The Full Committee Review plunder

The Office of Laboratory Animal Welfare (OLAW) recognizes two methods of protocol review: Full-Committee Review (FCR) and Designated Member Review (DMR).

The Great Eastern University's (GEUs) IACUC was confident that they understood the mechanisms of protocol review until Dr. Jerry Silverman's protocol was approved but did not include critical information identified during the FCR process. During the first round of IACUC review, one of the assigned Designated Member Reviewers (DMRs) for Jerry's protocol was concerned about the proposed use of food restriction - specifically, whether the duration was too long - and called for FCR.

On the day of FCR, the DMR gave a brief summary of the protocol's goals and described the concern about the duration of food restriction and the potential impact on the animals' well-being. The committee's discussion on this matter was quite robust; the DMR who called the protocol for FCR was satisfied with the veterinarian's recommendation to add additional monitoring criteria. However, as the committee discussed the food restriction, Dr. Watson, a scientific member of the IACUC, raised a few other concerns about the protocol, including the need for more detailed humane endpoints and concerns about an animal user's apparent lack of experience. Finally, a motion was made to send the protocol back to the PI for revision and the revised application could be reviewed by DMR subsequent to FCR (DMR/S/FCR). The motion was unanimously approved.

A month or so later, while reviewing an amendment to Jerry's protocol, Watson was upset to find that the protocol was not revised according to the concerns he raised during FCR. Watson called the IACUC Chair, Dr. Crick for advice. Crick indicated that once the protocol went DMR/S/FCR, the DMR(s) have the authority to act on the behalf of the IACUC and could decide what changes were required for approval. This did not sit well with Watson, and he wondered how the protocol could be approved without addressing his concerns. Is the GEU IACUC conducting FCR and DMR/S/FCR correctly, according to the regulations? ❐

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COMPLIANCE CONSIDERATIONS

The Protocol Review coordinators off the following compliance considerations:

Did the GEU process meet the regulatory requirements?

1. Literally speaking, the scenario indicates that the protocol was discussed before the full committee, and, during that review, the IACUC decided modifications were required before approval could be granted. Once the FCR was complete, the IACUC agreed that the modified protocol could be reviewed using the DMR/S/FCR process. The protocol was returned to the PI with the modification requests.
2. In accordance with the proper conduct of DMR, the modified protocol was provided to the IACUC as an opportunity to call for FCR and to the DMR for review in the absence of an FCR request. The DMR then conducted their review using the criteria that they could approve, require modifications prior to approval, or ask that the protocol be reviewed following the FCR process. Based on the DMRs assessment of the revised protocol, they granted approval.
3. This process complies with the regulatory expectations for the proper conduct of FCR, DMR, and DMR/S/FCR.

Does GEU's IACUC have an adequate process for ensuring required modifications identified during the FCR process are addressed in a protocol before approval (i.e., were Watson's comments included in the protocol modifications request)?

1. If the IACUC voted to require modifications before approval, then all of the questions or concerns identified during FCR must be sent to the PI for consideration. The initial review of the protocol occurred during the convened meeting, and the points identified during that review constitute required actions.
2. Once the protocol with modification is returned to the DMR(s), the adequacy of the PIs responses to all of the questions or concerns identified during FCR is at the discretion of the DMR(s), providing any member of the IACUC does not ask for FCR.
3. The discrepancy between the concerns raised by Watson and the content of the approved protocol suggests that the GEU IACUC should discuss and formalize its own expectations for DMR/S/FCR.
4. Further, the GEU IACUC may wish to develop an internal business practice that ensures all required modifications identified during FCR are communicated to the PIs as required modifications. This business practice may benefit from including language that further defines the DMRs' responsibility to ensure the required modifications identified during the IACUC FCR are adequately addressed by the PI. As part of the guidance document, GEU's IACUC may choose to remind the DMR(s) that the protocol can be returned to FCR if the DMR(s) questions the adequacy of a response.

GEU is a vehicle for addressing everyday challenges that we all experience. If your institution is challenged with an issue, send us a scenario or an idea and we may include it as part of an upcoming column. ❐

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DMR/S/FCR is working right

The Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR)[1] provides institutions with the ability to conduct DMR subsequent to FCR without the full IACUC being in attendance or carrying the protocol over to the next month.

A WORD FROM THE USDA AND OLAW

In this scenario, Dr. Silverman's protocol undergoes Designated Member Review (DMR) followed by Full Committee Review (FCR) and then another DMR. In the process, the protocol is approved by the second DMR but not all concerns raised during the FCR are addressed in the final approved version.

Under the AWA regulations, the decisions that could be made during FCR are approve, require modifications to secure approval, approval withheld[1], or suspension of an animal activity[2]. The IACUC during FCR can agree to send a protocol to DMR. Under the regulations, DMR decisions are approve, require modifications to secure approval, or request FCR[3]. In this scenario the concerns raised by Dr. Watson about the food restriction were not addressed during the second DMR before approval was given. No details were provided as to why this occurred. As a result, Watson felt the protocol should not have been approved.

