there will be no lapse in the study approval.
      i. The PI should allow at least one month for a full committee continuing review and two weeks for an expedited CR (should there be instances of CR for Expedited research).
   b. The eIRB system will direct the PI through the submission process.
      i. The eIRB will prompt the PI for information regarding the status or progress of the research during the last approval period. The information will include:
         1. A summary of the research providing sufficient information to address the approval criteria at 14 CFR 1230.110;45CFR46.111 and 21CFR46.110.
         2. A status report on the progress of the research, including significant findings
         3. The number of participants enrolled and withdrawn and the reason for withdrawals
         4. A description of any Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), Adverse Events and subject complaints about the research
         5. Any change in research team Conflicts of Interest
         6. A summary of major amendments to the research
         7. Relevant recent literature
         8. References to all publications/abstracts/posters
         9. Interim findings, relevant multi-center trial reports, if applicable, and an assessment by the researcher of the current risk-potential benefit based on study results to date.
   c. Amendments to the protocol or study documents may be submitted at the same time as the continuing review.
   d. PIs of projects that require CR review will be notified on the Approval Letter of the time frame for CR. As a courtesy, the eIRB will send out reminders at 90, 60, and 30 days before the expiration date of the protocol.
   e. PIs of projects that are eligible for no continuing review will be required to submit any changes to the IRB-approved study to eIRB. This process will be applicable to research approved for the first time by Expedited Review procedures and to greater than minimal risk research that has reached certain milestones on or after January 21, 2019.
      i. Reportable Events: UPIRSOs, AEs, etc.
      ii. Changes to the research, including personnel
      iii. Protocol Amendments
      iv. Recruitment materials
v. Current ethics certifications
vi. New COIs
vii. Completion of the research through study closure

Procedures

1. Making the Determination:
   a. At least 1 week prior to the convened meeting, each NASA IRB member will be provided with detailed continuing review materials sufficient to conduct substantive and meaningful reviews.
      i. Materials (via access to eIRB) will include the currently approved informed consent document, a protocol documents, and the Continuing Review Application.
   b. For studies where CR is required, the convened NASA IRB or designated reviewer and the rationale determines the IRB approval period that dictates when the first CR is required.
      i. Criteria for Continuing Review of Research are set forth by NASA 14CFR1230.111 and shall provide the framework for NASA IRBs evaluation of research. In order to re-approved the research at CR, the NASA IRB must determine that all of the requirements at 14CFR1230.111 and 45CFR46.111 are met.
      ii. The determination of the continuing review period can only be made after the research study has proceeded through its appropriate review/approval procedure (e.g. NASA IRB, Expedited Review, etc.).
      iii. CR will be conducted by the convened NASA IRB unless the research falls into one or more of the categories appropriate for expedited review.
         1. The primary reviewer should, whenever possible and not conflicted, be the NASA Center representative [e.g. Ames, Langley, KSC].
      iv. When appropriate, CR will continue until the study is complete.
   c. For studies where no CR is required, the convened IRB or designated reviewer will determine that the criteria are met for the designation of no CR. The removal of the requirements of an expiration date and CR for non-exempt minimal risk studies will be documented
      i. In the reviewer note in eIRB when the study is either initially approved or when an existing study is transitioned to the no CR status.
      ii. In the Approval letter.
         1. There will be an approval date but no expiration date attached to studies and the respective documents with no CR.
   d. For studies that are no greater than minimal risk but do not meet criteria for no CR requirement, the CR requirement remains and the designated reviewer determines the IRB approval period which dictates when the first CR is required.
2. Documentation:
   a. If CR is required
      i. The NASA IRB Office or reviewer must document in the NASA IRB record (eIRB and
         on the initial Approval letter) the rationale for the CR and the approval period for
         which CR is required to secure approval again; including identification of research
         that warrants review more often than annually and the basis for that
         determination.
   b. If CR is not required:
      i. When no CR is required, the NASA IRB shall remind PIs on an annual basis – via an
         automated email originating in eIRB – that the study remains open and under
         NASA IRB oversight, and that the PI must report changes to the NASA IRB that may
         affect CR requirements (changes to the IRB-approved study, Reportable events,
         etc.).

