Guidance on Changes That Involve Human Subjects in Active Awards and That Will Require Prior NIH Approval

Notice Number: NOT-OD-12-129

Key Dates

Release Date: August 2, 2012

Related Notices

NOT-OD-12-130

Issued by

National Institutes of Health (NIH)

Purpose

This notice provides detailed guidance on the types of changes in human subjects research awards that will require prior NIH approval and provides information on the process for submission of such requests.

Background

Current NIH policy requires prior approval from the NIH awarding Institute/Center (IC) for a change in scope (NIH Grants Policy Statement (GPS) 8.1.2.5). One of the potential indicators of a change in scope is a change from the approved involvement of human subjects. The guidance in this document further characterizes such changes. This will result in a more consistent approach across the NIH to the management of on-going awards that involve human subjects and will further NIH’s goal of supporting projects with a high degree of scientific merit, program relevance, and appropriate protections for human participants.

Description of Changes from the Approved Involvement of Human Subjects Requiring Prior NIH Approval:

In general, any change in research procedures in an active award that would result in an increased risk to human subjects will require prior NIH approval before implementation. This would include the following:

1. An addition or change to the study design/protocol that would result in the need to change the overall human subjects designation or clinical trial designation of the grant:
   - From non-human subjects research to human subjects research (exempt or non-exempt):
   - From exempt to non-exempt human subjects research; or
   - From “No Clinical Trial” to “Includes a Clinical Trial”; see NIH definition of “clinical trial”

2. The new inclusion of subject populations that are covered by additional regulatory protections under 45 CFR 46 subparts B, C or D (pregnant women, human fetuses, and neonates; prisoners; or children)

3. Any change to the study protocol that would result in an overall increase in risk level for subjects, including physical, psychological, financial, legal or other risks. This could include the addition of a new study population that would be at higher risk from existing research procedures, the addition of new study procedures that are greater than minimal risk, any modification of existing study procedures that would increase overall risk, or the addition of a new clinical study or a new clinical trial intervention arm not originally proposed that is greater than minimal risk.

4. New information that comes to light after a study is underway which indicates a higher level of risk to participants than previously recognized for a study intervention, procedure, or pharmacological treatment.

Process for Submitting Prior Approval Requests:

Individuals designated as an award’s Program Director/Principal Investigator (PD/PI) are strongly encouraged to discuss any potential changes in human subjects research under consideration with the Grants Management Officer (GMO) and Program Official (PO) at the funding IC to determine if the proposed changes will require prior approval as a change from the approved involvement of human subjects.
A request for an increase in support in a current budget period for activities which the IC determines to be a clear expansion of the project’s approved scope must be submitted as a competing revision type 3 application, in accordance with IC-specific submission requirements, and must undergo formal peer review. Determining if a proposed change represents an expansion of scope is a scientific judgment that will be made by the PO in light of the aims, goals, and methodologies of the existing award.

Prior approval requests must be submitted in writing (including submission by e-mail) by the Authorized Organization Representative (AOR) to the GMO of the funding IC no later than 30 days before the proposed change, in accord with the GPS, 8.1.3. NOTE: Although proposed changes may be addressed in the annual progress report, the formal prior approval request must be submitted as a separate request to the funding IC, prior to initiating the new human subjects activities.

**Required Documentation in the Prior Approval Request:**

- If the request is submitted by e-mail, include the complete grant number in the subject line. The e-mail request must also include the name of the grantee, the name of the initiating PD/PI, the PD(s)/PI(s) telephone number, fax number, and email address, and comparable identifying information for the AOR.
- Documentation of the proposed changes (such as a new/revised protocol) as required by the funding IC.
- New or revised human subjects section as described in Part II of NIH competing application instructions that clearly describes risk, protections, benefits and importance of the knowledge to be gained by the revised or new activities.
- New or revised Inclusion Plans for Women, Minorities, and Children, if applicable.
- New or revised Targeted Enrollment Table, if applicable.
- New or revised Data and Safety Monitoring Plan (DSMP) and Board (DSMB), if applicable.
- Certification that Key Personnel have taken appropriate education in protection of human subjects, if not provided previously.
- Certification of Federal-wide Assurance (FWA) (if not previously provided) and IRB approval of the IC approved plans will be required before the newly proposed human subjects activities can begin.

**Inquiries**

Questions about specific awards should be directed to the funding IC. Inquiries about the general policies in this notice may be directed to:

Office of Extramural Programs  
Office of Extramural Research  
National Institutes of Health  
6705 Rockledge Dr., Suite 300  
Email: OEPmailbox@mail.nih.gov

**Weekly TOC for this Announcement**

NIH Funding Opportunities and Notices

Note: For help accessing PDF, RTF, MS Word, Excel, PowerPoint, Audio or Video files, see Help Downloading Files.
NOT-OD-12-129: Guidance on Changes That Involve Human Subjects in Active Awards and That Will Require Prior NIH Approval