

Helpful Hints for Completing the Frederick National Lab Animal Study Proposal Form

The goal of the [Frederick National Lab Animal Care and Use Committee](#) [ACUC] is to promote the well-being of research animals and to ensure that investigators obtain reliable scientific data for their research endeavors. The ACUC has developed these helpful hints in an effort to assist investigators with the Animal Study Proposal [ASP] submission process. Before writing the ASP, the ACUC strongly encourages investigators to consider the following to ensure timely ASP review and processing:

- Take a look at the [Frederick National Lab Animal Care and Use Committee](#) website for assistance and reference materials
- Discuss the project with the [facility manager and technical staff](#) to ensure that the resources are available to support the study
- Be sure to download the most current version of the [Frederick National Lab Animal Study Proposal Form](#)
- Discuss the project with the [LAM veterinary staff](#) regarding the use of anesthetics and analgesics, proposed surgical procedures, preoperative and postoperative care, and/or necessary training that may be required for the study
- Review the current [ACUC Guidelines](#) to ensure applicable refinements and recommendations are incorporated into the text of the proposal submission
- If interested in using imaging technology in conjunction with the study, please discuss the project with the Director of the Frederick National Lab Small Animal Imaging Program [kalenj@mail.nih.gov] in advance of proposal submission
- Please send the proposal submission [signature pages can be submitted by interoffice mail, fax, or e-mail] by e-mail to stahlam@mail.nih.gov. Please be sure to include any appendices, tables, and references with the submission.
- If there are any questions or concerns, feel free to contact the ACUC Office [301-846-7544 or stahlam@mail.nih.gov] for guidance and assistance

SECTION A – ADMINISTRATIVE DATA

- Please be sure to complete all blanks in Section A
- Ensure that all individuals working on the study [including LASP and dedicated technicians] are listed here
- List all of the procedures they will be performing [to include tail clipping, injections, blood collections, surgical/experimental procedures, euthanasia, etc.].
- List their relevant experience [# of years] for the procedures that they will perform under this study

- Please be sure that all individuals listed have taken one of the following courses: [1] [The Animal Care and Use Introductory Online Training](#) course or [2] [NIH Office of Animal Care and Use Training Course](#).

SECTION B – ANIMAL REQUIREMENTS

- Please be sure to complete all blanks in Section B
- For multi-species proposals, please be sure to provide a breakdown of the animal numbers by species for each year
- Please be sure to check the math
- Please be sure that the total number of animals requested under Section B, matches those outlined in Sections D, E, and G [as applicable]

SECTION B1 – INSTITUTIONAL BIOSAFETY COMMITTEE

- This section was designed to ensure appropriate coverage by the Institutional Biosafety Committee [IBC] for studies proposing the use of transgenic/knock-out animal models, Recombinant DNA, transfected cell lines, human or other primate tissues or cell lines, or potentially infectious materials
- The ASP is not permitted to be released for approval until the necessary IBC registration documents have been secured. Therefore, if proposed work involves any of these materials, please contact the IBC Office [301-846-5860] in advance to ensure that the work is in compliance with safety requirements and to alleviate potential delays in the ASP approval.
- Please refer to the [Institutional Biosafety Committee](#) web page for additional guidance.

SECTION C – STUDY OBJECTIVES

- Describe the objectives of the research activities
- Describe the important benefits and/or outcomes expected as a result of performing this research project
- For support service studies, provide an overview of the service and for whom the services will be performed
- Use lay language; this section should be easily understood by the average high school student
- Define all abbreviations and acronyms

SECTION C1 – PROGRESS TO DATE

- This section must be completed for all renewals
- Briefly describe the study progress to date
- Provide a list of publications, abstracts, and presentations resulted from data generated on the study
- Include what research aims have been completed and the number of animals used in the previous proposal

SECTION D – RATIONALE FOR ANIMAL USE

- Explain why a non-animal model [i.e., in vitro, chemical technique, computer simulation, etc.] cannot be used to fulfill the research objectives
- Explain why a less sentient animal species cannot be used for this study

