ACRP Regulatory Affairs Committee Review of FDA & HHS OHRP Joint Draft Guidance

Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs

What is the guidance?
This guidance document was prepared as a joint effort between the Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) to help IRBs meet the regulatory requirements for preparing and maintaining minutes of IRB meetings.

The guidance covers specific sections and offers recommendations to IRBs to achieve compliance in each of these aspects:

- Documentation of attendance at meetings, including any non-IRB members and non-voting members and documentation of quorum and assurance that quorum is maintained throughout a meeting
- Documentation of actions taken by the IRB, including details regarding approval, requirement for modifications, disapproval, suspension or termination of approval. The guidance offers reminders and explanations of specific regulatory requirements pertaining to criteria for approval, special populations, etc.
- Documentation of votes and suggested methods of documentation
- Documentation of required changes to research
- Documentation of controverted issues and their resolution

Who does it impact & how?
This guidance primarily impacts IRBs responsible for conducting reviews according to regulatory requirements. Individuals also impacted by this draft guidance are individual IRB members, auditors, and recipients of IRB correspondence.

What did ACRP RAC have to say about it?
ACRP's RAC offered a number of comments for Agency consideration. Some of the key points include request for more guidance regarding membership and quorum at meetings to ensure that members with "representative capacity" are involved in the review and decisions. Additionally, ACRP recommends that quorum vote be required to ratify or confirm a decision to terminate or suspend approved research outside of a meeting by either a Chair or Institutional Official. Another suggestion by ACRP's RAC is to provide more emphasis in the guidance document about the process of informed consent rather than the form itself.

When were the RAC's comments sent to the agency?
February 2, 2015

Where can I access this document?
http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM470154.pdf

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February 1, 2016

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

In reference to docket number: **FDA-2015-D-3638**

The Association of Clinical Research Professionals (ACRP) is the primary resource for clinical research professionals in the pharmaceutical, biotechnology and medical device industries, and those in hospital, academic medical centers and physician office settings. ACRP was founded in 1976 to address the educational and networking needs of research nurses and others who supported the work of clinical investigations. Almost 40 years later, ACRP is a global association comprised of individuals dedicated to clinical research and development. Our mission is "ACRP promotes excellence in clinical research." The Academy of Physicians in Clinical Research (APCR) is an affiliate of ACRP and is the leading professional organization, exclusive to physicians, that supports and addresses these unique issues and challenges of all physicians involved in clinical research.

ACRP appreciates the opportunity to provide the FDA with our comments on the Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs draft guidance as this issue has a significant impact on our membership. The attached document provides detailed comments/suggestions/recommendations on specific sections of the draft guidance.

We applaud the FDA's efforts on this important issue and hope that our feedback helps improve the final version of the document. Please let me know if you have any questions regarding our comments, or if we may otherwise serve as a resource on issues related to clinical research.

Sincerely,

Jim Kremidas
Executive Director

FDA-2015-D-3638 : Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs			
Page Number	**Text Line**	**Reference** *(if applicable)*	**Comments**
3	Par. 1 under "Members…"		"Representative status" is insufficient to adequately describe the role of an IRB member, except in a cursory way. For example, simply identifying someone as "scientist, non-scientist, unaffiliated" does not connote whether an IRB is fulfilling its obligations to have one or more members with the "Representative capacity" to review many types of research especially with vulnerable populations, e.g., pediatric, decisionally-impaired adults, etc. It is suggested that the Guidance include a recommendation to describe the representative capacity of IRB members, in addition to the representative status.
3-4	Part 1 under "Member…" & Part 2 "Quorum"	Part 1 second paragraph & Part 2 fourth paragraph	ACRP requests more clarification for how IRB minutes should document **when** the members attending were **actually present** and who was present for deliberations and votes. For members attending by 'alternative mechanisms' a suggestion would be to include their log in/log off times. ["The minutes should make clear which members, if any, participated in the convened meeting via an alternative mechanism…"] ACRP notes that not being 'present' during the whole meeting speaks to quorum issues as well as deliberation and voting and sufficient minutes language assuring members are present via the alternate mechanism can be important. ["If quorum is lost during a meeting, then the IRB may not take any further action or vote on proposed research. Because IRB members may occasionally enter or leave the room at various times during a convened meeting (e.g., arrive late, depart early, or leave the meeting temporarily)"]
3	Members, Alternates…		Many IRBs use a primary reviewer system, which may not always be conducted by the most appropriate person. Further, it may promote a less than fulsome review if other IRB members do not receive, or have access to, all the study related documents, e.g., full protocol, consent form, Investigator Brochure, etc. Therefore, it is recommended that the FDA discuss its expectations of the use of a primary reviewer system and guidance on use of alternates to cover for primary members of the reviewer system, if applicable.
4	Part 2 "Quorum", relevance to Part 3 Other Regulatory	Par. 2, sentences 2 & 3, Par. 4	Paragraph 2 defines quorum, Par. 3 discusses need to maintain quorum throughout the meeting. The regulatory requirement for a majority of members to be present is repeated, including at least one whose primary concerns are in non-scientific areas. However, in order to achieve a more robust and meaningful research review especially where vulnerable populations are concerned, ACRP suggests that the FDA recommend that quorum should

