University of North Carolina at Greensboro
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE STANDARD OPERATING PROCEDURES

Spring 2014
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The University of North Carolina at Greensboro (UNCG) is committed to the responsible and humane treatment of animals used in programs at or conducted in collaboration with the university.

First and foremost, and in accordance with U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used In Testing, Research, and Training, the university ensures that all of its animal activities are designed and performed “with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society”.

1. Animal Care Overview
UNCG animal care personnel are responsible for the continuous provision of appropriate animal environments, housing, and management. All animal care and use-related programs implemented by animal supervisory staff are developed, reviewed, evaluated and modified, as deemed necessary, in consultation with the Attending Veterinarian, and are reviewed and evaluated by the IACUC, at least semi-annually during program reviews and facility inspections.

1.1 Animal Supervisory Staff Responsibilities
The responsibilities of animal supervisory staff include, but are not limited to:

1. To assist the IACUC in the oversight of animal care and use activities to ensure institutional compliance with all applicable federal, state and local animal welfare laws and regulations as well as relevant voluntary guidelines, company and IACUC policy
2. To ensure that all animal supervisory staff are appropriately trained
3. To ensure that animals are procured from only reputable and USDA-licensed sources (if applicable) and other reputable vendors (unregulated species).
4. To monitor and document animal procurement to ensure animals are purchased only for use on current IACUC-approved activities and to help track numbers of animals (that animal numbers do not exceed those approved for use), including internal transfers between IACUC-approved programs
5. To develop and implement appropriate animal procurement procedures
6. To develop and implement the Animal Facility Manual for providing appropriate animal environment, housing, and management necessary to ensure the safety and health of research animals and the quality of the research program
7. To oversee maintenance of laboratory animal facilities and equipment
8. To ensure the availability of appropriate equipment and supplies to support all IACUC-approved animal use activities
9. To develop and implement a program for monitoring the health of animals on a daily basis
10. To develop and implement an appropriate health quality assurance program to ensure the continued health of animals

11. To develop in consultation with appropriate health and safety personnel, and to implement, monitor and document participation in, an occupational health and safety program, designed to protect health and ensure safety of all personnel involved in animal care and use activities

12. To participate in the development an action plan in the event of facility problems during regular working hours, after hours, on weekends, on holidays.

13. To participate in the development of an animal facility disaster plan, in consultation with the ORI, and as part of the overall safety plan for the animal facility, that takes into account both personnel and animals, in the event of a disaster.

2. The Institutional Animal Care and Use Committee: Lines of Authority and Responsibility

The Institutional Animal Care and Use Committee recognizes that each member is appointed by the Chancellor of the University of North Carolina, Greensboro (UNCG) and consists of no less than five voting members. Efforts are made to appoint and maintain a diverse membership with a collectively broad spectrum of expertise and knowledge necessary to ensure a quality Institutional Animal Care and Use Program. With the exception of appointing IACUC members, the Chancellor has delegated their authority of Institutional Official to the Vice Chancellor of the Office of Research and Economic Development

Appropriate lines of authority and responsibility for administering the program are critical for ensuring regulatory and voluntary compliance. There is a direct line of authority from The Institutional Official to the Institutional Animal Care and Use Committee (IACUC). The Attending Veterinarian, a voting member of the IACUC, reports directly to the Institutional Official. (See table I below)
Table I

DIAGRAM OF THE REPORTING CHANNELS FOR THE ANIMAL CARE AND USE PROGRAM AT THE UNIVERSITY OF NORTH CAROLINA AT GREENSBORO

2.1 Institutional Official

The Institutional Animal Care and Use Committee recognizes that the Institutional Official is an individual of high-level authority within the institution and designated (documented in writing) by the UNCG Chancellor. The IO is authorized to legally commit on behalf of the institution that it is in compliance with the PHS Policy and the animal welfare Act. The IO has the administrative authority to promulgate, implement and enforce policies as well as the financial authority to approve necessary funding if required to meet the needs of the animal care and use program as recommended by the IACUC.

2.1.1 Responsibilities and Authority of the Institutional Official

The responsibilities of the Institutional Official include:

1. Authority to legally commit on behalf of the institution:
   • Authority to sign the UNCG’s PHS Assurance, making a commitment on behalf of the institution that the requirements of PHS Policy will be met
• Authority to sign the USDA research facility registration application and subsequent USDA annual reports (if applicable)

2. Direct oversight of the Institutional Animal Care and Use Program
3. Authority to administer the Institutional Animal Care and Use Program
4. Coordination of administration, IACUC, investigators and animal resources to ensure a clearly defined chain of authority
   (Note: The Institutional Official’s authority to formally appoint members to the IACUC has been retained by the UNCG Chancellor).

2.2 Definition of a "Quorum": Requirements for All Official Actions and Granting Exceptions

A quorum of the IACUC is defined as a majority of the voting members, which shall not include any member who has a conflicting interest with the activity under review.

Requirements for All Official Actions

All official actions must take place at a convened meeting of a quorum of the voting IACUC-membership and upon a majority vote.