- Explain why the animal model/strain selected is being used for this study [i.e., unique characteristics, etc.]
- Provide a mathematical calculation to justify the number of animals requested in Section B [tables and charts are highly recommended to outline the procedures and the associated numbers]. Please be sure that this number matches those outlined in Sections E and G [as applicable].
- For breeding studies, please be sure to include the number of breeders, the breeding scheme used, the number of offspring expected [% of correct genotype as applicable], etc.
- Refer to the [LASP Animal Numbers for Research Calculator](#) for assistance with calculating the number of animals required for the breeding study
- As an alternative to in-house [Monoclonal Antibody Production](#), please check out the [Developmental Studies Hybridoma Bank](#) website. This site was established under the auspices of the National Institute of Child Health and Human Development to supply investigators with monoclonal antibodies at cost

SECTION E – DESCRIPTION OF EXPERIMENTAL DESIGN AND ANIMAL PROCEDURES

Only procedures on live animals that have been approved by the Frederick National Lab ACUC in advance are permitted to be conducted. Conducting procedures that have not been listed in an approved ASP form* can result in the suspension of animal activities. Section E is where all the procedures that live animals will undergo in the study will be described. This includes, but is not limited to the following:

- Breeding details [scheme, breeder endpoints, endpoints for offspring not required for studies, genotyping, compliance with SOP 3.021]
- [Blood withdrawals](#) [volume, site, frequency, max number a single animals will undergo]
- [Injections/Treatments](#) [substance, volume, route, dose based on body weight as applicable]
- [Tailclipping](#) [anesthesia is required for re-tailclips]
- Sample collections
- Monitoring frequency for health issues [daily]
- [Tumors](#) [location, observation, palpation/measurement frequency, maximum burden]
- [Endpoints](#) [experimental and humane]
- Diets [manufacturer sheets should be provided]
- Body Weights [indicate frequency]
- [Anesthesia](#) [details to be provided in Section H]
- Imaging [a SAIP imaging request form will be required prior to approval]
- Radiation
- [Surgical Procedures](#) [details to be provided in Section F]
- Restraint method
- Resultant effects
- Potential adverse effects [please provide clinical descriptions for the veterinary and technical staff]
- [Deleterious phenotypes](#)
- [Euthanasia](#) [details to be provided in Section I]
- Maximum period of time a single animal remains under the study
- Please check the applicable [ACUC Guidelines](#) that will be followed in conjunction with the study
- Please check the applicable methods of identification that will be used
- If animal numbers have been outlined in this section, please ensure that they match those proposed in Sections B, D, and G

* If during the course of the study, if the investigator and/or technical staff determine that [changes, refinements, additions, etc.](#), are required, a [modification](#) MUST be submitted to the Frederick National

Lab ACUC and receive approval before proceeding. Modifications include, but are not limited to changes in personnel, strains to be used, diets, injection volumes, route of injections, doses of agents, blood collections, changes/additions of procedures specific to the study, facility location, increase in the number of animals to be used, method of euthanasia, etc.

SECTION F – CONDUCTING SURGICAL PROCEDURES

- Surgical preparation
- [Sterilization/Aseptic techniques](#)
- [Anesthetics](#) used [agent, volume, dose, route]
- Incision details [size, location]
- Procedure details/approach
- Wound closure [and removal]
- [Analgesics](#) used [agent, volume, dose based on body weight as applicable, route]
- [Post-operative care](#) [individual responsible, special housing, maintaining body temperature]
- Personnel experience
- Location where surgery will be performed
- Please contact the [LAM veterinary staff](#) in advance [301-846-5577] if proposing to conduct major survival surgery