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	Determinations and Review Responsibilities		include appropriate representative capacity for the study population, e.g., pediatrics, including the requirement to maintain such representative capacity amongst IRB members reviewing research in order to maintain quorum. It is also important for the IRB to have one or more persons with appropriate representative capacity participating in the review, as described in Section 3 Other Regulatory Determinations and Review Responsibilities; it is therefore recommended that "representative capacity" be addressed in this section, as well to meet the unique characteristics of the research under review.
5	Section B	Actions Taken by the IRB	This section notes: *The minutes should serve as a central repository for IRB decisions on proposed research activities.* The amount of information recommended to be documented in the meeting minutes is significant within the guidance. In some cases this would require documenting something in more than one place or multiple times, and increasing burden on IRBs. ACRP asks the FDA to include any recommendations for better efficiencies in IRB documentation practices. Additionally, large amount of documentation in meeting minutes and potential redundancies and duplications brings with it risks of inconsistent information or that not all of the information will support the meeting proceedings. Note that Later on page 6, section 3, ***Other IRB Regulatory Determinations and Review Responsibilities*** FDA recommends *"that IRBs document all required findings and determinations in the minutes* ***or elsewhere in the IRB records*** *(e.g., IRB reviewer form/checklist, database entries, or other forms of physical or electronic records),"* ACRP suggests that Section III DISCUSSION on page 2 include the suggestion that additional documentation can be elsewhere outside the meeting minutes yet still in the IRB records and available for access by stakeholders when appropriate.
6	Suspension or Termination of IRB Approval	IRB approval suspended or terminated outside a	The last sentence in this section stipulates that a decision to terminate or suspend the approved research is made outside meeting by, for example, the IRB Chair or Institutional Official be simply reported to the convened IRB and the discussion summarized in the minutes. Since approval for the research is granted by a majority vote of all IRB members present at a convened meeting, it is ACRPs' view that the IRB ought to be asked to ratify/confirm this

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		convened meeting	decision, that any further action regarding possible re-approval or lifting of any suspension be discussed at the meeting, voted upon by the IRB, and appropriately documented in the minutes.
7	Informed Consent	Informed Consent Form	In ACRP's view, this section places inordinate emphasis on the informed consent **form**, rather than the informed consent **process,** which should include methods of documentation of which a formal consent form with the required and additional elements of consent under 21CFR50 is but one approach. There have been many commentators remarking on the increasing length and complexity of such forms, which can be counterproductive and mitigate against subject understanding and true informed consent. Therefore, it is recommended that the FDA cite some other possible methods of documentation of informed consent, such as e-consent, or an information letter with the 21CFR50 information requirements, and a single page consent form for signatures, together with necessity to record the IRB's discussion and decision in the IRB minutes
8	Devices: SR/NSR Determination		The draft guidance states that the IRB minutes need only document the IRB's SR/NSR determination in the minutes. ACRP believes that it is also important for the IRB to document in the minutes its rationale or basis for the SR/NSR determination it makes.
General			ACRP asks that FDA include guidance to IRBs in relation to sharing meeting minutes with Investigators and Sponsors and potential implications on confidentiality related to IRB members in attendance at a meeting and related to other research reviewed during a given meeting.

