IACUC Feature of the Month

Correct Conduct of Full-Committee and Designated-Member Protocol Reviews

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Only two protocol review methods fulfill USDA and PHS requirements—full committee and designated member. The author attempts to lessen the confusion surrounding this issue by describing these methods, along with examples of faulty hybrids and convenient strategies to bring unacceptable methods into compliance.

Although the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy)\(^1\) has existed since 1986 and the United States Department of Agriculture’s (USDA) Animal Welfare Act\(^2\) regulations governing Institutional Animal Care and Use Committees (IACUCs) have been extant since 1989, continuing questions and misunderstandings exist regarding the procedures used for protocol review.

During the past several years, a significant number of Animal Welfare Assurance submissions to the Division of Assurances, Office of Laboratory Animal Welfare (OLAW) have proposed protocol review procedures that are not compliant with PHS Policy. There seem to be various reasons for this noncompliance, ranging from lack of clear understanding of the requirements to efforts by IACUCs to improve or streamline the processes. Previously published articles and letters to the editor have attempted to clarify federal requirements on these issues\(^3\,^6\). This article will address the appropriate methods, review some faulty “hybrids,” and suggest simple steps that can be taken to make an unacceptable method acceptable.

If an institution must comply with the Animal Welfare Act by virtue of the animal species used or the PHS Policy because it receives support from one of the PHS agencies (e.g., National Institutes of Health, Food and Drug Administration, Centers for Disease Control and Prevention), then the procedures for protocol review must be compliant with the aforementioned documents. The review procedures are nearly identical for both USDA and PHS and consist of only two acceptable methods, namely full-committee review and designated-member review. The following discussion will focus on the PHS Policy/OLAW perspective. Nothing in this article should be interpreted to establish new PHS policy or to reflect a change in official OLAW animal care and use guidelines. Work with animals may not commence until appropriately approved through one of the two recognized methods of protocol review.

Full-Committee Review

A literal reading of the PHS Policy at IV.C.2 is imperative to understand what is expected regarding IACUC review of PHS-conducted or -supported research projects. The Policy states that “prior to review, each IACUC member shall be provided with a list of proposed research projects to be reviewed. Written descriptions of research projects that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full committee review of those research projects.” The Policy explains the actual full-committee review method as follows: “If full committee review is requested, approval of those research projects may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest (e.g., is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum.”
Of the two methods, the concept of full-committee review is usually easier to understand and results in fewer permutations or “improvements.” Ordinarily, the IACUC members meet in a room to review and vote on the acceptability of research proposals (protocols) involving research animals submitted by a principal investigator (PI). A quorum (i.e., one person more than one half of the total number of voting members of the IACUC) of a properly constituted IACUC (as defined in PHS Policy IV.3.b) must be present to proceed with any official business requiring a quorum. It is important to remember that anyone who may have a conflict of interest cannot contribute to the quorum. The full-committee review is to take place in real time with interaction of the members. Previous OLAW guidance has indicated that it is acceptable to use long-distance communication methods such as video-conferencing in exceptional circumstances.

Many IACUCs use primary reviewers during the meeting to present a protocol to the rest of the members. A primary reviewer should not be confused with the designated reviewer of the designated-member review method defined later. A primary reviewer, IACUC coordinator, or other member may be involved in some initial interaction with the PI to prepare the protocol for review by the full committee by checking for obvious inconsistencies, omissions, or clerical errors. Either a primary reviewer can make the presentation, or the members can discuss the protocol collectively with direction from the Chair.

When a vote is called for, there can be several possible outcomes. Outright approval requires an affirmative vote by a majority of the convened quorum present. In the event that substantive questions prevent final approval, the committee can wait until the next meeting for revisions to be reviewed by the full committee. Alternatively, the committee can decide to handle the resubmission by the designated-member review process, with appropriate notation in the minutes. Although PHS Policy does not recognize protocols in this status, IACUCs often refer to them as “conditionally” or “provisionally” approved. However, this designation does not allow animal work to begin, nor can the date of the meeting serve as an IACUC approval date for use on a grant application.

The committee members can also vote to withhold approval if they feel that the requirements of PHS Policy or other stipulations have not been satisfied. Other officials at the institution cannot overturn this decision. The PI must receive written notification, including the reason for this decision, and must have an opportunity to respond in person or in writing.

IACUCs may invite consultants to assist in the review of complex protocols, but consultants cannot vote unless they are officially appointed voting members on the committee.

**Designated-Member Review**

The second accepted method of protocol review is known as “designated-member review.” The actual Policy description of this method is as follows: “If full committee review is not requested, at least one member of the IACUC, designated by the Chairperson and qualified to conduct the review, shall review those research projects and have the authority to approve, require modifications in (to secure approval) or request full committee review of those research projects.”

This method is equally acceptable for use by IACUCs when conducting protocol review, but it must proceed as outlined in the PHS Policy. Using this method, all IACUC members receive a list of proposed research projects and access to the necessary information on the protocol to be reviewed. If any member feels that this protocol should go before a full committee, then its review must be deferred to the next full IACUC meeting. Any member can make the decision to send the protocol to full-committee review at any time during the time period designated for providing this opportunity. It is useful for IACUCs to allow a predetermined time period during which members may indicate which method of review is preferred. If no member calls for a full-committee review, then the Chair can refer the protocol in question to a designated reviewer. The Chair may select one or more members, qualified to review this specific protocol, who will act on behalf of the entire IACUC to approve the protocol, request additional information from the PI to approve it, or refer it.
for full review. The designated reviewer does not have the power to withhold approval, however, but must in such cases refer the protocol for full-committee review.