SECTION G – PAIN, DISTRESS, GENERALIZED DISCOMFORT

- Any animal receiving an [anesthetic](#) or [analgesic](#) must be listed under Category 2 [unless used for restraint purposes only]
- If conducting a study for which animals are placed in [Category 3](#), a literature search is required to demonstrate that [alternatives](#) to procedures that may cause more than momentary pain, distress, or generalized discomfort have been considered
- The literature search statement must include the database[s] searched [at least two], the date of the search, the period covered, and the keywords that were used
- For [Category 3](#), scientific justification for performing the proposed procedure and a description of considerations to alternative procedures and why they cannot be utilized in this study must be included
- Please ensure that the total number of animals outlined in this section match those proposed in Sections B, D, and E [as applicable]

SECTION H – ANESTHESIA, ANALGESIA, TRANQUILIZATION

- Agents used
- Volume
- Route
- Dose [based on body weight as applicable]
- Frequency

SECTION I – METHOD OF EUTHANASIA OR DISPOSITION

- Please be sure to utilize the appropriate method [species and/or age specific]

- If using CO₂, please indicate the source [gas cylinder, in-house line, etc.]
- Please refer to the ACUC [Guidelines for Euthanasia of Rodents](#)
- If using cervical dislocation in mice, please provide scientific justification, indicate the individual performing the procedure and their experience
- If [PHL](#) services may be utilized, list additional known methods of euthanasia that may be performed by PHL staff [i.e., terminal perfusion under anesthesia]

SECTION J – HAZARDS

- This section was designed to inform the animal facility staff of potential hazards associated with the research study
- Complete Sections I and II as they relate to human health hazards
- Attach all Material Safety Data Sheets, Recombinant DNA Documents, and/or Human Pathogen Registration Documents

SECTION K – BIOLOGICAL MATERIALS AND ANIMAL PRODUCTS

- List all materials that are to be used in the study [tumors, cell lines, matrigel, collagenase, rodent derived antibodies, natural cytokines, any other unpurified or nature materials/rodent by products]
- Include copies of all [MTBM Results](#)
- It is recommended that test results [greater than 10 years old](#) for lines that have not been used recently be submitted for re-testing
- All human tumor cell lines must be manipulated according to Biosafety Level 2 [BSL2] practices
- If using synthetic materials, please provide the manufacturer sheet that indicates that no murine products were involved in the making of the material and/or the purification process
- Indicate if lines have been manipulated in any way [i.e., transfected]; this may prompt additional testing requirements.

SECTION L – TRANSPORTATION

- Verify that all transportation will be in accordance with [approved policies and procedures](#)
- List all locations [Building and Room] where live animals will be transported
- Provide details on the procedures to be performed at that location [i.e., tissue collection]
- State the time point and method of euthanasia [i.e., within 6 hours by CO₂]
- If transporting to Bethesda, please provide the NCI-Bethesda proposal that covers the work
- List the individual responsible for care in the new location
- If applicable, refer to the [ACUC Policy on Transportation of Newborns](#)

SECTION M – SPECIAL CONCERNS AND ENVIRONMENTAL ENRICHMENT

List all of the special requirements of the study, this includes [but is not limited to]:

- *Special caging*
- *Special diets*
- *Treated water or feed*
- *Fasting*

- *Exceptions to ACUC Guidelines*
- *Biohazard waste disposal*
- *Body weight measurement frequency*

For environmental enrichment, please check the appropriate boxes for singly housed and group housed animals.

SECTION N – INVESTIGATOR CERTIFICATIONS

This section is where the investigator certifies the following:

- All individuals listed under Section A have taken one of the following courses: [1] [The Animal Care and Use Introductory Online Training](#) course or [2] [NIH Office of Animal Care and Use Training Course](#)
- All individuals under Section A are adequately trained to perform the procedures proposed in the study
- The proposed work is NOT duplicative
- That the literature has been reviewed to confirm that there are no [alternatives](#) to procedures that may cause pain and/or distress to the animals
- That staff are enrolled in the appropriate occupational health and safety surveillance programs
- That if changes are required to the study, that a [modification](#) memorandum is submitted in advance to the ACUC for review and approval
- That animals used in the study are in compliance with the [Technology Transfer Branch](#) requirements

SECTION O - ANIMAL AUTHORIZATION DISPOSITION

- Complete this form in its entirety
- List all adverse clinical symptoms and/or signs that the technical and veterinary staff should be aware of in relation to the study
- Please provide at least two contact names with their cell/home/pager numbers
- Please specify what is to be done with the animal prior to or after euthanasia [i.e., bleeding, collect specific tissues, necropsy, refrigerate, etc.]