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Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

Submit electronic comments to http://www.regulations.gov.

Submit comments on paper, disk, or CD-ROM by mail/hand delivery/courier to:

Office for Human Research Protections
Division of Policy and Assurances
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Food and Drug Administration
Division of Dockets Management (HFA-305)
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U.S. Department of Health and Human Services

Office for Human Research Protections **Food and Drug Administration**

November 2015

Contains Nonbinding Recommendations

Draft – Not for Implementation

Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs

Additional copies are available from:

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http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ProposedRegulationsandDraftGuidances/default.htm

For questions on the content of this guidance, contact the Office for Human Research Protections or the Office of Good Clinical Practice at the address/phone number listed above.

U.S. Department of Health and Human Services

Office for Human Research Protections **Food and Drug Administration**

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Minutes of Institutional Review Board (IRB) Meetings: Guidance for Institutions and IRBs

This draft guidance, when finalized, will represent the Office for Human Research Protections' (OHRP's) and the Food and Drug Administration's (FDA's) current thinking on this topic. This guidance does not create or confer any rights for or on any person and does not operate to bind OHRP, FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the appropriate OHRP or FDA staff responsible for implementing this guidance. If you cannot identify the appropriate OHRP or FDA staff, call the appropriate number listed on the second title page of this guidance.

I. INTRODUCTION

This draft guidance has been prepared jointly by the Department of Health and Human Services (HHS) Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA). This guidance is intended for institutions and institutional review boards (IRBs) responsible for oversight of human subject research under HHS and FDA regulations.

This draft guidance is intended to assist institutions and IRBs responsible for preparing and maintaining minutes of IRB meetings (also referred to in this guidance as minutes). This draft guidance document describes requirements for minutes and provides recommendations for meeting the regulatory requirements for minutes.

OHRP's and FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe OHRP's and FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in OHRP and FDA guidances means that something is recommended or suggested, but not required.

II. BACKGROUND

The institution, or where appropriate an IRB, must prepare and maintain adequate documentation of IRB activities, including minutes of IRB meetings (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). IRBs have been cited in OHRP Determination Letters[1] and FDA Warning Letters[2] for failing to prepare and maintain adequate minutes. For this reason OHRP and FDA believe providing recommendations on the type and amount of information to include in minutes will help IRBs meet the regulatory requirements for minutes.

[1] OHRP Determination Letters are posted at http://www.hhs.gov/ohrp/compliance/letters/index.html and can be viewed by the date issued.

[2] FDA Warning Letters are posted at http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm and can be viewed via multiple browsing options (e.g., by date, by company, by subject).

Examples of noncompliance related to minutes include:

- Minutes are missing.
- Minutes lack sufficient detail to show the vote on actions taken by the IRB, including the number of members voting for, against, and abstaining.
- Minutes are incomplete and only describe voting actions as "passed unanimously."
- Minutes do not clearly indicate, or contain discrepancies about, what the IRB approved.
- The IRB maintains multiple sets of minutes with different information for the same meeting.
- Minutes fail to include a summary of the discussion of controverted issues.

Minutes are intended to provide a summary of what occurred during a convened meeting and document the IRB's findings and determinations. Minutes provide information to persons not present at the meeting (e.g., institutional officials, regulators, IRB members who could not attend) about the IRB's decisions and provide documentation of the IRB's compliance with regulatory requirements. Minutes should be detailed enough for OHRP and FDA to be able to determine compliance with the applicable regulations.

When reviewing proposed research, IRBs must make certain findings and determinations to fulfill specific regulatory requirements (e.g., that the study meets the approval criteria found in the regulations at 45 CFR 46.111 and 21 CFR 56.111). We recommend that IRBs document their findings and determinations in the minutes, or elsewhere in the IRB records (e.g., IRB reviewer form/checklist, database entries, or other forms of physical or electronic records).

The regulations for IRB records at 45 CFR 46.115(a)(2) and 21 CFR 56.115(a)(2) provide institutions and IRBs with flexibility in choosing how to prepare minutes. Institutions and IRBs may adopt procedures for preparation and maintenance of minutes that best suit their particular organization.