3. Modifications:
   a. If the modification changes the determination of a currently approved study or a
      study that previously had the CR removed, a new determination will be made by
      the NASA IRB or designated reviewer.
      i. The new determination and rationale for resuming CR will be
         documented in the eIRB by the Designated Reviewer and in the Approval
         letter to the PI.

4. CR for existing Approved studies:
   a. At the time of CR, a determination regarding whether future CRs are needed will
      be made. For minimal risk non-exempt studies, the presumption is no CR.
      i. If a study is eligible for no CR and the NASA IRB or designated reviewer
         determines a CR will continue to be needed, the rationale must be
         included in the IRB record (eIRB and in the Approval letter to the PI).

5. Reportable Events (or RNIs):
   a. If a report of new information changes the determination regarding the CR
      requirement, a new determination will be made by the NASA IRB or designated
      reviewer.
      i. Upon submission of a new Reportable Event, the NASA IRB Office will
         review the protocol for CR status and assess whether a change is
         warranted. If the NASA IRB Chair or designated reviewer notes that CR is
         required for a study that previously had the CR removed, a new
         determination will be made by the convened NASA IRB or the NASA IRB
         Chair/designee, whichever is appropriate (based on the risk category and
         qualifications for expedited review).
      ii. The rationale for reinstating an expiration date should be documented in
          the new CR.
      iii. The new expiration date will be established at the time of the CR and
           should reflect the time approval period determined by the IRB or
           designated reviewer.

6. Communication to the PI:
a. The NASA IRB Office will communicate to the PI the determination regarding if a CR is required in the Approval/Determination Letter (Initial Review, Modification, CR, or RNI).
   i. If a CR is required, the NASA IRB Approval letter will contain the study’s approval period and the IRB’s expectation for submission for the CR prior to the end of the NASA IRB approval period.
   ii. The rationale for maintaining the CR requirement will be communicated to the PI in the approval letter.
   iii. For studies which no longer need CR, the IRB approval letter will confirm that the CR is not required, the study will not expire, and that modifications, reports of new information, and study closure submissions are still required and the responsibility of the PI.

7. Lapses in Approval:
   a. If a NASA IRB approval expires, All Research Activities Involving Human Subjects Must Cease (See HRP – 450 – SOP).
      i. Research activities include participant enrollment, recruitment, informed consent, data collection, data analysis and storage of identifiable data, and sharing of identifiable data. The only exception to this requirement is for activities that are needed for participant safety. No new subjects may be enrolled.
      ii. In cases where research activities must continue for participant safety, the PI must provide the rationale for continuation with their request to continue to the NASA IRB. The NASA IRB determines on a case-by-case basis whether treatment may continue for currently enrolled subjects. The NASA IRB will notify the investigator if it is permissible under federal guidelines to continue limited research activities.

Definitions

Full Committee Review: reviews conducted at convened meetings at which IRB membership requirements [14CFR1230.107; 45CFR46.107] are met and a quorum consisting of the majority of the members of the IRB is present.

Minimal Risk [14CFR1230.102(j); 45CFR46.102(j)]: the probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine or psychological examinations or tests.

FDA Regulated: The US Food and Drug Administration (FDA) regulates clinical studies conducted on drugs, biologics, devices, diagnostics, and in some cases dietary supplements and food additives. All such research studies must be conducted in accordance with FDA requirements for the protection of human subjects and IRBs, regardless of funding (21 CFR Parts 50 and 56). NOTE: Until such time as the FDA harmonizes its Continuing Review requirements with the revised Common Rule, minimal risk research regulated by the FDA will require annual continuing review.
When FDA regulated test articles are used in research conducted under the purview of NASA IRB oversight, more than one set of regulations may apply. For example, clinical trials involving FDA regulated test articles that are supported by the DHHS fall under the jurisdiction of both the FDA and DHHS Office for Human Research Protections (OHRP). Such trials must comply with the FDA and the DHHS human participant regulations. Where regulations differ, the NASA IRB will apply the stricter regulation.

References

NASA
1. 14 CFR 1230.109, 14CFR 1230.110
2. NPR 7100.1B

DHHS Regulations
3. IRB review of research: 45 CFR 46.109
4. Criteria for IRB Approval of Research: 45 CFR 46.111

FDA Regulations and Guidance
6. FDA 21CFR 50 and 56

AAHRPP Elements: I.3

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