2.2.1 Exceptions

The IACUC may grant exceptions to its own voluntary guidelines, position statements and policies. Under special circumstances, it may be necessary for the IACUC to seek review and approval of exceptions to federal laws, regulations and policies from the appropriate agency.

2.2.1.1 Exceptions to Voluntary Guidelines, Position Statements and Policies

The IACUC may exercise its authority to grant exceptions to voluntary guidelines and its own established recommendations (position statements and policies), if the IACUC determines that such an exception is in the interest of animal health and well-being or if the exception can be scientifically justified and with due consideration to the cost-benefit to animal well-being and scientific advancement. Exceptions will be handled on a case-by-case basis and must be accompanied by written justification, supporting need. All exceptions must be approved by majority vote of a quorum of the IACUC and documented in the IACUC minutes.

2.2.1.2 Exceptions to Federal Law and Regulations

If an exception to federal animal welfare laws, regulations and/or policies cannot be clearly supported by satisfactory justification. The IACUC will seek the review and approval of the exception from the appropriate agency. If the federal agency approves the exception, the exception must be then be approved by majority vote of a quorum of the IACUC and documented in the IACUC minutes.
2.3 General Overview of the IACUC Membership
At a minimum, the IACUC membership will meet the applicable federal, state and local requirements including Public Health Service requirements, the Guide for the Care and Use of Laboratory Animals, USDA regulations 9CFR2.31 (if applicable), and institutional policy.

2.3.1 Membership Terms and Membership Overlap
Voting IACUC members are typically appointed for three-year terms with the option for renewal of additional terms thereafter. If possible, staggered terms, necessary to ensure at least one-half of the membership has a minimum of one to two years of experience at any given time, will be implemented. If possible, the mechanism of membership overlap will be implemented to permit a new member to serve as a non-voting member on the IACUC for a period of time prior to the resignation of a voting member as a means of training.

Appointment terms of non-voting members will be determined on a one-on-one basis, commonly dependent on IACUC needs and availability of qualified replacements.

2.3.2 Minimum Membership Requirements
At a minimum, the UNCG IACUC will consist of five voting members including a:

- **Doctor of Veterinary Medicine** with training or experience in laboratory animal science and medicine, who has direct or delegated program authority and responsibility for activities involving animals at the institution

- **Unaffiliated Member** who is not affiliated with the institution in any way other than as a member of the IACUC, who is not a member of the immediate family of a person who is affiliated with the institution, and who represents community interests with respect to the use of animals in research; preferably, an individual whose primary expertise is in a non-scientific area and who is not a laboratory animal user

- **Practicing Scientist** with experience in research involving animals

- **Non-Scientist** with primary interests in a nonscientific discipline

As long as the committee meets the minimum membership of 5 members, an individual who satisfies more than one of the required qualifications may fulfill more than one requirement. For example, the unaffiliated member may fulfill the role of community representative and the role of non-scientist. However, based on USDA policy, the position of IACUC Chair, Veterinarian (V) and Non Affiliated Member (NAM) will be filled by three unique individuals.

Due to perceived undue influence over the IACUC, the Institutional Official will not be appointed to the IACUC.
2.3.3 IACUC Titles and Responsibilities - USDA

In addition to other required appointments, and in accordance with the USDA requirement that the IACUC consist of a minimum of 3 individuals, the Chancellor has appointed the following members with the following titles and responsibilities:

**IACUC Chair**

One individual is appointed IACUC Chair. This individual is selected based on their familiarity with the recognized standards for humane animal care and use, transgenic technology, and the role of animals in this process. The IACUC Chair serves to represent the institution, the IACUC and the animal research area, collectively. Because of the possibility of real or perceived potential conflict of interest, and based on USDA policy, the Veterinarian or the Nonaffiliated Member will not be appointed to the position of IACUC Chair.

**Attending Veterinarian**

The Doctor of Veterinary Medicine appointed to the IACUC is also the designated (or delegated) with expertise in the areas of laboratory animal medicine and science and direct or delegated animal care and use program authority and responsibility for activities involving animals. In the capacities of Attending Veterinarian and IACUC member, you have a direct reporting line to the Institutional Official.

**Non-Affiliated Member**

The Non-Affiliated member (NAM) is selected based on his/her ability to represent an unbiased view of the community’s interests and concerns with regard to the care and use of animals in research. This individual is not affiliated with the institution in any way other than by their participation on the IACUC. This individual is not a research animal user.

Based on the IACUC’s enormous responsibility and substantial time-commitment, the IACUC membership will also include non-voting individuals and/or support staff to help alleviate the administrative burden on the committee by providing administrative support for IACUC activities.

2.3.4 IACUC Advisors/Consultants

The IACUC membership may include additional voting members or ad hoc (non-voting) advisors (e.g. regulatory consultants, legal representatives, biostatisticians, or safety officers) who bring additional expertise to the IACUC in the conduct of facility inspections, animal care and use program reviews and other IACUC activities. Additional voting members or ad hoc (non-voting) advisors may be necessary to help ensure committee effectiveness in the development and maintenance of a quality program customized to meet the unique needs of the
institution while ensuring regulatory and voluntary compliance and desired program outcomes.