The designated-reviewer approval has equal validity to full-committee review approval and does not require subsequent reapproval or notification by a convened meeting. It is always possible for the IACUC to discuss protocols approved by either method in future meetings as a form of continuing review or in response to animal welfare concerns.

**Common Errors**

In efforts to facilitate the designated-member review procedure, many IACUCs have suggested incorrect variations. Even if these methods result in faster review or other perceived benefits, one must remain aware that the two recognized methods are the only presently acceptable ones as a condition of PHS support. No changes in the current IACUC review requirements are permissible without a formal change in the PHS Policy. Along with the following examples of faulty use of designated-member review, I offer suggestions for making the review compliant.

**Unacceptable Method 1**

Each IACUC member receives a copy of the protocol (paper or electronic), decides on approval, and sends a “vote” back to the Chair. The Chair notes that a majority approves, concurs, and signs the protocol as approved. This is a hybrid of both recognized methods that does not meet the requirements of either.

Correction: The feedback from the members should only concern their concurrence with the use of a designated-member review or a call for full-committee review. If there is no call for full-committee review, it is still acceptable for members to share comments with a designated reviewer, who can use this information in conducting the designated-member review as described earlier.

**Unacceptable Method 2**

The IACUC members receive a copy of the protocol. As soon as a quorum of the members reply that they do not request full-committee review, and before the end of the predetermined time period provided to all members to request full-committee review, the Chair initiates designated-member review.

Correction: In this case, not all members were given sufficient time to reply. The committee should determine a definite time frame during which members must submit replies. IACUCs may consider the lack of a reply as equivalent to declining to call for full review, but only after the full time period has elapsed. If all voting members reply before the end of the predetermined time period and there are no requests for full-committee review, the Chair is at liberty to initiate designated-member review.

**Unacceptable Method 3**

The IACUC members receive a copy of the protocol, no one responds, and hearing no negative comments or call for full review, the Chair automatically considers the protocol approved.

Correction: This does not meet the requirements of designated-member review because no one was appointed designated reviewer. It also appears that no review was conducted; this is a violation of PHS Policy. The absence of a request for full review must lead to the appointment of a designated reviewer(s), and the correct procedure followed.
Unacceptable Method 4

The IACUC members indicate that a protocol can be handled by designated-member review and the Chair selects three reviewers. Two reviewers vote to approve and one votes to withhold. The Chair considers the protocol approved.

Correction: Under designated-member review, all participants must either approve or require (the same) modifications for approval; failing this, they must submit the protocol for full-committee review. In this case, the reviewers will not actually be voting with a majority-rules outcome.

Unacceptable Method 5

The designated reviewer considers a protocol to be marginally acceptable and assigns a “provisional approval” but thinks it would be best for a final decision to come from a full-committee review at the next meeting. The PI starts the work with the possibility of having to stop once the full committee meets.

Correction: Again, this situation constitutes an unacceptable hybrid. The designated reviewer should fully approve a protocol, allowing the work to start without additional review needed, or require modification, or submit the protocol for full-committee review. Designated members should be qualified to conduct the specific review to allow a competent final decision.

Unacceptable Method 6

The IACUC develops a flowsheet whereby certain studies (e.g., primate, dog, survival surgery) automatically must have full-committee review whereas other studies (e.g., antibody production, rodent behavior) are directed to a standing committee of designated reviewers.

Correction: The routing to a full committee is acceptable, as is the default submission to the designated reviewers, provided the remainder of the committee has the opportunity to call for full-committee review. Only after all members have, as a minimum, received a list of proposed research projects, had written descriptions of those projects available to them, and decided that full-committee review is not necessary, can the designated reviewers handle it.

Unacceptable Method 7

The IACUC Chair prereviews submitted studies, decides that certain benign proposals would result in a unanimous decision by the members in favor of designated-member review, and therefore chooses to be the reviewer and approves the study, informing the committee at the next meeting.

Correction: Here the Chair has bypassed the committee members, who do not have the opportunity to call for full review. Only after all have had the opportunity and no one expresses the need for full review can the Chair become the designated reviewer and approve on behalf of the entire IACUC.

Potentially Acceptable Method 8

All members receive a copy of the protocol and all are designated reviewers. This arrangement can work in theory but may be difficult to accomplish logistically. In this instance all reviewers need to examine each subsequent revision. Every IACUC member must approve, rather than just the majority of the members. Abstention is not permissible because this approach does not operate on a majority-rule basis.
Conclusions

In all of the cases just presented, the critical issue in bringing them into compliance is the initial inclusion of all members in the opportunity to examine the protocol and subsequently to decide to forgo a full review in favor of the designated-member review. Once members have chosen designated-member review, then the reviewer(s) assumes the responsibility for the full committee in granting unanimous approval, requiring modification, or sending the protocol for full review.

Everything discussed here regarding the recognized methods of protocol review is equally applicable to the review of proposed significant changes to ongoing, approved protocols and to the PHS triennial continuing-review requirement. The IACUC should formulate, in advance, a list of what changes it would consider significant (see ref. 8 for examples) and apply exactly the same methodology for review. All members must have a chance to examine proposed significant changes, either in full-committee review or in determining whether to use the designated-member review method. As in protocol review, any member can request that the change be presented to the full committee and have this request honored.

When an Assurance is submitted to OLAW, it is important to outline clearly and accurately the methods that the IACUC used under discussion for reviewing protocols and significant changes. The description should clearly explain the method for conducting the procedures at that institution, so that OLAW can assess whether the method is compliant. Once an Assurance is approved, the described method is considered acceptable for review of protocols and significant changes at that institution. The annual report to OLAW should include any changes to the institution’s approved protocol review process. OLAW welcomes questions on this subject; it is the office’s mission to ensure that Assured institutions remain compliant.

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References