

Guideline for Review, Approval, & Post Approval Monitoring of Animal Study Proposals Including Designated Member Review

In the NIH Animal Study Proposal review process, Animal Care and Use Committees (ACUC) do not judge the scientific merit of the study. Judgments concerning the merits of the science as well as the potential advances/benefits of the studies are performed through the programmatic reviews by the NIH Institutional Boards of Scientific Counselors that provide expert review of the laboratory's programs, including the merits of the proposed research. The Branch/Lab Chief/Scientific Director plays a role in this review and their required signature on all ASPs attests to the appropriateness of conducting the study. The ACUC is responsible to assure that the scientific review process has been completed.

Public Health Service Policy on the Humane Care and Use of Laboratory Animals and the Animal Welfare Regulations permit only two methods of Animal Study Proposal and proposed significant changes review:

- 1) Full committee review at a convened meeting of the Animal Care & Use Committee
- 2) Designated member review *in lieu* of FCR at a convened meeting

Definitions:

ACUC – Animal Care and Use Committee

ASP – Animal Study Proposal

AWR – Animal Welfare Regulations

Conflict of interest – principal investigator and animal users listed on the ASP

DMR – Designated Member Review

FCR – Full Committee Review

Guide – Guide for the Care and Use of Laboratory Animals

PHS Policy - Public Health Service Policy on the Humane Care and Use of Laboratory Animals

Minor administrative changes - typographical or arithmetic errors, misspellings, incorrect room or telephone numbers, etc., are not considered substantive. While these corrections must be made, additional ACUC review is not required.

Substantive information - the information the ACUC needs to evaluate the proposal for humane animal care and use in accordance with the requirements of the PHS Policy at IV.C.1., and in adherence to provisions of the Guide.

Quorum – greater than 50% of the voting members (VM), i.e. VM of 8, need 5; VM of 7, need 4

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. 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 should weigh the procedures of the study against potential animal welfare concerns in accordance with the study description of alternatives that have been considered, justification of the number of animals required and experimental refinement. Protocols with procedures that have the potential for more painful or distressful adverse

effects, such as column E procedures, may garner more discussion 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.

Full Committee Review at a Convened Meeting:

The standard or default method for review and approval of ASPs by the NIH ACUCs is through the deliberative process during convened meetings. For those meetings, a quorum must be present for the ACUC to conduct business. Copies of or a list of new or renewal ASPs or proposed significant changes are distributed to the ACUC members for their review prior to the convened meeting. The members are asked to identify ahead of time any ASPs which they feel must be reviewed and deliberated only by FCR. It is further understood that any ASP initially subjected to FCR may require modification and the adequacy of that modification may be assessed by either: (1) return of the modified ASP to the full committee, or (2) in the absence of a call for FCR, return of the modified ASP to the DMR process (detailed in Appendix 1).

ACUC members having a conflict of interest with any particular ASP (or proposed significant change) may participate in questions and answers regarding the ASP, but must recuse themselves during deliberation and voting on that action. During that deliberation, the member(s) in conflict of interest must not be counted as part of the quorum, which must still be present to render a decision.

Designated Member Review In Lieu of a Convened Meeting:

When an expedited review is required, DMR can be proposed by the ACUC Chair. The Chair appoints at least one member of the ACUC, who is qualified to conduct the review, and who shall have the authority to approve, require modifications (to secure approval) or request FCR of those research proposals or significant changes. Implementation of this form of the DMR process is detailed in Appendix 2.

Approval of Designated Member Review Use:

The use of the DMR process for either review process (i.e. FCR + DMR or DMR alone) will be agreed to by the Committee members, by unanimous consent, and in advance of its use, by one of the following: 1) establishing and approving an ACUC standard operating procedure on DMR which follows these guidelines or 2) by acknowledgement and approval of this ARAC Guideline which is then documented in the IC ACUC's minutes as part of their permanent records. Once established the ACUC does not have to re-approve this process as new members are added; however new members should be informed of this and all standing ACUC procedures as they join the Committee.

Disposition of ASP Deliberations:

- Approved [Note: administrative changes can be made]
- 'Tabled' or 'Modifications required to secure approval', if substantive changes are needed
- Disapproved

The intermediate disposition (i.e. 'tabled' or 'modifications required to secure approval') requires a decision from the Committee as to whether the revised protocol will be further reviewed via DMR or FCR (either method is acceptable).

Final Approval:

Chair signs and dates the ASP or proposed significant change. This denotes the date and finalization of the approval process. Animal ordering and initiation of animal activities described in that ASP/amendment can then proceed.

If an IACUC uses DMR, the approval date is the date that the designated member(s) approve the study.

Post Approval Monitoring:

Continuing ACUC oversight of animal activities is required and can be accomplished through a variety of mechanisms. Monitoring animal care and use is required by the PHS Policy, but the Policy does not explicitly require specific post approval monitoring (PAM) procedures to compare the practices described in approved protocols and SOPs against the manner in which they are actually conducted.

ACUCs are charged, however, with program oversight and as such are responsible for program evaluations, annual and triennial reviews of protocols, reporting noncompliance, ensuring that individuals who work with animals are appropriately trained and qualified, addressing timely reports from investigators of adverse or unanticipated events and addressing other concerns involving the care and use of animals at the institution. The veterinarian with program authority and responsibility for animal activities along with the animal care and technical staff, add another important level of program supervision.