2.3.5 Appointment Terms
IACUC appointments for IACUC Advisors/Consultants will be indefinite, based on the needs of the IACUC and the institution.

2.3.6 Subcommittees
The IACUC may appoint subcommittees to act on behalf of the IACUC and under clearly defined circumstances as deemed necessary to enhance the effectiveness of the IACUC in ensuring institutional compliance, research animal welfare and personnel safety and education (e.g. Animal Alternatives Subcommittees, Training, or monitor Occupational Health and Safety). However, in all cases, the IACUC will retain oversight and responsibility for all activities.

2.3.7 Alternate IACUC Members
The Chancellor may also appoint alternates to the IACUC membership if needed to ensure meeting quorum and/or for the purpose of training future full-voting IACUC members.

Each alternate must replace a specific IACUC member (a “primary” or full-voting) and be appropriately trained. More than one individual can be appointed alternate for the same primary member but only one alternate can be empowered with the vote during official business in the absence of their designated primary member. Similarly, one individual can be appointed alternate for more than one primary member, but can only represent one “absent” member (not multiple members) during official business. Each alternate must meet the criteria for the primary member’s specific role on the IACUC (i.e. practicing scientist replaces a practicing scientist; veterinarian replaces veterinarian; community member replaces community member). Alternates must vote their own conscience and not that of their primary member. Alternates cannot vote or contribute to the quorum unless their designated primary member or one of their designated primary members (if appointed as an alternate for more than one primary members) is physically or “technically” (due to conflict of interest) absent. Alternates must be appointed by the Chancellor in writing and each letter of appointment must be specific and one-to-one.

2.4 Attending Veterinarian
The Doctor of Veterinary Medicine appointed to the IACUC is also the designated (or delegated) with expertise in the areas of laboratory animal medicine and science and direct or delegated animal care and use program authority and responsibility for activities involving animals. In the capacities of Attending Veterinarian and IACUC
member, you have a direct reporting line to the Institutional Official. This authority and responsibility include, but is not limited to:

- Authorization via IACUC activities to contribute to the establishment of appropriate policies and procedures for ancillary aspects of veterinary care including, but not limited to, animal care and husbandry, animal health quality assurance, environmental and psychological enrichment programs for resident animals, exercise programs for canines, occupational health and safety programs for animal care and use personnel, animal facility disaster plans, and to conduct periodic evaluations of their associated outcomes, at least semiannually.

- Appointment as a full-voting member of the IACUC.

- As Attending Veterinarian and full voting member of the IACUC, the role of the Attending Veterinarian is vital to ensuring that the institution continues to maintain a program of adequate veterinary care including but not limited to the following provisions by semi-annual inspection and IACUC protocol review:
  - Appropriate facilities, personnel, equipment, and services are available to comply with federal animal welfare requirements.
  - Appropriate living conditions for each research animal species that contributes to their health and comfort.
  - Appropriate housing, feeding, and nonmedical care of the animals directed by the AV or other designated scientist(s) trained and experienced in the proper care, handling, and use of the species being maintained or studied.
  - Guidance to principal investigators, and other personnel, involved in the care and use of animals regarding handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia.
  - Ensure the provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices.
  - Adequately qualified and trained personnel conducting procedures on the species being maintained or studied.
  - Ensure that no animal is used in more than one major operative procedure from which it is allowed to recover unless satisfactorily justified for scientific reasons by the principal investigator, in the IACUC protocol.

- With respect to procedures that are potentially painful or distressful, the AV is authorized to:
  - Consult with research animal users to ensure the minimization of pain and distress during the conduct of animal research, and in particular, with regard to procedures that may cause more than momentary pain or distress.
- Ensure that procedures which may cause more than momentary pain or distress are performed with appropriate pain relieving drugs unless withholding such drugs is justified for scientific reasons, in writing, by the principal investigator and will continue only for the necessary period of time.

- Ensure that procedures that may cause more than momentary pain or distress are NOT performed with the use of paralytics without anesthesia.

- In addition, the AV will share the following responsibilities with the other voting members of the IACUC including, but not limited to:
  - Semi-Annual Program Evaluation including Program Review and Facility Inspections
  - Reports and Recommendations to the Institutional Official
  - Review and Approval of Proposed Animal Use Activities and Significant Modifications to IACUC-Approved Animal Use Activities
  - Suspension of On-Going Animal Activities (if warranted)
  - Assessment of Animal Care and Use Personnel Qualifications
  - Review of Institutional Training Programs for Animal Care and Use Personnel and the Institutional Animal Care and Use Committee
  - Provision of and participation in appropriate Occupational Health and Safety Programs and associated training for animal care and use personnel as well as others at risk
  - Reporting and Record Keeping Requirements
  - Provision of training in the recognition and reporting of animal care and use deficiencies or departures and the mechanism for voicing animal welfare concerns
  - Review and Investigation Animal Welfare Concerns
  - Endorsement of an Animal Facility Disaster Plan

- Authorized to ensure that adequate veterinary care is provided at all times.
  - Methods to control, prevent, diagnose, and treat diseases and injuries and the readily availability of appropriate weekend, holiday, and emergency care.