SECTION P – LAB/BRANCH CHIEF CONCURRENCE

- The Principal Investigator is not permitted to sign this section
- The PI lab/branch chief or division director MUST sign this section

ASP SUBMISSION/REVIEW PROCESS

After the ASP is submitted to the ACUC office, it is assigned a number and added to the ACUC meeting agenda for review. A copy is then sent to the Environment, Health, and Safety (EHS) representative for review, comment, and signature. It is also checked for proper Pathogen Registration, rDNA registration, and radiation program registration, if required.

A copy is simultaneously sent to the respective Animal Facility Manager(s) for resource/space review and signature (i.e., is there sufficient space to house these animals? Is the required technical expertise

available? Are there any anticipated problems?). The Animal Facility Manager also works with EHS to ensure that if any hazards exist, that the appropriate facility staff members are informed and trained and then sign Section J (Hazardous Agents) as well as receive a copy of the approved ASP upon release.

A copy is simultaneously sent (as applicable) to the Institutional Biosafety Committee (IBC) office for review and approval.

The form is also reviewed by the ACUC Coordinator and the Attending Veterinarian. Requests for clarification or further explanation on any items relating to animal care and use are addressed (by e-mail) with the investigator at this time. Upon receipt of acceptable responses, the Attending Veterinarian signs the ASP form.

A complete copy of the ASP (with incorporated clarifications as required) and subsequent email correspondence with the Principal Investigator is delivered to the ACUC members one week in advance of the ACUC meeting. One member is identified as the Primary Reviewer to obtain additional clarifications and to present each study to the Committee at the meeting.

After review at a convened ACUC meeting, an ASP may then be:

- Approved or (Approved with clarifications): Minor clarifications are requested of the Principal Investigator by the Primary Reviewer (i.e., need to append copies of Mouse Antibody Production tests; further justification of animal numbers; need further definition of experimental endpoints, etc.). Once the Primary Reviewer, Attending Veterinarian, and Chairperson are satisfied that the indicated condition has been resolved, the ASP is released for final approval.
- Approved with stipulation: The ACUC requests that the LAM veterinary staff observe a procedure in advance of initiation of the study (i.e., intracranial injection procedure) and/or the completion of a pilot study. Once LAM is satisfied that the stipulated requirement has been fulfilled, the study is released for final approval. LAM reports to the ACUC its findings on a monthly basis as part of the post-approval monitoring process. If LAM is not satisfied with a procedure and/or technique, the ACUC will discuss the issue at a convened meeting and determine how to proceed (i.e., require additional training, request refinements to a procedure, etc.).
- Deferred: Additional clarifications are requested of the Principal Investigator by the Primary Reviewer. Upon receipt of the clarifications from Principal Investigator, the proposal is either reviewed during a regularly scheduled ACUC meeting or via designated member review.
- Not Approved: The ASP is returned to the Principal Investigator for resubmission with notification of non-approval status and recommendations for improvement.

After the ACUC meeting, an email is sent to the Principal Investigator to communicate the approval status of their reviewed ASP. Principal Investigators are strongly encouraged to contact their Primary Reviewer to resolve any outstanding clarifications.

**ELECTRONIC COPIES OF THE ASP SHOULD BE SENT TO STAHLAM@MAIL.NIH.GOV
COPIES OF THE APPLICABLE SIGNATURE PAGES CAN BE SENT BY MAIL OR FAX
THE ACUC HAS IMPLEMENTED [PROPOSAL SUBMISSION DEADLINES](#)
FOR QUESTIONS, PLEASE CONTACT THE ACUC OFFICE AT 301-846-7544**