**Regulatory Issues Related to IRB Review – IRB Member Retreat**

**May 15, 2017**

**Links:**

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM470154.pdf>

<https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/continuingreview2010.pdf>

<https://www.hhs.gov/ohrp/compliance-and-reporting/types-of-determinations/index.html>

**Inadequate Continuing Review**

Continuing review of research must be substantive and meaningful. HHS regulations at 45 CFR 46.111 set forth the criteria that must be satisfied in order for the IRB to approve research. The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review. The procedures for continuing review by the convened IRB may include a primary reviewer system. In conducting continuing review of research not eligible for expedited review, **all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including:**

1. the number of subjects accrued;
2. a summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review;
3. a summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review;
4. any relevant multi-center trial reports;
5. any other relevant information, especially information about risks associated with the research; and
6. a copy of the current informed consent document and any newly proposed consent document.

At least one member of the IRB (i.e., a primary reviewer) also should receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member also should have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting. The minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol.

**Documentation of Required IRB Findings in IRB Minutes**

HHS regulations at 45 CFR 46.116(d) require that the IRB make and document four findings when approving a consent procedure which does not include, or which alters, some or all of the required elements of informed consent or when waiving the requirement to obtain informed consent. OHRP recommends that when approving such a waiver for research reviewed by the convened IRB, these findings be documented in the minutes of the IRB meeting, including protocol-specific information justifying each IRB finding. Similarly, where HHS regulations require specific findings on the part of the IRB, such as

(a) approving a procedure which waives the requirement for obtaining a signed consent form [see 45 CFR 46.117(c)];

(b) approving research involving pregnant women, human fetuses, or neonates (see 45 CFR 46.204-207);

(c) approving research involving prisoners (see 45 CFR 46.305-306); or

(d) approving research involving children (see 45 CFR 46.404-407), the IRB should document such findings.

OHRP recommends that for research approved by the convened IRB, all required findings be fully documented in the minutes of the IRB meeting, including protocol-specific information justifying each IRB finding.

For research reviewed under an expedited review procedure, these findings should be documented by the IRB Chairperson or other designated reviewer elsewhere in the IRB record (e.g., approval letters).

**FDA-Regulated Medical Device Studies**

For FDA-regulated research involving an investigational medical device, sponsors are responsible for determining whether the device study is significant risk (SR) or nonsignificant risk (NSR) and presenting this information to the IRB. The IRB must then make its own SR or NSR determination about the study, and either agree or disagree with the sponsor, by reviewing relevant information provided by the sponsor at a convened meeting (21 CFR 56.108(a)(1); 21 CFR 812.66). FDA considers this determination to be part of the IRB’s responsibilities for conducting its initial review of a study. FDA recommends that the IRB document each SR/NSR determination in the minutes

**Controverted Issues and Their Resolution**

The minutes of IRB meetings must be in sufficient detail to show a written summary of the discussion of controverted issues and their resolution (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). Many IRBs struggle with the amount of detail that is necessary to satisfy this regulatory requirement.

Controverted issues are those that cause controversy and dispute among the IRB membership during a convened meeting. Controverted issues that arise during the convened meeting usually are the result of opposition to some aspect of the proposed research. During the review of proposed research, IRB members may express a difference of opinion, or raise issues, questions or concerns that cause debate among the IRB members, or even result in disagreement. Some research, by its very nature, is considered to be controversial (e.g., emergency research where informed consent may not be obtained for all subjects or some research involving vulnerable populations).

IRB members may resolve controverted issues and concerns with continued discussion and deliberation, decide to seek further clarification from the investigator or sponsor of the proposed research, or decide to settle the issue by vote. If resolution was not reached about a controverted issue and the IRB seeks additional information, the minutes must summarize the IRB’s discussion and plans for seeking resolution (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

Similarly, when resolution of controverted issues is reached, the minutes must summarize the IRB’s discussion and how they were resolved (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). If there were no controverted issues, this should also be noted in the minutes.

**Contingent Approval of Research with Substantive Changes and no Additional Review by the Convened IRB**

OHRP finds that the IRB frequently approves research contingent upon substantive modifications or clarifications without requiring additional review by the convened IRB. OHRP recommends the following guidelines in such cases:

(a) When the convened IRB requests substantive clarifications or modifications regarding the protocol or informed consent documents that are directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111, IRB approval of the proposed research should be deferred, pending subsequent review by the convened IRB of responsive material.

(b) Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB Chair or another IRB member designated by the Chair subsequently approve the revised research protocol on behalf of the IRB under an expedited review procedure.

**Lack of Prisoner/Prisoner Representative for IRB Review of Research Involving Prisoners**

HHS regulations at 45 CFR 46.304 require modification of IRB membership for review of research involving prisoners. In specific, at least one member of an IRB that reviews the research shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.

When the convened IRB reviews research involving prisoners (including initial review, continuing review, review of protocol modifications, and review of unanticipated problems involving risks to subjects or others), the prisoner or prisoner representative must be present as a voting member. OHRP finds that the IRB failed to meet this requirement when reviewing research projects involving prisoners.