  - Daily or more frequent observations of all animals by you to assess health and well-being; if such observations are performed other than by you directly, a mechanism of direct and frequent communication must be in place to ensure the timely and accurate notification of you in the event of a problem or concern related to animal health.

  - Availability and provision of medical care for animals by you as necessary.

- Authorized to oversee the adequacy of all aspects of animal care and use for all animals.

- Responsible for developing and implementing the Veterinary Care Program
• With respect to procedures that involve surgery, the AV is authorized to:
  ▪ Ensure the provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices.
  ▪ Ensure that all survival surgery is performed using aseptic procedures, including surgical gloves, masks, sterilized instruments, and aseptic techniques.
  ▪ Ensure that all major operative procedures on non-rodents are conducted only in facilities intended for that purpose and that these facilities are operated and maintained under aseptic conditions.
  ▪ Ensure that non-major operative procedures, and all surgery on rodents, are performed using aseptic procedures.
  ▪ Ensure that no animal is used in more than one major operative procedure from which it is allowed to recover unless satisfactorily justified for scientific reasons by the principal investigator, in the IACUC protocol.

• With respect to any and all euthanasia procedures, the AV is authorized to:
  ▪ Ensure that the method produces rapid unconsciousness and subsequent death without evidence of pain or distress, or utilizes anesthesia produced by an agent that causes painless loss of consciousness and subsequent death such as those described in the most current version of the AVMA Panel on euthanasia.

• With respect to the Animal Facility Disaster Plan,
  ▪ Fulfill the role of an “official responder” within the IACUC Emergency Plan, and should participate in the response to a disaster.

2.5 IACUC Support through Office of Research Integrity (ORI)

Responsibilities
The responsibilities and support of the IACUC will be overseen by the Director and the Research Integrity Coordinator of the ORI and include, but are not limited to:

• Participation in the development of IACUC calendars, agendas, meeting minutes, program and inspection reports, position statements and operating procedures, institutional guidelines
• Facilitation, tracking and documentation of the IACUC animal research review and approval process
• Provide assistance in the conduct of program reviews and facility inspections
• Record keeping requirements associated with the animal welfare regulations and institutional requirements by active documentation and maintenance of IACUC reports, records, and activities

• Participation in the development, implementation and documentation of training programs for IACUC members, animal users and animal supervisory staff

• Participation in the development, implementation and documentation of Occupational Health, Safety and Medical Surveillance Programs

• Provide guidance and all necessary checks and balances to ensure the timely address of the IACUC’s regulatory, voluntary and institutional obligations

3. IACUC Responsibilities

Other critical responsibilities delegated to the UNCG IACUC in its review and approval of proposed animal activities includes ensuring:

• Animal use is justified
• Animal species is appropriate
• Animal numbers are the minimum necessary to achieve statistical significance
• Non-animal alternatives have been considered
• Alternatives to potentially painful procedures have been considered
• A written description of the methods and sources used to determine that alternatives to painful procedures are not available is provided
• Research is not unnecessarily duplicative
• Humane endpoints are addressed

3.1 Alternatives and Investigator Responsibilities

Investigators are obligated to conduct a comprehensive review of the scientific literature prior to proposing an animal use activity. Literature searches are conducted to ascertain the most appropriate research model (e.g. non-animal or animal), the most appropriate species if an animal model is indicated, the minimum number of animals necessary to obtain reliable information, the available refinements to minimize study length, degree of invasiveness and pain and distress, and finally, to ensure that research will not unnecessarily duplicate previous research.

3.1.1 Alternatives to Animal Testing AltWeb or PubMed

The IACUC encourages investigators to conduct animal alternatives literature searches using available mechanisms. For example, the Alternatives to Animal Testing Web (AltWeb) Search Engine is designed to allow investigators to search selected sites on the Internet that contain information about alternatives or animal welfare. The AltWeb Site is found at URL http://altweb.jhsph.edu.
3.1.2 The “3Rs” of Animal Research

Animal alternatives are commonly referred to as the 3Rs of Russell and Burch: Replacement, Refinement and Reduction (Russell, W. M. S., Burch, R. L. 1959. The principles of humane experimental technique. Methuen & Co., Ltd., London.)

- **Replacement** is the use of non-animal technologies such as computer and mathematical models, or the use of in vitro techniques in place of whole-animal systems, or the modification of methods for use of a lower order or a less sentient animal species.

- **Refinement** is the minimization of pain and distress during animal research including the use of pain-relieving agents or the incorporation of refined techniques, which prevent or minimize pain and distress.

- **Reduction** is the use of the minimum number of animals necessary to obtain statistically significant results. Reduction of animal numbers may be achieved in a variety of ways including the use of more sensitive or combined endpoint assays.