III. DISCUSSION

IRBs that review research subject to HHS and FDA regulations (45 CFR part 46 and 21 CFR parts 50 and 56, respectively) must comply with the requirements in those regulations. Both the HHS regulations at 45 CFR 46.115(a)(2) and the FDA regulations at 21 CFR 56.115(a)(2) specifically require that institutions, or where appropriate, an IRB, prepare and maintain adequate documentation of IRB activities, including minutes in sufficient detail to show:

- Attendance at the meetings;

- Actions taken by the IRB;
- The vote on these actions, including the number of members voting for, against, and abstaining;
- The basis for requiring changes in or disapproving research; and
- A written summary of the discussion of controverted issues and their resolution.

A. Attendance at the IRB Meeting

Minutes of IRB meetings must be in sufficient detail to show attendance at the convened meeting of the IRB (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). In addition, except when an expedited review procedure is used, the IRB must review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it must receive the approval of a majority of those members present at the meeting (45 CFR 46.108(b); 21 CFR 56.108(c)).

1. Members, Alternates, Consultants and Guests

It is important for IRBs to keep an accurate record of who attended each convened meeting of the IRB. OHRP and FDA recommend that the minutes include the full names of the IRB members present and participating in the convened meeting and the representative status for each member (e.g., scientist, nonscientist, unaffiliated). We recommend that attendance information be listed at the beginning of the minutes so it is clear who was present at the meeting.

IRB members may participate in a convened meeting of the IRB via telephone or video conferencing when those members have received in advance of the meeting a copy of the documents for research proposals that are to be reviewed at the meeting. The minutes should make clear which members, if any, participated in the convened meeting via an alternative mechanism, such as telephone or video conferencing.

If the IRB has appointed alternate members who may substitute for primary members at a convened meeting, the minutes should document any circumstance in which an alternate member is replacing a primary member. An alternate may substitute for a primary IRB member for an entire meeting (e.g., when the primary member is not able to participate in the meeting), or at any time during a meeting for the review of particular research proposals (e.g., when the primary member has a conflict of interest and is recused from review of a particular study). In any situation in which an alternate member replaces a primary member at a convened meeting, the minutes must provide the alternate's name and representative status, the name of the primary member for whom the alternate is substituting, and the reason for the substitution (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). Even if an alternate substitutes for a primary member for only a portion of the meeting, we recommend that the reason for the substitution be documented in the minutes.

IRBs may invite consultants to assist in the review of a particular study. If the IRB uses a consultant, the minutes should include the name of the consultant and a brief description of the consultant's expertise. Because a consultant is prohibited from voting (45 CFR 46.107(f); 21 CFR 56.107(f)), we recommend that IRBs document in the minutes that the consultant did not vote on the study.

If the IRB permits non-members and guests to attend a convened meeting (e.g., IRB support staff, the investigator whose study is being reviewed, study coordinator), then the minutes must record the name(s) of all such attendees (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). The minutes should be clear that the non-member or guest did not participate in the deliberation and voting. The institution and the IRB may consider having a written policy covering the attendance of non-members and guests at a convened meeting. This policy may help to ensure that those who attend an IRB meeting understand the confidential nature of the information being reviewed and promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects.

2. Quorum

The attendance information documented in the minutes assists in determining which and how many IRB members must be present to convene a meeting (i.e., quorum) and whether proposed research receives enough votes (i.e., a majority of those present) to be approved.

A quorum is the minimum number and type of IRB member that must be present at a convened meeting for the IRB to conduct business. In order to review proposed research at a convened meeting, a majority of the members of the IRB must be present, including at least one member whose primary concerns are in nonscientific areas (45 CFR 46.108(b); 21 CFR 56.108(c)). If a majority of the IRB membership is not present, or if a nonscientist is not present, then quorum has not been met.

