Changes to Eliminate Immediate Hazards to Subjects Guidance

Version Date: June 1, 2007  Revised: January 1, 2013

Guidelines for implementation of changes of protocol for safety reasons prior to IRB approval

Per institutional policy and the Federal regulations governing human subjects research, any change in an approved human subjects research protocol must be reviewed and approved by a UW-Madison IRB before the change can be implemented by the investigator, except under certain circumstances. The Health Sciences IRBs Office is available for consultation (608-262-2362) if you have any questions about whether the implementation of a change prior to IRB approval is appropriate.

Changes to eliminate an apparent immediate hazard to subjects

Changes in approved research initiated without prior IRB review and approval to eliminate apparent immediate hazards are allowed both under both the Common Rule and FDA regulations ONLY to eliminate apparent immediate hazards to subjects. These changes are expected to be rare. Any such changes made must be reported to the applicable IRB within fourteen (14) business days of implementation as both an unanticipated problem and a change of protocol.

- Using the Change of Protocol form. In the unanticipated problem report, the investigator must give an overview of the situation including what changes were implemented prior to IRB approval and why these changes needed implementation prior to IRB approval to prevent immediate hazard to study subjects.
- In the change of protocol form the investigator needs to specifically explain whether any changes to the protocol and study documents (e.g., or informed consent documents) that are required. Changes should not be made to avoid the IRB review process or merely for the sake of convenience.

The IRB then will review the unanticipated problem report change of protocol to determine if that: (1) the action taken by the investigator was necessary to eliminate an apparent immediate hazard to the subject(s). The Change of Protocol will be reviewed to determine if the changes implemented are), and (2) the change of protocol is consistent with ensuring the subjects' continued welfare.

If a change of protocol is implemented prior to IRB approval and the IRB determines that the change was not necessary to eliminate apparent immediate hazards to a subject, the investigator’s action may be considered to represent noncompliance with the regulations governing human subjects research and result in additional action by the IRB.

Other Changes Needed for Subject Safety Reasons That Do Not Present an Apparent Immediate Hazard to Subjects
Study sponsors may require Changes made for subject safety reasons but no apparent immediate hazard

Situations arise when changes in study procedures in response to are required by sponsors, which are often based on new safety information. In many cases, however, the changes are not required to eliminate an apparent immediate hazard to subjects. Prior IRB review and approval of these types of changes is required before any changes in study procedures can be implemented. Investigators who required... In the case of clinical research involving drugs, biologics, or devices, there will be instances when the investigator, in his or her role as a treating physician, may think a change to study procedures must be made should be implemented prior to IRB review to ensure the well-being of the subject-patient even though the an immediate hazard is not present. In these situations a change of protocol still should be submitted to the IRB for review as soon as possible. If any patient-subjects are treated under the revised protocol procedures prior to IRB approval of them, the principal investigator for that protocol should inform the IRB via a formal letter of this protocol deviation within fourteen (14) business days of the occurrence. Changes should not be made to address subject safety issues should contactavoid the IRB review process or merely for the sake of convenience.

The issue of informed consent and changes implemented prior to IRB approval

If a change of protocol is implemented prior to IRB approval, note that the IRB cannot approve a revised consent form or process that results in obtaining retroactive consent from subjects to undergo revised study procedures.

Protocols exceptions and deviations

Investigators frequently enroll subjects, usually with permission from the study sponsor, who may deviate from the eligibility criteria in a minor way or who may have a study visit outside the timeframe required by the study. Consequently, the Health Sciences IRB determined that if the investigator and sponsor (when applicable) determine that the protocol "exception" or "deviation" does not present a significant safety risk to the subject or potential subject then the "exception" or "deviation" is not required to be reported to the Health Sciences IRB until the time of continuing review. See the Health Sciences IRBs office for Protocol Exception and Deviations guidance before making any changes without IRB approval.

WHEN IN DOUBT, CALL YOUR IRB OFFICE