NCI-Frederick ACUC Guidelines and Recommendations made at Committee Meetings (June 1998 – December 2007)

ANALGESICS, ANESTHESIA & EUTHANASIA

Post-surgical anesthesia is required in any instance where a body cavity is invaded [5/99].

The *2000 Report of the AVMA Panel on Euthanasia* has recently been released. Following are the changes from the previous edition: Decapitation is considered conditionally acceptable. Scissors used for decapitation must be sharp, in good working order and maintained specifically for that purpose. It is recommended that scissors be sharpened or replaced twice yearly. Facilities must be able to document that they meet the guidelines. The use of dry ice is no longer considered an acceptable source of CO2 for euthanizing animals. Compressed CO2 gas must now be used. A subcommittee was formed to facilitate compliance with this new guideline by the May 1, 2001 deadline [4/01].

The ACUC determined that the following procedure will be followed for studies requesting cervical dislocation as a method of euthanasia: [a] When the procedure is conducted in a NCI-Frederick Animal Facility: the investigator must state which individual[s] will conduct the procedure and his/her experience. Based on the attending veterinarian's knowledge of the staff performing the procedure, she will either approve the individual to conduct the procedure or she will observe the individual performing the procedure prior to approval; or [b] when the procedure is conducted in a laboratory setting: the investigator must use CO_2 unless they can scientifically justify the need for cervical dislocation and the ACUC will determine if the justification is adequate for approval [7/02].

Previously any animal that underwent anesthesia for any reason [including restraint] was placed in Pain/Distress Category 2. It was noted by the ACUC that placing these animals into Pain/Distress Category 2 is misleading. The NCI-Frederick is required to report annual usage by Pain/Distress Category to the USDA for regulated species. While the NCI-Frederick does not currently house regulated species, it was noted that the data should be categorized accurately. Therefore, any animal sedated for restraint purposes will be placed in Pain/Distress Category 1 [6/05].

The NCI-Frederick *Guidelines for Euthanasia of Rodents* was revised and approved to reflect the results of the LAM euthanasia study [5/04, revised 3/05 and 10/05].

MAP TESTING

A. All cell lines to be injected into rodents at NCI-Frederick will be MAP tested prior to use. Cell lines that originated from animals at Frederick and have never left Frederick are exempted from this requirement.
B. Any biological material of rodent origin will be MAP tested prior to its use in animals at NCI-Frederick. Material from the same lot will not require a second MAP test, BUT the same material from another lot will require another MAP test.
C. Murine recombinant proteins grown in non-mammalian cells will not need a MAP test. However, if grown in mammalian cells, a MAP test will be required.

D. Investigators are encouraged to submit information as to the method[s] of purification of any biological material to be injected into animals in order to aid the ACUC in determining if the purification procedures are virucidal.
E. MAP testing of human tissues of primary origin is encouraged, but is not mandatory [5/99].

The document *Biological Material Risk Factors* was disseminated to investigators as a reminder regarding testing requirements and recommendations [12/02].

The NCI-Frederick *Testing Requirements for Biological Materials Proposed for Use in NCI-Frederick Animal Study Proposals* was approved [7/07].

ANIMAL STUDY PROPOSALS

Blanket proposals: According to Dr. Nelson Garnet at the OPRR, blanket breeding proposals were in compliance with OPRR policy. Therefore, Frederick will continue to approve such proposals.
Blanket proposals for experimental use of animals were not recommended. The Committee voted in favor of requiring that, for proposals covering the production of polyclonal and/or monoclonal antibody, each investigator completes sections A,B,C,D and O for his/her specific requirement while the other sections could be of a blanket nature [6/98]. A method for individually tracking modifications to blanket proposals was presented and the Committee recommended that it be instituted [4/01].

In response to an AAALAC inspection suggestion that ACUC members be more actively involved in interacting with the investigator concerning questions and concerns about an ASP, as opposed to having the Facility Veterinarian obtain all of the answers, effective immediately, the assigned primary reviewer would become responsible for obtaining answers to all questions and concerns about an ASP. The ACUC member should try to anticipate and obtain answers prior to the meeting at which the ASP is discussed. However, they will also be responsible for obtaining answers to any questions raised during discussion of the ASP at the ACUC meeting [6/99].