IRBs often calculate majority by using the "half-plus-one" technique. This technique works well for IRBs with an even number of IRB members. For example, if the total IRB membership is 10, then majority is 6 (half of 10 is 5, plus 1 equals 6). However, if the IRB has an odd number of members, then majority should be calculated by taking half of the total number of IRB members, and rounding up to the next whole number. For example, if the IRB membership is 15, then majority is 8 (half of 15 is 7.5, and rounding up to the next whole number is 8).[3]

A quorum must be maintained throughout the meeting in order for the IRB to conduct business (45 CFR 46.108(b); 21 CFR 56.108(c)). If quorum is lost during a meeting, then the IRB may not take any further action or vote on proposed research. Because IRB members may occasionally enter or leave the room at various times during a convened meeting (e.g., arrive

[3] Note that the regulations do not prohibit IRBs from having more stringent requirements for quorum.

late, depart early, or leave the meeting temporarily), we recommend that the minutes provide sufficient information to indicate that a quorum is present throughout the meeting.

B. Actions Taken by the IRB

The minutes of IRB meetings must be in sufficient detail to show the actions taken by the IRB at the convened meeting (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). OHRP and FDA interpret "actions taken by the IRB" (also called "IRB actions") to refer to any vote taken by the IRB related to a proposed research activity. The minutes must summarize all research activities being reviewed by the IRB at that meeting, and must document actions taken by the IRB (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). The minutes should serve as a central repository for IRB decisions on proposed research activities.

1. Approve, Require Modifications to Secure Approval, Disapprove

OHRP and FDA regulations require that an IRB review and have the authority to approve, require modifications in (to secure approval), or disapprove all proposed research activities covered by the regulations (45 CFR 46.109(a); 21 CFR 56.109(a)). Additionally, the IRB or institution may develop a range of other allowable actions the IRB may take when reviewing proposed research activities (e.g., approve with conditions, table the proposed research until additional information can be obtained, or defer a decision).

The minutes, or other IRB record, should show that the IRB made all of the findings and determinations required for approval under the regulations. If a proposed research activity is approved with conditions, the minutes should state the process to be followed to ensure the conditions are met (e.g., the IRB Chair, or other individual(s) designated by the IRB, will review and determine whether the changes, clarifications, and/or additional documents submitted by the investigator are satisfactory). Both OHRP and FDA have issued guidance that addresses the authority of IRBs to approve research with conditions.[4]

The minutes should identify the effective date of approval and the approval period (continuing review interval) for any study approved by the IRB. IRBs must determine which protocols require continuing review more often than annually (at intervals appropriate to the degree of risk) (45 CFR 46.103(b)(4)(ii); 21 CFR 56.108(a)(2); 45 CFR 46.109(e); 21 CFR 56.109(f)). Both OHRP and FDA have issued guidance on continuing review of research to assist the IRB in determining the effective date of the initial approval and the subsequent date of continuing review.[5]

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[4] OHRP's Guidance on IRB Approval of Research with Conditions can be found at http://www.hhs.gov/ohrp/policy/conditionalapproval2010.html; FDA's Guidance on IRB Continuing Review after Clinical Investigation Approval can be found at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf.

[5] OHRP's Guidance on IRB Continuing Review of Research can be found at http://www.hhs.gov/ohrp/policy/continuingreview2010.html; FDA's Guidance on IRB Continuing Review after

2. Suspension or Termination of IRB Approval

Both OHRP and FDA regulations authorize an IRB to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects (45 CFR 46.113; 21 CFR 56.113). Any IRB action to suspend or terminate IRB approval that occurs at a convened meeting must be summarized in the minutes (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). The summary should include the reason(s) for the IRB's action(s) and any follow-up action items. Any decision to suspend or terminate IRB approval that occurs outside of a convened meeting (e.g., as determined by the IRB Chair or Institutional Official for subject safety reasons) should be reported to the convened IRB and the discussion summarized in the minutes.

3. Other IRB Regulatory Determinations and Review Responsibilities

IRBs must make certain regulatory findings and determinations in order to approve research (e.g., that research involving children satisfies the additional protections provided for children at 45 CFR part 46, subpart D and 21 CFR part 50, subpart D). Because these findings and determinations are made during IRB meetings, many IRBs document them in the minutes. OHRP and FDA recommend that IRBs document all required findings and determinations in the minutes or elsewhere in the IRB records (e.g., IRB reviewer form/checklist, database entries, or other forms of physical or electronic records), and include protocol-specific information justifying the findings and determinations.