Related components of the NIH intramural animal program provide monitoring by a multi-disciplinary team of individuals. Examples of such components include daily observation of animals by trained animal care personnel and communication to the veterinary staff for follow-up, facility monitoring by facility management personnel, post-operative care by trained personnel, evaluation of outcomes of animal procedures by investigators and staff, hands-on training in animal procedures, and appropriate reporting of incidents involving occupational health and safety. All of these functions and responsibilities constitute monitoring of the NIH intramural animal programs.

References:

Animal Welfare Regulations (AWRs) – Regulations promulgated by the United States Department of Agriculture, Animal and Plant Health Inspection Service, pursuant to the authority in the Animal Welfare Act, 7 U.S.C. 2131, et seq. and contained in 9 CFR, Parts 1, 2 and 3 (http://www.aphis.usda.gov/animal_welfare/downloads/awr/awr.pdf)

Public Health Service Policy (PHS Policy) - Public Health Service Policy on Humane Care and Use of Laboratory Animals, revised August 2002, or subsequent editions.
(<http://grants.nih.gov/grants/olaw/references/phspol.htm>)

[Guide for the Care and Use of Laboratory Animals](#); National Research Council, 2011

Office of Laboratory Animal Welfare '[Frequently Asked Questions](#)' webpage:

- For additional information regarding methods of ACUC approval refer to: [What are the possible methods of IACUC approval.](#)
- For additional information regarding substantive changes and the use of DMR, refer to: [May an IACUC use designated member review \(DMR\) to review an animal study protocol subsequent to full committee review \(FCR\) when modifications are needed to secure approval?](#)
- For additional information regarding post approval monitoring refer to: [Is post approval monitoring required?](#)
- For additional information regarding scientific merit review refer to: [Is the IACUC responsible for judging the scientific merit of proposals?](#)

Association for Assessment and Accreditation for Laboratory Animal Care, Int'l '[Frequently Asked Questions](#)' webpage:

- For additional information regarding use-benefit analysis refer to: http://www.aaalac.org/accreditation/faq_landing.cfm#B3

Approved - 12/11/02

Revised – 05/16/07; 09/08/10; 05/09/12

Appendix 1: Full Committee Review and Subsequent Designated Member Review

PHS Policy and the AWR require that copies or a list of each of the proposed ASPs or proposed significant changes are distributed to the each ACUC member prior to the convened meeting. In this case, it is the 'default' understanding by that ACUC that those ASPs or proposed significant changes are intended for discussion and probable vote by the convened ACUC at the upcoming meeting. The members are asked to identify ahead of time any ASPs or proposed significant changes which they feel must be reviewed and deliberated only by the FCR process (i.e., cannot be shifted to DMR). Since the Committee members must be informed of all agenda items prior to the convened meeting, this usually precludes bringing additional ASP or significant changes to the meeting as last minute items for consideration.

Following discussion by the convened quorum, the ACUC may agree that an ASP or proposed significant change is not ready for final approval as presented because the proposal lacks substantive information, and therefore decides additional information/clarification must be furnished before final approval can be granted. In that case, the Chair may suggest the use of the DMR process. If the DMR process is *unanimously* accepted (i.e. no call for FCR), the Chair will identify the designated reviewer(s). If the ACUC has 'standing' DMR reviewers, the Chair will inquire if any other members also wish to participate.

Following receipt of the additional information and/or clarifications, the designated reviewer(s) can: (1) grant final approval for that ASP or proposed significant change; (2) request further information/clarification (to secure approval); or (3) return the ASP or proposed significant change back for FCR. The decision for approval or further information must be made unanimously or the proposal must come back for FCR. The designated reviewers must all review identical versions of the protocol and, if modifications are requested by any one of the reviewers, the other reviewers must be aware of and agree to the modifications.

Appendix 2: Designated Member Review In Lieu of a Convened Meeting (FCR)

- The submitted ASP or proposed significant change is pre-reviewed to assure its readiness for consideration for designated review - submitted ASP determined to adequately address U.S. Government Principles, PHS Policy and the Guide standards.
- The ACUC Chair decides if the ASP or proposed significant change is ready and should be proposed for review by the designated review.
- The ACUC Chair appoints, unless pre-defined by ACUC policy, the DMR reviewer(s).
- All ACUC members then receive a copy of the ASP or proposed significant change to be reviewed, accompanied by the name(s) of the proposed DMR reviewer(s).
- The ACUC members are given five work days (or a sufficient time set by the ACUC) to respond back to the Chair/APD/ACUC Coordinator and indicate one of two dispositions for that ASP or proposed significant change:
 - 1) All members or a quorum of members respond to the request and have no objections to that particular proposal being reviewed and potentially approved by the DMR process. [Note: If all members respond prior to the 5 *day* period; the DMR reviewers can proceed at that point.]
 - Comments for the designated reviewers to consider may be provided, but they cannot be listed as contingencies for the document's approval.
 - 2) One or more members call for FCR for that particular proposal.
- Following receipt of responses from the ACUC members the DMR reviewer(s) reviews the proposal and can:
 - 1) Grant final approval for that ASP or proposed significant change; (2) request further information/clarification (to secure approval); or (3) return the ASP or proposed significant change back for FCR. This must follow the same requirements as listed in Appendix 1 for the DMR process.