It is the responsibility of the Principal Investigator to ensure that all investigators added to protocols are fully aware of the details and limitations of the work [8/99].

An electronic version of the NCI-Frederick *Animal Study Proposal* form will be put on the web and the NCI-Frederick animal users referred to this site for the new form [4/00].

The *Primary Reviewer's Summary and Recommendation* form will be put into use. Completed forms will be attached to the proposals [6/00, revised 2/03 and 5/06].

Approved proposals which exceed their animal numbers: The Principal Investigator, the Facility Manager and the LASP/ACUC Office should share equally in the responsibility of tracking animal numbers. The ACUC has recently instituted a system to identify when the approved animal numbers on the ASP's have reached 80% using information accessed from the Animal Information System [AIS] database. The office can then notify the PI so that if additional animals are required an amendment can be submitted for ACUC approval prior to reaching the 100% mark [10/00].

A tracking system [e.g. MS Excel database] will be developed to track the rabbits ordered in on the blanket polyclonal antibody production ASP to their respective PI and animal study

proposal number. As the current AIS database cannot be programmed to lock out animal orders on ASP's that have exceeded the approved numbers, a tracking system can be used to alert the LASP office and prevent approval of these orders. The PI can then be contacted and submission of a modification to their ASP requested. Once ACUC approval for additional animals is granted, the rabbits can be ordered [10/00].

The *Facility Space and Resource Review* sheet was developed to ensure that facility managers review resources and space issues prior to ACUC review [6/02, revised 2/03].

The ACUC approved the *Annual Review Notification and Statement Form* to comply with the Animal Welfare Act annual review requirement [8/02].

The *NCI Animal Study Proposal* form was revised to reflect administrative changes and to incorporate the additional information required for transportation from Frederick to Bethesda [9/02].

The *NCI Animal Study Proposal* form was revised to reflect environmental enrichment considerations [2/03, revised 7/03].

The *NCI Animal Study Proposal* form was revised to include an individual's experience in Sections A and F, as well as the new *Animal Disposition Authorization* form [7/03].

The *NCI Animal Study Proposal* form was revised to incorporate the LASP Right-to-Know Checklist into Section J of the form [8/03].

The *NCI Animal Study Proposal* form was revised to ensure consistency with the *Guidelines for Classifying Category 3 Procedures on Animals* [4/04].

The *NCI Animal Study Proposal* form was revised to include Section *B1 – Transgenic Animal Models* to address potential health risks to humans working with these animal models. The *Recombinant DNA in Animal Models* overview was posted on the ACUC website in conjunction with this form revision. If applicable, this section is forwarded to the NCI-Frederick Institutional Biosafety Committee for review/action [8/04].

The *NCI Animal Study Proposal* form was revised to include intellectual property issues as requested by the NCI Technology Transfer Branch [12/04, revised 5/05].

The *NCI Animal Study Proposal* form was revised to include information pertaining to core/service facilities in Section C [4/05].

The *NCI Animal Study Proposal* form was revised to include hyperlinks to various guidelines, recommendations, etc., as well as to include minor revisions to Sections B1, C, D, E, K, L, N, and the *Animal Disposition Authorization* form [5/05].

The *NCI Animal Study Proposal* form was revised to include deadline information and other typographical inclusions [10/05].

The *NCI Animal Study Proposal* form was revised to include ACUC guidelines, adverse effects, health monitoring, and administrative inclusions [3/06].

The *NCI Animal Study Proposal* form was revised to include changes in the title or instruction statements for Sections B1, D3, J [imaging hazards], and K [9/06].

The NCI Animal Study Proposal form was revised to incorporate a table for Section G - Category 3 study requirements [5/07].

The NCI Animal Study Proposal form was revised to include additional guidance, administrative inclusions, and a revision to Section J in regards to the change in paperwork processing [11/07].

ANTIBODY PRODUCTION

A clear description of all antigens and details on their purification in monoclonal and polyclonal antibody production proposals is now required [12/00].

