Common Issues with Human Subjects Research (HSR) Prior Approval (PA) Submissions

PURPOSE

Hubs, the CTSA Program Steering Committee, and NCATS all agree that the process of obtaining prior approval for Pilot and KL2 projects involving HSR can be frustrating if not onerous. The new requirement to use to the Human Subjects System (HSS) has led to additional challenges for all of us. This document was developed in response to a call by the Steering Committee for NCATS to develop a list of common issues with materials submitted for HSRPA.

Based on the NCATS experience of processing of hundreds of prior approval requests each year, the most common issues with CTSA Program requests fall into 4 main categories:

1) Inaccurate/incomplete HSS fields;
2) Incomplete submissions (missing, inaccurate, or inconsistent documents; inadequate information);
3) Overall quality of the materials; and
4) Adherence to NIH and NCATS policies.

Below are detailed descriptions of the most common issues encountered, and suggested approaches for decreasing such issues. We plan to make revisions to the NCATS HSRPA Addendum for additional clarification.

SUGGESTED APPROACHES

Approaches for developing successful submissions and greatly reducing the number of errors in Pilot Project and KL2 programs submissions are described below; these are practices used by several hubs.

1. If your site does not already do so, consider designating a POC to serve as a quality control specialist for all types of prior approval requests. This individual can enhance the process by:
    - Becoming a resource for relevant policies, procedures, and use of the HSS
    - Reviewing documents prior to submission to ensure the following:
        - Special attention that Section 1 of the HSS is completed correctly
        - Required documents are present, accurate, and consistent
2. If you receive a request for clarification, revision, or inclusion of a missing document into the HSS, provide to the Grants Management Specialist and Program Officer a Summary Change Table that indicates all submitted changes/amendments (i.e., what the changes are and where they are located). This will facilitate expedited reviews and decisions by NCATS.
3. Consider providing training to Pilot Project and KL2 Scholars on how to complete and compile submissions.
4. Applicants and their supervisors/mentors should ensure that submitted projects are clear, well-written, and scientifically sound, including study designs with adequate sample size and analysis plans, as well as provisions for patient protection such as DSMBs when appropriate. Additional involvement and input from mentors are expected to facilitate timely reviews and decisions.

DETAILED COMMON ISSUES

Incomplete Submissions

- Most commonly missing documents
    a. NCATS Addendum
    b. Assent documents
    c. IRB approval or institutional exemption determination
    d. Determination by the institution (or IRB) that the study is exempt; an explicit statement from the IRB regarding risk level can expedite NCATS' review

- Insufficient information provided

    a. NCATS HSRPA Addendum Section II *(note, the NCATS HSRPA Addendum Section II Q1 will be split into two portions, for clarity)*
        - Incomplete information regarding which specific research activities or staff being requested for NCATS funding
        - Budget justification: complete list of supplies, services, and personnel costs associated with the activities for which NCATS' funds are requested (Per NIH policy, generally only expenses greater than $1,000 require an itemized breakdown); ensure budget request does not exceed the allowable amount for KL2 projects
        - No budget justification explaining how requested funds will be used to address the research question/hypothesis; if there is scientific overlap with the parent study
        - Insufficient information provided to clarify the relationship between pilot and parent studies (e.g., often unclear whether request is to enroll additional subjects or perform additional experiments)
        - Incomplete and inconsistent details for key personnel or missing biosketches for the Study PI and for each Key Personnel involved in the proposed HSR study (those not originally provided in the CTSA application).

    b. Clinical Trial Information
        - Study is a clinical trial but HSS Section 4 is missing
        - Consent Form: incomplete or missing sections; inappropriate description of the risks
        - Human Subjects Protections Training: expired certificates
        - Safety Monitoring
            – Insufficient details to assess whether proposed level is adequate for the trial
            – Data Safety and Monitoring Plan: lack details; inadequate description of conditions for Adverse Event Reporting
            – Data and Safety Monitoring Board information is insufficient, e.g., composition and frequency of meetings are not described
        - Missing ClinicalTrials.gov registry number (NCT #)

Inaccurate Documents

- Inconsistencies between the protocol and IRB approval (e.g., study title)
- Sample size: inconsistent among the IRB approval, protocol, Inclusion Enrollment Report, and consent
- IRB expiration occurring within (or close to) the prior approval review process
- Discrepancy between the submission project description and the IRB approval letter (e.g., submission states "Exempt" but the IRB determination does not specify an exemption and/or no institutional exemption document is provided)
- Inaccurate assessment of HSS project (HSS Clinical Trial Questionnaire – Question 1.4)
- Enrollment information issues: cumulative enrollment vastly exceeds planned enrollment; cumulative enrollment is missing; planned enrollment total (sample size enrollment number) that varies throughout the application; instructions on how and when to complete the Planned vs Cumulative Tables are not followed appropriately.

Possible Confusion regarding Instructions and Tracking Requirements

- Human Subjects coding of applications and grants (see https://ncats.nih.gov/ctsa/funding/par-information). Awardees will not be able to add new studies to the HSS if a grant indicates "NO" for human subjects research; contact your Program Director if the human subjects research code needs to be changed.
    a. Inclusion should be "yes" on UL1s
    b. Inclusion should be "no" on KL2s and TL1s
- Confusion between Direct Funding, Voluntary Committed Cost Share, and Voluntary Uncommitted Cost Share, and the reporting requirements of each (Solution see: Post-Award Grant Actions: Prior Approval and Reporting of Research with Human Subjects and/or Vertebrate Animals)
- Period of Performance
    a. Pilot projects typically extend ≤12 months; the request should include a plan for managing any pilot project that will span more than one budget period, as funds generally cannot be carried over from the prior budget period.
    b. The pilot project activity may cross over budget periods. However, per NIH Grants Policy and the Notice of Award, the institution CANNOT carry over funds from one budget period to another without NIH prior approval. Repeated prior approval requests to transfer funds from one budget period to another for the same/similar program costs, e.g., a hub's Pilot Project Program entity, will be denied. Pilot project submissions that span beyond a budget period should include a plan for how the funding will be managed.

Overall Quality of Submission Materials

- Adobe PDF files that are unopenable
- Documents that appear to be in draft form (e.g., in tracked changes format)

Subsequent Reporting

- Pilots that received prior approval during the last budget period are not included in the RPPR
- Progress reported in the RPPR goes beyond the scope of the granted pilot project prior approval request
- Pilot projects are reported in the RPPR that did not receive, but require, NIH prior approval

Resources

NCATS Human Subjects Research Prior Approval (HSRPA) Requests
https://ctsa.ncats.nih.gov/governance-guidelines/guidelines/prior-approval-of-planned-research-involving-human-subjects/ (*See Section VIII. Resources in the document "NCATS Human Subjects Prior Approval Addendum and Instructions for PIs and SOs – New 02.05.2019")

Post-Award Grant Actions: Prior Approval and Reporting of Research with Human Subjects and/or Vertebrate Animals
https://ncats.nih.gov/ctsa/funding/prior-approval-paga

Further Assistance

For assistance with the NCATS Addendum or requested content, please contact NCATSDOPAinquiry@mail.nih.gov

For assistance with the eRA HSS, please contact the eRA Service Desk
https://grants.nih.gov/support/index.html
Toll-free: 1-866-504-9552 (Press 1 for eRA Commons or ASSIST)
Phone: 301-402-7469 (Press 1 for eRA Commons or ASSIST)
Hours: Mon-Fri, 7 a.m. to 8 p.m. ET (closed on federal holidays)