- **Criteria for IRB Approval of Research**

  In order to approve research, the IRB must determine that all of the criteria for IRB approval of research are satisfied (45 CFR 46.111; 21 CFR 56.111). These criteria apply to both initial review and continuing review of research and provide the framework for the IRB's evaluation of research. The minutes, or other IRB record, should summarize the IRB's consideration of the approval criteria and should include a determination as to whether the criteria were met, as applicable.

- **Informed Consent**

  In order to approve a study, the IRB must determine that informed consent will be sought from each prospective subject or the subject's legally authorized representative (LAR) in accordance with the informed consent regulations (45 CFR 46.111(a)(4); 21 CFR 56.111(a)(4)). The IRB must also determine that informed consent will be appropriately documented in accordance with the regulations (45 CFR 46.111(a)(5); 21 CFR 56.111(a)(5)).

Clinical Investigation Approval can be found at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf.

The minutes should indicate that, as part of its review and approval of a study, the IRB reviewed the informed consent form(s) and determined that the form(s) meet the applicable regulatory requirements.[6] The minutes, or other IRB record, must also summarize any changes to the informed consent form(s) required by the IRB (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

Both OHRP and FDA regulations permit an IRB to waive the requirement that the subject or the subject's LAR sign a written consent if the IRB determines that certain criteria are met (45 CFR 46.117(c); 21 CFR 56.109(c) and (d)). We recommend that any such waiver of documentation of informed consent be documented in the minutes with protocol-specific information justifying the IRB's decision(s).

In addition, for HHS-conducted or -supported research, the regulations at 45 CFR 46.116(c) and (d) permit an IRB to approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the IRB finds and documents that certain criteria are met. When an IRB approves a waiver of consent for research reviewed by the convened IRB, these findings must be documented (45 CFR 46.116(c) and (d)). OHRP recommends that IRB decisions for waiver of consent be documented in the minutes and that the minutes include protocol-specific information justifying each IRB finding.

IRBs should be aware that FDA does not have similar regulatory provisions permitting an IRB to waive elements of consent, or to waive informed consent altogether.

- **Studies Involving Children**

  Each IRB that reviews studies involving children as subjects covered by 45 CFR part 46 subpart D and 21 CFR part 50 subpart D may approve only those studies that satisfy the criteria described in subpart D (45 CFR 46.403; 21 CFR 50.50).

  In its review of proposed research involving children, the IRB must find that the research meets the conditions of 45 CFR 46.404 or 21 CFR 50.51 (research/clinical investigations not involving greater than minimal risk); 45 CFR 46.405 or 21 CFR 50.52 (research/clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects); or 45 CFR 46.406 or 21 CFR 50.53 (research/clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition). If the IRB determines that the proposed research cannot be approved under these categories, then additional regulatory requirements under 45 CFR 46.407 or 21 CFR 50.54 (research/clinical investigations not otherwise approvable that present an opportunity to understand, prevent, or alleviate a serious problem

[6] See 45 CFR 46.116, 45 CFR 46.117, 21 CFR 50.20, 21 CFR 50.25 and 21 CFR 50.27.

affecting the health or welfare of children) must be met. Both OHRP and FDA have issued guidance to assist IRBs with handling clinical investigations that include children as subjects and that have been referred under 45 CFR 46.407 or 21 CFR 50.54.[7]

In addition to the findings and determinations described above, the IRB must also determine that requirements for permission by parents or guardians and for assent by children are met (45 CFR 46.408; 21 CFR 50.55). If the proposed research involves children who are wards of the State or other agency, institution or entity, then the IRB must ensure that additional protections are met (45 CFR 46.409; 21 CFR 50.56).

OHRP and FDA recommend that the IRB's findings and determinations for studies involving children be documented in the minutes.

- **Emergency Research**

  If the IRB reviews a proposal for research involving an exception from informed consent requirements for emergency research, the IRB must find and document that the proposed research satisfies the criteria found in OHRP's Secretarial Waiver[8] and/or FDA's regulations at 21 CFR 50.24.