A strong understanding of these concepts is necessary to perform successful animal alternatives literature searches.

The IACUC relies on the satisfactory completion of several sections in the IACUC application to evaluate animal use justification, animal alternatives and other related issues.

Resumes and/or statements of animal use experience may also be required by the IACUC for review and evaluation in order to secure full IACUC-approval of an animal use activity.

Subsequent addition of personnel to a current IACUC-approved IACUC Submission may be considered a significant modification that must be reviewed and approved by the IACUC through an amendment before new individuals can participate in the program. Individuals other than the PI who are deemed trained and qualified to perform their assigned responsibilities may be added administratively to the IACUC Protocol without additional approval by the IACUC. Written assurance from the principal investigator must be provided stating that new participants are qualified to conduct the indicated procedures and documented evidence of relevant and training and qualifications must be on file with the IACUC. In addition, the IACUC may exercise its right to require training or demonstrated proficiency before new personnel can participate in the activity.

New personnel or untrained personnel are permitted to engage following the approval of a protocol amendment in animal use activities as designated “trainees” and only under the strict supervision of individuals currently approved as trained and qualified.
The Principal Investigator notifies the IACUC in writing. This notification includes the names of the assigned trainers, the planned animal use training activities and a copy of the trainee’s resume and/or other relevant background information. If any IACUC member objects to permitting the individual to enter the program as “trainee”, they are directed to contact the Principal Investigator and Director of the animal program and the individual will not be permitted to enter the training process until the matter is discussed (and resolved) at a subsequent convened meeting of the IACUC. If no member expresses concern, the designated trainee is permitted to enter the program and their progress and proficiency is presented at a subsequent IACUC meeting. At that time, the IACUC will determine if additional training is needed or if the individual can be upgraded from “trainee” status to “Animal Handler” (without strict supervision) and approved for addition to the personnel sections of specified IACUC Form.”

Finally, and in order to secure IACUC-approval, the IACUC may require the Attending Veterinarian or his/her designee to perform or participate in certain aspects of a proposed program (determined on a case by case basis) or to provide prior training to designated individuals in specified animal use techniques in order to secure IACUC-approval.

3.2 Justification of Animal Use and Species Rationale

The USDA Animal Welfare Regulations obligate investigators proposing animal research to provide “A rationale for involving animals and for the appropriateness of the species and numbers of animals to be used”. In the Animal Use Section of the IACUC Form, the investigator must justify the use of animals and the proposed animal species, and describe the relevance of the animal research to human or animal health and/or the advancement of knowledge including the specific characteristics that make the proposed species the best choice for the work.

3.2.1 Animal Numbers

In the Animal Use section of the IACUC application, the investigator provides approximate numbers of animals to be used in a study (i.e. number of animals per group, number of groups per study and total number of animals per year).

In addition, the investigator must identify the sources supporting the proposed numbers of animals (e.g. supporting historical data, published literature, statistical analysis, regulatory requirements, dictated by in vitro requirements, other specified sources).

3.2.2 Animal Alternatives

In the Pain/Distress section of the IACUC application, the investigator must answer to the availability of alternatives to painful and/or distressful or potentially painful and/or distressful procedures. This section obligates the investigator to seek out and consider, if available, alternative methods and systems that may REPLACE animal use with non-
animal systems, non-whole animal systems or systems which use a lower order species; may REDUCE animal numbers by utilizing fewer animal numbers without compromise to the statistical significance of the data; and/or REFINE the research design by preventing or minimizing the degree and/or duration of pain or distress.

If alternatives are available, the investigator must explain and satisfactorily justify why available alternatives cannot be used (i.e. why the use of the alternative would compromise research objectives).

In addition, the investigator must identify the methods and sources used (e.g. literature databases), the date of the literature search, the period covered, and key words searched, to seek animal alternatives information including alternatives to painful or potentially painful procedures, distressful or potentially distressful procedures.

3.2.1 Painful/Distressful or Potentially Painful/Distressful Procedures
Anesthetic, analgesic, or tranquilizing agents should be administered for any procedure with the potential for causing more than minimal and/or transient pain or distress to the animal. If a potentially painful/distressful or painful/distressful procedure is proposed, the investigator is required to

• Develop the procedure in consultation with the Attending Veterinarian
• If pain-relieving agents must be withheld, provide scientific justification for withholding them
• Provide assurance that the painful/distressful procedure will continue only for period of time necessary
• Clearly establish the steps to monitor for pain/distress and to respond to animals in pain/distress

Even in those programs that incorporate the use of pain relieving agents to prevent or minimize pain or distress, the availability of alternatives must be addressed for each procedure with a potential for causing greater than slight or momentary pain or distress (i.e. pain or distress greater than that caused by routine injections or venipuncture). That is, the use of pain relieving agents to prevent or minimize pain or distress does not rescind this responsibility.