The ACUC will request technical data sheets from an investigator to confirm the antibody purification process that was used. If this information cannot be found on the data sheet, the investigator is responsible for contacting the company and obtaining the purification process information [3/03].

A new form entitled *LASP Immunization and Ascites Request* form was approved for use. This form will accompany animal study proposal submissions for immunization and/or ascites production [11/03].

GUIDELINES

The NCI-Frederick *Guidance for Animal Numbers Justification* was approved [6/98].

A revised version of the NCI-Frederick *Guidelines Involving Experimental Neoplasia in Mice and Rats* was approved [10/99, revised 11/03, 5/04 and 4/06].

The NCI-Frederick guideline regarding *Perioperative Analgesia in Rodents* was approved [10/99, revised 5/04, 7/07].

The NCI-Frederick guideline regarding *Responsibilities of Principal Investigators Maintaining Mutant Strains of Mice* was approved [11/99, revised 11/03].

The NCI-Frederick *Guidelines for Ascites Production* were approved [9/00, revised 2/04].

The NCI-Frederick *Guidelines on Tail Biopsy for DNA Analysis and/or Genotyping of Mice* were approved [10/00, revised 2/02 and 2/05].

The NCI-Frederick *Guidelines Regarding Significant and Minor Changes to Animal Study Proposals* were approved [7/01, revised 2/03, 5/03, and 7/06].

The NCI-Frederick *Guidelines Regarding Engraftment of Human Cells or Tissues into Immunodeficient Mice* were approved [7/01, revised 2/03 and 7/05].

The NCI-Frederick guideline regarding *Endpoints in Animal Study Proposals* was approved [12/01, revised 2/02 and 5/04].

The NCI-Frederick guideline regarding *Pain and Distress in Rodents: Responsibilities, Recognition, and Alleviation* was approved [12/01, revised 11/07].

The NCI-Frederick *Guidelines for Euthanasia of Rodents Using Carbon Dioxide* [name changed to *Guidelines for Euthanasia of Rodents*] were approved [2/02, revised 10/02, 5/04, 3/05, and 10/05].

The NCI-Frederick *Guidelines on Survival Bleeding of Mice and Rats* [name changed to *Guidelines for Rodent Blood Collection*] were approved [2/02, revised 2/05 and 3/06].

The NCI-Frederick *Guidelines on Transportation of Newborns from NCI-Frederick to Bethesda* were approved [10/02].

The NCI-Frederick *Guidelines for Classifying Category 3 Procedures on Animals* were approved [4/04].

The NCI-Frederick *Experimental Autoimmune Encephalomyelitis [EAE] and Paralysis Clinical Assessment Guidelines* were approved [5/04, revised 12/05 and 6/06].

The NCI-Frederick *Guidelines for Categorizing Significant Deficiencies and OLAW Reporting* were approved [8/04].

The NCI-Frederick *Guidelines for the Designated Member Review and Expedited Review Proce*sses were approved [9/04, revised 7/06].

The NCI-Frederick document *Rules of Order for the NCI-Frederick ACUC* was approved [1/05].

The NCI-Frederick document *Formal Process for Appointing/Renewing Members of the NCI-Frederick ACUC* was approved [1/05].

The NCI-Frederick *Guidelines for Investigating and Reporting Animal Care and Use Concerns* were approved [2/05, revised 10/05].

The NCI-Frederick *Guidelines for the Use of Tribromoethanol/Avertin Anesthesia* were approved [2/05].

The NCI-Frederick *Recommendations for Aseptic Technique and Post-Operative Care for Rodent Surgery* were approved [2/05, revised 8/07].

The NCI-Frederick *Guidelines for the Skin Painting of Mice* were approved [5/05].

To ensure due diligence in the review of all ACUC guidelines, on a yearly basis the ACUC Coordinator will disseminate a notice requesting that all ACUC members review the current guidelines to ensure that they are consistent with his/her own research practices along with the ACUC review of proposed studies [6/07].

The NCI-Frederick *Testing Requirements for Biological Materials Proposed for Use in NCI-Frederick Animal Study Proposals* were approved [7/07].

The NCI-Frederick *Recommendations for Anesthetics* were approved [10/07].

