Policy on Amendments

Effective date: 9/20/2019

I. Background
Once a study receives IRB approval or is determined exempt from IRB review, the study must be carried out as described in the application. Any changes must be submitted for IRB review and receive approval before being implemented, except for correcting typographical errors (not considered changes to the protocol) or when changes are “necessary to eliminate immediate hazards to the subject” per 45 CFR 46.103(b)(4). This policy outlines the request and review procedure for amending non-exempt research protocols. Please see Policy on Exemption Review for how to amend exempt studies.

II. Definitions
a. Amendments/modifications/changes: Any change made to an approved protocol other than correcting a typographical error. This may include (but is not limited to) changes in recruitment procedures, study population, study sites, data collection instruments, funding, personnel, informed consent procedures, etc.
b. Minor changes: Changes that do not significantly alter research aims or design and does not significantly affect the risk benefit assessment and therefore can be reviewed under expedited procedures (e.g., adding/changing personnel other than PI, adding or revising recruitment materials, adding a minimal risk procedure, etc.).

III. Amendment Request Requirements and Procedures
a. Researchers: The Principal Investigator (PI) is required to submit a Modification/Amendment Request Form outlining each proposed change, along with a modified protocol and/or any applicable supplemental materials (e.g., recruitment materials, consent documents, study instruments, data collection forms/instruments, reliance request forms, etc.). ORCA asks PIs to highlight all changes within the protocol and supplemental materials. Changes must be approved before being implemented except when changes are “necessary to eliminate immediate hazards to the subject.” “Hazards to the subject” is interpreted to mean that the health or livelihood of one or more subjects is in jeopardy and, in such cases, the situation must be reported to the IRB in an Event Report. The researcher must respond to any comments/requests from either ORCA administrators or IRB members before the request moves forward to the next action.
b. ORCA: ORCA does an administrative review of modification requests in the order of receipt and sends comments/questions to researchers if needed. Once researchers respond, proposed modifications to minimal risk research
that is eligible for Expedited Review are forwarded to the Chair or their designee. For proposed modifications to greater than minimal risk research that are not considered “minor,” the study must be reviewed at a convened meeting of the full board.

IV. IRB Review and Actions
The IRB will review the amendment to ensure that the protocol, as amended, meets the criteria for IRB approval outlined in 45 CFR 46 of the HHS Common Rule.

a. Expedited review: The IRB Chair or an experienced member designated by the Chair conducts the review. The expedited reviewer can approve it, require modifications, or refer it to the full Board.

b. Full committee review: A quorum of the IRB meets to discuss the protocol and reviews it based on the criteria for IRB approval. The Board can approve it, require modifications if the comments are specific and direct, defer it if they cannot determine whether criteria for approval are met based on the information provided, or disapprove the research if risks outweigh benefits.

c. The IRB will determine whether the currently approved informed consent document is adequate in light of the proposed amendment(s).

V. Criteria for Approval
In order to approve a proposed amendment,

a. The IRB determines that the criteria for IRB approval in 45 CFR 46 are met.

b. The IRB determines whether the amendment increases risks to subjects and, if so, that sufficient safeguards are in place to minimize risks.

c. The IRB determines that the informed consent document reflects changes to any required elements of consent or to anything that could affect subjects’ willingness to participate.

d. The IRB is guided by the three ethical principles described in the Belmont Report of the National Commission for the Protection of Human Subjects:

Respect for persons—researchers should obtain the informed consent of all human subjects invited to participate in research. In order to respect subject autonomy, the consent process should include giving subjects full and comprehensible information about the research and provide clear assurances of the subjects' voluntary participation.

Beneficence—the risk of harm to subjects should be the least possible, and that the sum of benefits to the subjects and the importance of the knowledge to be gained should so outweigh the remaining risk of harm to the subject as to warrant a decision to allow this risk.
Justice—the selection of human subjects should be fair and equitable and that the risks and benefits of research should be distributed among subjects in a fair and equitable manner, with particular concern for subjects whose personal status or condition as children, prisoners, patients, impoverished persons places them in a vulnerable or dependent status.

VI. Documentation and Notification of Determination

a. Modifications required: If either a designated reviewer or the full board requires modifications before the proposed amendment can be approved, ORCA will notify the researcher and provide them with the issues that must be addressed. For amendments that are eligible for expedited review, the required modifications are documented in an email to the researcher. For amendments requiring full board review, the required modifications are documented in a letter from the IRB Chair and in the IRB meeting minutes. Researchers must respond in writing. Regardless of whether the initial application required full board review, the researcher’s response to required modifications may be reviewed by an experienced IRB reviewer designated by the Chair (expedited procedures). The reviewer may determine that the IRB’s issues are satisfied or else request further modifications from the researcher, in which case ORCA will notify the researcher and provide them with the remaining issues in an email. Again, the researchers must respond in writing and the review cycle continues until all IRB issues are resolved.

b. Deferral: If the full Board votes to defer a proposed amendment, ORCA will notify the researcher and provide them with the issues that must be addressed. The IRB’s issues are documented in a letter from the IRB Chair and in the IRB meeting minutes. Researchers must respond in writing. The researcher’s response to a deferral must be reviewed by the full IRB at a convened meeting.

c. Approval: Once approved, ORCA will notify the researcher of the approval, including whether any consent waivers are granted and whether the inclusion of any special populations is approved, the effective date, and the approval period (see Policy on Continuing Review). The approval is documented in a letter from the IRB Chair and, if applicable, in the IRB meeting minutes. For amendments requiring full Board review, controverted issues and their resolution will be documented in the meeting minutes.

d. Disapproval: If the IRB disapproves the amendment, ORCA notifies the researcher and provides them with the IRB’s reasons for the disapproval. The reasons for the disapproval are documented in a letter from the IRB Chair and in the IRB meeting minutes. The researcher may submit a different amendment based on the IRB’s feedback, choose not to pursue any
amendment, or appeal the IRB’s determination in writing. Researcher appeals must be reviewed at a convened meeting of the full IRB.

VII. References
a. 45 CFR 46
b. Stanford University HRPP Policy Manual