3.2.2 Non-Duplication
No animal use activity should be performed without a thorough review of the literature to eliminate the possibility of unnecessary duplication of previously conducted research. The investigator identifies the literature databases searched to ensure that the proposed research does not constitute unnecessary-duplication In the Principal Investigator Assurance section of the IACUC application, and as required by the USDA regulations, the investigator assures that the proposed research is not unnecessarily duplicative.
4. IACUC Review and Approval of Proposed Animal Use

As an agent of the university, the IACUC is authorized to review and approve, require modification (in order to secure approval), or withhold approval of all proposed activities involving animals.

The Institutional Animal Care and Use Committee reviews and evaluates all research animal use activities conducted at the university at least every twelve months.

4.1 Animal Use Activity Defined

Animal use activities cover any and all activities involving animals including testing, teaching and research (e.g. animals used in specific research programs, sentinels in animal health surveillance programs, animals used for training personnel in both, animal care and animal use techniques, breeding programs, blood and tissue donors etc.).

These activities are not limited to those performed in-house but include all animal research programs without regard to where they are conducted, i.e. any collaborative or subcontracted animal research conducted at otherwise unaffiliated institutions which originate from the university and to which the university provides total or partial funding, or provides unique services/products/agents, or designates, directs or suggests the animal procedures to be followed, and from which the university has potential to derive benefit.

At institutions with an established IACUC and where animal research activities which originate in total or in part from the university, the university IACUC may choose to rely on the review and approval of the animal use activity by the non-affiliated IACUC. While dual IACUC review is not required by PHS Policy or the USDA Animal Welfare regulations, the UNCG IACUC retains its authority to assess the adequacy of IACUC review and approval of an animal activity by a non-affiliated institution. If the review and approval are deemed inadequate, the UNCG IACUC will not permit its initiation until the non-affiliated IACUC has reviewed the proposal and granted it full-approval.

4.2 Purpose of IACUC Protocol Review and Approval Process

The “Application for Use of Animals in Research and Teaching” and the “IACUC Protocol” review and approval process are the IACUC-established mechanisms to ensure that the IACUC fulfills its responsibilities in the review and approval of animal use activities prior to their initiation. This process permits the IACUC to evaluate proposed animal use activities and suggest significant changes to IACUC-approved activities to ensure that they will be conducted in keeping with all applicable federal laws, regulations and policy, the “Guide for the Care and Use of Laboratory Animals” (the Guide), and all IACUC and institutional guidelines, unless satisfactory scientific justification for a departure is presented by the investigator and approved by the Committee.
No animal use activity or significant change to an IACUC-approved animal use activity can be initiated unless it has been reviewed and granted IACUC approval.

4.2.1 Purpose of the IACUC Protocol
The IACUC uses an IACUC Protocol completed by the Principal Investigator (PI) for the review and approval of all proposed animal use activities.

A completed IACUC Protocol provides committee members with critical information required to evaluate and ensure:

- Use of minimum numbers of animals and the appropriate species
- Appropriate pre- and post-procedural housing, husbandry and veterinary care
- Satisfactory evidence and assurance that the activity does not constitute unnecessary duplication
- Consideration of non-animal alternatives, and evidence that non-animal alternatives are not available or, if available, will not fully meet the research objectives
- Satisfactory measures to prevent or minimize pain and distress that are consistent with sound research design.
- Consideration of alternatives to painful procedures
- Written account of the methods and sources used to determine that alternatives to painful procedures are not available
- Potentially painful and distressful procedures are supported by satisfactory scientific justification and appropriate established measures to prevent and/or minimize pain and distress
- Use of appropriate anesthetics, analgesics and tranquilizers during painful and distressful procedures unless withholding pain relieving agents is scientifically justified and the procedures are permitted to continue only for the time period necessary
- Potentially painful or distressful procedures including those which utilize anesthetics, analgesics and tranquilizers to prevent, minimize or alleviate pain and distress are developed in consultation with the Attending Veterinarian or his/her designee
- If paralytic agents are used in conjunction with anesthesia, proper monitoring of the animal’s vital signs are performed to ensure an unconscious state including but not limited to the following:
  - Blood pressure
  - Heart rate
  - Respiratory rate and effort
  - Assessment of oxygenation (pulse oximetry, capnography, arterial blood, gas, mucous membrane coloration)
• Assessment of the level of anesthesia (i.e. responsiveness to stimuli, changes in anesthetic regimen)
• Euthanasia at the end of the procedure or, if appropriate, during the procedure, of animals that would otherwise experience severe or chronic pain or distress that cannot be alleviated
• Aseptic technique for all survival surgeries
• Major surgical procedures on non-rodent species are performed in dedicated facilities
• Multiple major survival surgeries, within the same protocol, is supported by satisfactory scientific justification (e.g. necessary and related components of a research activity) or evidence supporting their conduct in order to conserve scarce animal resources or for clinical reasons as determined by the Attending Veterinarian or his/her designee. Multiple major survival surgeries using a USDA-regulated species among different IACUC protocols is not allowed unless the UNCG Institutional Official has been given approval from the USDA Animal Care Regional Director.
• Appropriate pre-surgical and post-surgical care
• Continued animal participation in applicable enrichment and exercise programs during the conduct of the activity unless supported by scientific justification or upon the recommendation of the Attending Veterinarian to ensure animal well-being
• Appropriate methods of euthanasia, consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia, unless a deviation is scientifically justified and complies with the PHS policy on humane care and use of laboratory animals clarification regarding use of carbon dioxide for euthanasia of small laboratory animals
• Appropriate animal housing and care which contributes to animal health and comfort
• Housing, feeding, and non-medical care activities directed by qualified individuals trained and experienced in the animal's species-specific needs
• Appropriately trained and qualified personnel are designated to participate in the activity
• Availability of a qualified veterinarian for the provision of medical care usually for field studies or off campus studies
• Implementation of appropriate safety precautions throughout the procedure for the protection of personnel and animals
4.2.2 Pre-Requisites for Submission