MISCELLANEOUS

The *Deleterious Phenotype Reporting Form* was approved and disseminated to investigators for use [2/01, revised 7/04]. The reporting mechanism for deleterious phenotypes is to be expanded to include the animal technical staff as they are the most likely to first observe an abnormal phenotype. The PI and the Attending Veterinarian would be notified, the information recorded on the *Deleterious Phenotype Reporting Form* and the completed form sent to the ACUC [3/01].

The final draft of the SOP *Action Plan for Unexpected Positive Diagnostic Tests* was presented to the Committee and approved as written [6/01].

The final draft of the *LASP Right-To-Know Checklist for Chemical and Biological Age*nts was presented to the Committee and approved as written [02/03].

Effective April 2002, the ACUC will require the use of an environmental enrichment device for all singly housed animals and animals that are housed for greater than 90 days unless an exception is requested and approved by the ACUC [02/03]. The NCI-Frederick ACUC revised its environmental enrichment requirement to only cover singly housed animals [7/03].

The NCI-Frederick ACUC reviewed and approved a revised designated member review process to ensure compliance with Federal regulations [2/03, revised 9/04].

A *Facility Inspection Checklist* was developed for use by ACUC members during the semiannual program review facility inspections [2/03].

The NCI-Frederick LAM post-approval monitoring log was implemented for monthly review of updates at the ACUC meetings [1/04].

The NCI-Frederick ACUC began its distribution of a newsletter [on an as needed basis] to provide investigators, technicians, facility staff, and animal users with updated information on animal care and use issues [2/04].

The NCI-Frederick ACUC posted the *LASP Animal Numbers for Research Use Calculator* and the *Recommended Needle Sizes, Sites, and Volumes for Injection* on its website for reference [2/04, revised 8/07].

The NCI-Frederick ACUC approved the LAM *Skin Lesions in Research Mice* treatment policy for distribution [3/04].

The NCI-Frederick ACUC launched its *Animal Care and Use Introductory Online Training Course* to ensure that all individuals listed on a proposal have taken the required training before proposal approval [6/04, revised 5/07, 9/07].

The NCI-Frederick ACUC is updated on a monthly basis of the LASP facility staff retraining occurrences [7/04]. This initiative was placed on hold in 2005.

The document *Recombinant DNA in Animal Models* was disseminated to investigators [8/04].

The NCI-Frederick ACUC reviewed and approved an expedited member review process to ensure compliance with Federal regulations [9/04].

The document *Reporting Animal Care and Use Concerns* was disseminated to investigators and animal users from the Institutional Official [8/05].

The NCI-Frederick ACUC posted the *Helpful Hints for Completing the NCI-Frederick Animal Study Proposal Form* [9/04, revised 10/05 and 05/07].

The NCI-Frederick ACUC began conducting unannounced animal facility inspections [10/04].

The NCI-Frederick ACUC will implement proposal submission deadlines [effective January 2006] three weeks in advance of the regularly scheduled meeting date [9/05].

The NCI-Frederick ACUC initiated the online Refresher Animal Care and Use Training Course requirement. Individuals must complete this course every three years [subsequent to lecture training course attendance] [11/05].

The NCI-Frederick ACUC and IBC disseminated information pertaining to submission deadlines and safety requirements to alleviate approval delays [11/05].

The NCI-Frederick created an online animal number justification website to assist investigators with proposal submissions [2/06].

The NCI-Frederick ACUC discontinued the semiannual lecture training course [the online introductory and refresher training course replace the lecture requirement] [5/06].

A new LASP Animal Facility and ASP Online Access System was initiated to provide investigators with an overview of active Animal Study Proposals [11/06].

A Murine Norovirus information sheet was created for investigators [11/06].

An official post-approval monitoring notification [e-mail] process was implemented to notify the investigator of the status and if additional requirements are needed to fulfill stipulations [1/07].

Guidance for Calculations for Making Drug Preparations, Proper Drug Concentrations for Compound Delivery to an Animal, and Cell Preparations was created for investigators [3/07].

A Material Safety Data Sheet resource site was provided for investigators and facility staff [3/07].

The DTP Surface Area Dosage Conversion Factor chart was posted on the website for investigators and ACUC members [8/07].