Guidelines for Review and Approval of Animal Study Proposals and Significant Changes

Public Health Service (PHS) Policy on the Humane Care and Use of Laboratory Animals and the Animal Welfare Regulations permit several standard methods of review for Animal Study Proposals (ASPs) and proposed significant changes to previously approved animal activities:

- Full committee review by a convened quorum of the members of an ACUC, or
- Designated member review by one or more members.

Additionally, IC ACUCs have some discretion to establish and use approved policies and guidance documents to define what constitutes a significant change in accordance with OLAW guidance[1] (see ARAC Guidelines Regarding Changes to Animal Study Proposals).

Full Committee Review (FCR):
The standard or default method for review of ASPs and proposed significant changes by the NIH IC ACUCs is through the deliberative process conducted by a quorum of ACUC members during a convened meeting. Copies of or access to new or renewal ASPs or proposed significant changes are distributed to the ACUC members for their review prior to the convened meeting.

ACUC member(s) having a conflict of interest with any ASP or significant change (e.g., Principal Investigator, or animal user) *may* participate in questions and answers regarding the ASP but *must* recuse themselves and leave the room during final deliberation and voting. During that final deliberation, a quorum must still be present to render a decision, however, the member(s) in conflict must not be counted as part of the quorum.

FCR Dispositions:

- Approval;
- Require modifications to secure approval; or
- Withhold approval

Please note that if the ACUC determines that an ASP or significant change is approvable, contingent on receipt of a very specific administrative modification or clarification (e.g., typographical or arithmetic errors, misspellings, incorrect telephone numbers, etc.), the ACUC may handle the issue as an administrative detail that an individual (e.g., ACUC Chair or Coordinator) may verify. While these corrections must be made, additional ACUC review is not required.

Designated Member Review (DMR):
At the discretion of the ACUC Chair, DMR can be used to review ASPs and proposed significant changes in lieu of FCR. The ACUC Chair can propose the use of DMR by providing copies of or access to the ASP or significant change to all ACUC members. If FCR is not requested, at least one member of the ACUC, designated by the ACUC Chair and qualified to conduct the review, can review the ASP or significant change. If more than one member conducts the review, the designated reviewers must all review identical versions of the ASP or significant change and, if

modifications are requested by any one of the reviewers, the other reviewers must be aware of and agree to the request for further modifications.

DMR Dispositions:

- Approval;
- Require modifications to secure approval; or
- Request FCR

Modifications Required to Secure Approval:

When modifications are required to secure approval following FCR, the ACUC may take the following actions:

If **all** members of the ACUC **are present** at the meeting, the ACUC may:

- Vote for FCR, or
- Vote for DMR (vote must be unanimous)

If **all** members of the ACUC **are not present** at the meeting, the ACUC may:

- Vote for FCR, or
- Vote for DMR, if: All ACUC members agree in advance and in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR. Provided that any member of the ACUC may, at any time, request to see the revised ASP or significant change and/or request FCR.

If all members are not present **and** the ACUC lacks the above procedure, the ACUC may:

- Vote for FCR, or
- Vote for DMR, if: All ACUC members, including the members not present at the meeting, must have the revised research protocol made available to them and have the opportunity to call for FCR. If all members of the committee have had the opportunity to request FCR and none have done so, the DMR may then be conducted.

Approval of DMR Process:

The use of the DMR for either review process (i.e., DMR alone, or DMR subsequent to FCR) will be agreed to by the ACUC members, by unanimous consent, and in advance of its use, by one of the following:

1. Establishing and approving an ACUC procedure on DMR which follows these guidelines, or
2. Documenting the acknowledgement and approval of these guidelines as the standing ACUC procedure. Once approved, the ACUC does not have to re-approve this guidance as new members are added; however new members must be informed of this and all standing ACUC procedures when they join the committee.

ASP Deliberations:

Description of Procedures - The ASP must present a clear description of the animal procedures. This standard can be met through language in the protocol, simple flow charts or diagrams, and

through deliberations by the ACUC during review. The ACUC composition, which meets PHS Policy standards, ensures a well-rounded, knowledgeable committee that represents the interests of scientific, animal welfare, and local communities. Such a committee can collectively ensure the procedures are understood and animal welfare concerns are discussed and addressed.

Use-Benefit Analysis – As the impact of the proposed procedures on the animal's well-being increases, the ACUC must decide if the benefits of the study to medicine and science outweigh the costs to the animal's well-being by using the ASP's explanation of procedural alternatives that have been considered, number and justification of animals required, experimental refinements, and other factors upon which to base their decision. This analysis should be performed prior to the final approval of the ASP and should be a primary consideration in the review process. ASPs with procedures that have the potential for more painful or distressful adverse effects, such as column E procedures, may deserve more discussion and significant analysis by the Committee. Deliberations should be documented in the ACUC minutes or the comments provided to the investigator for incorporation into the revised/final ASP.

Scientific Merit - ACUCs do not judge the scientific merit of the study. Judgments concerning the merits of the science are performed through the programmatic reviews by NIH Institutional Boards of Scientific Counselors and other scientific review boards appointed by the scientific directors or their representatives. These boards review research programs and proposals for their scientific merit and appropriateness of attaining an answer to a study question. The Branch/Lab Chief/Scientific Director signs all ASPs as a certification of their approval of the ASP's scientific merit.

Final Approval:
Following ACUC review, approval, and collection of all required signatures, the ACUC Chair signs and dates the ASP or significant change. This denotes the approval date and finalization of the approval process. Animal ordering and initiation of animal activities described in that ASP or significant change can then proceed.

References:
- Animal Welfare Act and Regulations
- Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), 2015
- Guide for the Care and Use of Laboratory Animals; National Research Council, 2011.
- Office of Laboratory Animal Welfare 'Frequently Asked Questions' webpage regarding: 1) methods of ACUC approval; 2) use of Designated Member Review; 3) methods for conducting post approval monitoring; and 4) scientific merit review for protocols.
- AAALAC International Frequently Asked Question regarding harm-benefit analysis.
- OLAW NOT-OD-09-035: Guidance to IACUCs Regarding Use of Designated Member Review for Animal Study Proposal Review Subsequent to Full Committee Review
- [1]OLAW NOT-OD-14-126: Guidance on Significant Changes to Animal Activities

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