

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

In the NIH Animal Study Proposal (ASP) 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 ASP template provides a signature block for the Branch/Lab Chief/Scientific Director's signature as acknowledgement of this review.

Public Health Service (PHS) 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:

- Full Committee Review (FCR) at a convened meeting of the Animal Care & Use Committee
- Designated Member Review (DMR) *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 changes - typographical or arithmetic errors, misspellings, incorrect room or telephone numbers, etc., as defined by the ARAC [Guideline Regarding Significant Changes to Animal Study Proposals](#) and companion IC ACUC policies and SOPs. While these corrections must be made, additional ACUC review is not required.

Significant changes – as defined by the ARAC [Guideline Regarding Significant Changes to Animal Study Proposals](#) and companion IC ACUC policies and SOPs

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. A query regarding the ASP or significant change is sent to the full committee with instructions regarding the DMR process with a request to proceed. Implementation of this form of the DMR process is fully 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 are informed of this and all standing ACUC procedures as they join the Committee.

Disposition of ASP Deliberations:

- Approved [Note: minor changes can be made with this status]
- 'Tabled' or 'Modifications required to secure approval', if significant/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.

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 standard operating procedures (SOP) 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 Act and Regulations, 9 CFR, Parts 1-3](#) –
- [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](#).

Approved - 12/11/02

Revised – 05/16/07; 09/08/10; 05/09/12; 03/03/13; 10/08/14; 01/25/17

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, and they have called for modifications to secure approval as the outcome of their deliberations, 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 (DMR) 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, the DMR reviewer(s), unless pre-defined by ACUC policy.
- 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), unless the DMR reviewers and/or standing issues are defined in written standard procedures/ACUC policy.
- The ACUC members are given sufficient time, e.g. 2-5 days (which is set by the ACUC), to call for full committee review. When that timeframe has been met, and in the absence of one or more members calling for full committee review, the DMR can proceed. Comments for the designated reviewers to consider may be provided, but they cannot be listed as contingencies for the document's approval.
- The DMR reviewer(s) can:
 - Grant final approval for that ASP or proposed significant change;
 - Request further information/clarification (to secure approval); or
 - Return the ASP or proposed significant change back for FCR.

The decision for approval or request for further information must be made unanimously by the reviewers 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.