The ACAP Animal Use Application, available on the ACAP website, must be completed.

The PI must be a member of the UNC Greensboro faculty. If a student desires to conduct animal research, he/she must identify a faculty member to take full responsibility as PI.

All Individuals that will have handle animals as part of a proposed IACUC Protocol are required to take CITI Training Modules “Working with the IACUC: Investigators, Staff and Students” and the CITI module that is specific for the species used. Also, if you are conducting studies that have the potential to cause “more than momentary pain and distress” in mice or rats, you must take the Minimizing Pain and Distress module. If conducting major surgery on non-rodent species you must take the aseptic surgery module.

The PI must complete the ACAP Animal Use Application. As of 8/12/2013, PIs are required to request scientific merit review (Departmental Review) and general acceptance review from their Department Reviewer before submission is completed in ACAP. This review is to include verification of funds to support the project if external funds will not be sought.

Each department can determine the basis for conducting the review but at a minimum, reviewers should consider a brief synopsis of the background, hypothesis tested, animal numbers and proposed data analysis. Reviewer comments should be forwarded to the PI as they may provide helpful suggestions for improving the experimental design. Please note that the departmental review is not intended to be an editorial review of the IACUC protocol, but any added feedback the departmental reviewer can provide the PI will aid in the overall review process. The review may include, but should not be limited to, the IACUC application, which focuses on animal welfare.

In addition, departmental review may also wish to evaluate the proposal for adequacy of the following areas (adapted from the NIH peer review process):

- Significance: does the project address an important problem in the field?
- Investigator: are the PI and other researchers capable of carrying out the project?
- Innovation: do the experiments challenge current scientific paradigms?
- Approach: are the overall strategy, methodologies, and analyses appropriate to accomplish the specific aims of the project?
• Environment: is the scientific environment adequate for successful completion of the work?

Upon acceptance, the Department Reviewer must notify the ORI that the Departmental Review has been completed.

Once the Departmental Review is completed, the PI submits the completed IACUC Protocol to the ORI and Attending Veterinarian for review. During veterinary review, the Attending Veterinarian corresponds with the PI via e-mail that is copied to the IACUC Chair. The Attending Veterinarian will examine the medical aspects of the study (such as drugs or substances), housing, light/dark cycle, animal welfare, and any other experimental treatment. All stipulations and recommended changes are incorporated into the IACUC Protocol.

After veterinary review, the PI submits the final IACUC Protocol to the Attending Veterinarian and IACUC Chair. If requested by any reviewer, the PI will complete any hazard review forms specified by the Department of Environmental Health and Safety (EHS) in order to provide a summary of health risk to the IACUC.

As of 8/12/2013, all new protocols will be reviewed by the full IACUC at regularly scheduled meetings. In order to get your new study reviewed at the next IACUC meeting, please allow at least two weeks of review time and make sure all requested changes are made at least ten (10) days ahead of the next meeting date.

Approved protocols are forwarded to the Attending Veterinarian and Manager of the Animal Facility.

4.2.3 Field Studies

In compliance with UNCG’s Assurance with PHS-policy, the UNCG IACUC is responsible for oversight in accordance with research involving vertebrate animals. IACUCs must know where field studies will be located, what procedures will be involved, and be sufficiently familiar with the nature of the habitat to assess the potential impact on the animal subjects.

Principal Investigators who wish to study on free-living wild USDA-covered species that involve invasive procedures, harms or materially alters the behavior of an animal under study is covered by USDA animal welfare regulations and requires IACUC review and approval as well as state and/or federal permit approval. Permits should be obtained prior to submission of the IACUC protocol, since changes to the protocol may occur during the application process for the issued permit based on the review of the permit application. The IACUC must also ensure compliance with the regulations and permit requirements of pertinent local, state, national, and international wildlife regulations.
If the activity alters or influences the activities of the animal(s) that are being studied, the activity must be reviewed and approved by the IACUC (e.g., capture and release, banding). If the activity does not alter or influence the activity of the animal(s), IACUC review and approval is not required (observational, photographs, collection of feces).