  FDA has issued guidance on the exception from informed consent requirements for emergency research.[9] As outlined in FDA's guidance, FDA anticipates that an emergency research study in which informed consent is not obtained for all subjects is, by its very nature, controversial. Therefore, IRBs must summarize their discussions and decisions about the required elements for these studies in the minutes (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

- **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.[10] 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

[7] OHRP's guidance on Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process can be found at http://www.hhs.gov/ohrp/policy/populations/guidance_407process.html; FDA's guidance on the Process for Handling Referrals to FDA Under 21 CFR 50.54, Additional Safeguards for Children in Clinical Investigations can be found at http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm127605.pdf.

[8] Information about OHRP's Informed Consent Requirements in Emergency Research can be found at http://www.hhs.gov/ohrp/policy/hsdc97-01.html.

[9] FDA's guidance on the Exception from Informed Consent Requirements for Emergency Research can be found at http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm249673.pdf.

[10] See FDA's Information Sheet Guidance on Significant Risk and Nonsignificant Risk Medical Device Studies at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf.

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.

- **Studies Involving Pregnant Women, Human Fetuses and Neonates**

  The regulations for research conducted or supported by HHS require specific findings for research involving pregnant women, human fetuses and neonates as subjects (45 CFR 46 subpart B). OHRP recommends that when such research is approved by the convened IRB, all required findings should be documented in the minutes, including protocol-specific information justifying the IRB's findings.

  IRBs should be aware that FDA regulations do not require specific findings for research involving pregnant women, human fetuses, and neonates as subjects. If an IRB reviews an FDA-regulated study that is not HHS conducted or supported research, and the study is expected to involve pregnant women, fetuses, and neonates as subjects, IRBs may find 45 CFR 46 subpart B to be helpful.

- **Studies Involving Prisoners**

  The regulations for research conducted or supported by HHS require specific findings for research involving prisoners as subjects (45 CFR 46 subpart C). OHRP recommends that when such research is approved by the convened IRB, all required findings should be documented in the minutes, including protocol-specific information justifying the IRB's findings.

  IRBs should be aware that FDA regulations do not require specific findings for research involving prisoners as subjects. If an IRB reviews an FDA-regulated study that is not HHS conducted or supported research, and the study is expected to involve prisoners as subjects, IRBs may find 45 CFR 46 subpart C, and OHRP's guidance on research in prisoners[11] to be helpful.

- **Reporting of Expedited Review Activities**

  Each IRB that uses an expedited review procedure must adopt a method for keeping all members advised of research proposals which have been approved under the expedited review procedure (45 CFR 46.110(c); 21 CFR 56.110(c)). There are various methods IRBs can use to keep the IRB members appraised of expedited actions. One method that may be used is to present a report of expedited actions during a convened meeting. If this

[11] OHRP's guidance on the Involvement of Prisoners in Research can be found at http://www.hhs.gov/ohrp/policy/prisoner.html, and the Prisoner Research FAQs can be found at http://answers.hhs.gov/ohrp/categories/1568.

method is used and the IRB reviews a report summarizing expedited review actions at a convened meeting, the minutes should describe what was presented to the IRB, indicate that the IRB members had an opportunity to ask questions or raise concerns, and summarize questions or concerns, if any, raised by the IRB members.

- **Unanticipated Problems, Serious or Continuing Noncompliance, Suspension or Termination of IRB Approval**

  If at a convened meeting, the IRB reviews an issue that requires prompt reporting to the IRB under 45 CFR 46.103(b)(5) or 21 CFR 56.108(b), the minutes should summarize the report and must document the IRB's action, if any, resulting from that review (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). Any review of such information and any decisions made outside of a convened meeting (e.g., as determined by the IRB Chair or Institutional Official for subject safety reasons) should be reported to the convened IRB and documented.

C. The Vote on IRB Actions

The minutes of IRB meetings must be in sufficient detail to show the vote on IRB actions as determined during the convened meeting, including the number of members voting for, against, and abstaining (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)). Individual voting records by name are not required. The following are examples of acceptable formats for documenting the votes on actions taken by the IRB in the minutes. Each example assumes that 15 members were present for the vote:

- Total Voting = 15; Vote: For = 14, Opposed = 0, Abstained = 1.

OR

- Total Voting = 14 [1 member was recused and did not vote]; Vote: For = 12, Against = 1, Abstained = 1.