Under the AWA regulations, an IACUC member can request FCR of a protocol at any time[3]. In this scenario, the concerned member can request another FCR review, however, requesting a FCR after the PI was notified of approval could be burdensome. Considering this, it would be in the best interest of all parties to work together to address the concerns. In the event the IACUC elects to take no further action, the concerns could be captured in the semiannual report to the Institutional Official as a minority view[4].

Under the PHS Policy, to approve proposed animal activities, the IACUC is allowed to require modifications using either FCR or DMR[5,6]. OLAW's guidance on DMR subsequent to FCR offers the opportunity for the IACUC to expeditiously move the protocol from FCR to DMR and address identified concerns requiring clarification[7,8]. The IACUC Chair is correct in stating that the DMR, once assigned, is acting on behalf of the IACUC to review and approve protocol clarifications identified by the IACUC during FCR. However, it is incumbent on the IACUC in its business practices to ensure that all points for clarification raised during FCR and agreed to by the members present are transmitted to the DMR and the PI for reconciliation. Watson's recourse is to bring his concerns to the full committee and request that the IACUC re-review the protocol[9–12]. If his concerns are not addressed, the PHS Policy allows minority views to be expressed as recommendations to the Institutional Official (IO), or in the semiannual report to the IO, and must be reported in the Annual Report to OLAW[5,13]. ❐

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First, we will need to make the assumption that all the members of the Great Eastern University's IACUC were present or that all members agreed in advance in writing that a quorum of the members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR. Second, Dr. Watson must have a great memory to remember exactly what his concerns where on Dr. Silverman's protocol that he wasn't the DMR on a month or so later.

However, as long as the reviewers designated as DMRs received and reviewed the identical versions of the protocol, then Dr. Crick was correct, the IACUC acted in accordance with the regulations regarding DMR subsequent to FCR. While Watson may not agree with the DMRs decision to not have his concerns addressed, the protocol was approved appropriately.

Crick could offer the following options to Watson regarding his current review of the Silverman amendment:

1. Call the amendment to FCR for discussion of his previous concerns. The IACUC could discuss the reasons why his original concerns were not addressed and if they are still relevant.
2. Continue with the DMR process, but first discuss with the initial DMRs the reasons why his concerns were not addressed. There could have been some discussion between the DMRs and the Principal Investigator (PI) that warranted those concerns not getting addressed at the time of the initial protocol approval.
3. Continue with the DMR process, and just have the PI address the concerns. ❐

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Who is qualified to conduct the review?

Both the OLAW and USDA allow use of Designated Member Review subsequent to Full Committee Review (DMR/S/FCR) when the IACUC determines that substantive information is lacking from a protocol.[1,2] However, use of DMR/S/FCR requires some forethought and planning. In brief, GEU IACUC's use of DMR/S/FCR would have only been valid if one of the following applied:

1. All IACUC members were present at the FC meeting and voted to disposition the protocol to DMR/S/FCR.
2. All IACUC members agreed in advance in writing to allow the quorum of members present at a convened IACUC to unanimously vote to use DMR/S/FCR. If this review method was not already described in GEU Assurance with OLAW, GEU should provide it in their next Annual Report to OLAW.
3. The IACUC FC voted to employ Designated Member Review (DMR) of the protocol, with DMR and approval occurring only after all members of the Committee had the revised research protocol available to them and had the opportunity to request FCR and none had done so.

The next question would be if the designated member reviewer was designated by the Chairperson and qualified to conduct the review.[3,4] In this scenario, it could be interpreted that a qualified IACUC member would have been someone with knowledge of the FCR discussion and an understanding of the critical information that may have been lacking from this protocol to ensure these were addressed during the review.

Once designated, the designated member reviewer has the authority to approve, require modifications in (to secure approval), or request FCR of the protocol. They not obligated to ensure that all IACUC members are satisfied with the final protocol prior to their approval; however, the GEU IACUC is obligated to ensure the review of animal care and use is in accordance with *the PHS Policy*, *Animal Welfare Act/Regulations*, and provisions of *the Guide*. This includes ensuring that animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be euthanized at the end or during the procedure (e.g., humane-endpoints) and personnel conducting animal procedures are qualified and trained.[3–5] The designated member reviewer is the last-step in ensuring the IACUC has appropriately evaluated a protocol and any substantive information should be captured in the protocol, unless captured elsewhere.

We cannot determine that required information was lacking from the protocol, but Dr. Watson is within their authority as an IACUC member to re-review and/or request FCR of the protocol.[1,6] This scenario may have been avoided if the Chairperson designated Watson as a designated member reviewer, if Watson requested FCR of the protocol, and/or if the GEU IACUC had a mechanism to ensure substantive information and/or modifications needed to secure approval identified by the FC is captured during the DMR/S/FCR process. It may be appropriate for the IACUC Full Committee to re-review this IACUC protocol to determine if substantive information was indeed lacking from the protocol and discuss the best approach to resolve this protocol concern and mitigate similar situations in the future. ❐

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