OHRP and FDA recommend that minutes identify any member who has a conflicting interest in a research study, and as such, is excluded (recused) from participation in the IRB's review of that particular research including the reason for the recusal. As shown in the examples above, the minutes of the meeting must reflect a vote count (i.e., for, against, and abstaining) that is consistent with the number of non-conflicted IRB members present (45 CFR 46.107(e); 21 CFR 56.107(e); 45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

Members who are recused from voting on a specific study because of conflicting interests may not be counted toward the quorum. That is, their recusal may not be recorded as an abstention.

IRB members who participate in a convened meeting via telephone or video conferencing may vote and be counted towards the quorum. The IRB must ensure that the votes of such members are recorded (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

IRB members may not vote outside of the convened meeting (e.g., via email prior to the convened meeting). IRB members who cannot attend a convened meeting may not send someone (e.g., from their department or office) to vote in their place. Opinions of absent members that are transmitted prior to the convened meeting by mail, telephone, telefax or email may be considered by the attending IRB members but must not be counted as votes or towards the quorum for convened meetings (45 CFR 46.108(b); 21 CFR 56.108(c)).

D. Requiring Changes or Disapproving Research

The minutes of IRB meetings must be in sufficient detail to show the basis for requiring changes in (to secure approval) or disapproving research (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

If the IRB requires that the investigator make specified changes to the research protocol or informed consent document(s) and to resubmit such documents to the convened IRB for subsequent review, these IRB decisions must be documented in the minutes (45 CFR 46.115(a)(2); 21 CFR 56.115(a)(2)).

If the IRB disapproves a research activity, the IRB must include a statement of the reasons for its decision in the written notification to the investigator and the institution, and provide the investigator an opportunity to respond in person or in writing (45 CFR 46.109(d); 21 CFR 56.109(e)). The minutes should summarize the IRB's discussion and deliberations for its decision to disapprove proposed research, and clearly indicate the IRB's reasons for its decision.

E. 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.

IV. ADDITIONAL CONSIDERATIONS

We recommend that institutions and IRBs decide who is responsible for preparing and maintaining minutes at their institutions and outline the process in the IRB's written procedures. If the institution and IRB have a process for review and either acceptance or approval of minutes, this process should be covered in the IRB's written procedures. Institutions and IRBs may consider creating a standard template to assist in the preparation of their minutes.

OHRP and FDA recognize that in addition to documenting the IRB's findings and determinations in the minutes, or elsewhere in the IRB records, IRBs may also choose to document other activities that occur during the meeting. For example, some IRBs provide continuing education and training to the IRB members at a convened meeting and document such training in the minutes. IRBs may also communicate announcements or other information to the IRB members and attendees at the meeting and document this in the minutes (e.g., upcoming meeting schedule, staff or membership changes). This practice is acceptable to OHRP and FDA.

IRBs may choose to record IRB meetings (e.g., video, audio tape) and use the recording as a tool to assist in the preparation of written minutes. This process, if used, should be described in the IRB's written procedures.[12] However, retention of complete recordings of meetings does not relieve an IRB of its obligation to keep written minutes in accordance with the requirements of 45 CFR 46.115(a)(2) and 21 CFR 56.115(a)(2). We do not expect the minutes to include a verbatim transcription of what each member said during the course of the meeting.

Records required by the regulations, including meeting minutes, must be retained for at least 3 years after completion of the research subject of the review and must be accessible for inspection and copying by authorized representatives from OHRP and FDA at reasonable times and in a reasonable manner (45 CFR 46.115(b); 21 CFR 56.115(b)). Many sets of minutes will have records of review of multiple studies; those minutes must be retained until all of the studies that were reviewed at that meeting have been completed for at least 3 years. Institutions and IRBs can expect that representatives of OHRP conducting a compliance oversight assessment, or representatives of FDA conducting a Bioresearch Monitoring inspection, will review minutes and other appropriate IRB records to assess compliance with the regulations.

[12] Institutions and IRBs should ensure recording is permitted by institutional policy and, if applicable, state law. All members, and any others attending the meeting, should be informed that the meeting is being recorded and how the recording(s) will be used.