**4.2.4 UNCG Health and Safety Program for Personnel Using Animals in Teaching and Research**

The University of North Carolina at Greensboro is committed to ensuring the health and safety of individuals working with animals in their professional activities, both on and off campus. The goal of the UNCG Health and Safety Program for Personnel Using Animals in Teaching and Research (HSPUSTR) is to prevent occupational injury and illness while working with animals by avoiding, controlling or eliminating hazards on campus and, to the extent possible, off campus. The emphasis of such a program is the prevention of illness and injury, but our program also includes provisions for early diagnosis and treatment when necessary.

There are two programs for preventing occupational injury and illness while working with animals at UNCG. One is for personnel hired by the Animal Facility and one is for individuals that work with animals within a research study. Animal Facility personnel include individuals who work in the Animal Facility on a full or part-time basis. Individuals who work with animals within research include faculty, staff, and students engaged in funded or unfunded research projects or teaching in a class or field setting. Personnel in the Animal Facility must follow guidelines established by the Animal Facility. Research staff working with animals must follow the guidelines contained in this document.

HSPUSTR is supported by the Office of Research Integrity. It requires effective interactions among researchers, the Animal Care and Use Committee (IACUC), the Consulting Veterinarian, the Environmental Health and Safety Office and Student Health Services. HSPUSTR has four (4) key points: Hazard Identification and Risk Assessment, Personnel Training, Personal Hygiene/Protection, and Medical Evaluations.

**4.2.3.1 Hazard Identification and Risk Assessment**

It is the responsibility of lead professors and principal investigators (PI) who work with animals to assess dangers associated with their work and to select safeguards appropriate to the risks. In some cases the IACUC may determine there is a need for an additional risk assessment to be conducted by UNCG Environmental Health and Safety. The Anna M. Gove Student Health Center will perform medical evaluations to ensure that the risks remain at acceptable levels.
4.2.3.2 Personnel Training

Individuals who work with animals should be given clearly defined procedural training for the risks they incur by working with animals. This training should include chemical safety; zoonosis (any infectious disease that may be transmitted from animals, both wild and domestic, to humans or from humans to animals); proper handling of waste materials; microbiological and physical hazards (including those related to radiation and allergies); unusual conditions or agents that might be part of experimental procedures (e.g., immunocompromised animals), personal hygiene, and other considerations (e.g. precautions to be taken if personnel are pregnant, ill, or have decreased immunocompetence) as appropriate to the risk imposed by their workplace/environment. The PI is responsible for providing this training. Any and all trainings must be reported the IACUC and ORI. If needed, he or she may draw upon input from the occupational health doctor at Student Health Services, the Attending Veterinarian, the Office of Research Integrity, and/or the UNCG Environmental Health and Safety. This training must provide appropriate instructions for conducting duties, an understanding of the hazards involved, and assurance that proficiency is attained in implementing the required safeguards. This training is in addition to the IACUC required Collaborative Institutional Training Initiative (CITI) modules.

4.2.3.3 Personal Hygiene and Protection

It is essential that all personnel maintain a high standard of personal cleanliness. Individuals who work with animals should wash their hands and change clothing as often as necessary to maintain good personal hygiene. They should wear clothing suitable for use in the Animal Facility, classroom laboratories, or field studies. Disposable gloves, masks, head covers, coats, coveralls, and shoe covers may be desirable in some circumstances. Laboratory coats worn in the Animal Facility should not be worn outside it. Likewise, clothing worn in field studies should be contained in a safe and sanitized manner.

4.2.3.4 Medical Evaluations

All individuals who have a potential risk from their work with animals are required to have a medical evaluation prior to initiating the work, referred to in this document as the initial medical evaluation. Thereafter, a follow-up evaluation is required annually, as long as the work with animals continues. All individuals that submit an IACUC protocol will be required to have a medical evaluation, unless the PI identifies particular individuals who will not have any risks associated with animal exposure.
Both the initial and the follow-up medical evaluations are conducted by the Anna M. Gove Student Health Center. After satisfactory completion of either evaluation, the Anna M. Gove Student Health Center will notify the ORI and the individual.

The first step of the initial medical evaluation, and frequently the only step required, is for the individual who will be working with animals to complete a medical questionnaire. In the questionnaire individuals disclose existing medical conditions, species to which they will be exposed, and other relevant personal health information. This questionnaire may be taken in person or sent via interoffice mail to Anna M. Gove Student Health Center, located at 107 Gray Drive, Greensboro on the UNCG campus. Researchers may also fax completed questionnaires to 336-334-3299. The purpose of this evaluation is to provide early identification of conditions, if any, that may present an increased risk of adverse health effects that could result from working with animals. The questionnaire is evaluated by the Anna M. Gove Student Health Center for a nominal fee for UNCG faculty and staff. Students who are currently enrolled at UNCG will not be charged a fee. A fee will be charged to the appropriate department for students from another institution who are working at UNCG. Work with animals may begin unless Anna M. Gove Student Health Center identify that additional steps are necessary. Then work should be delayed until they are completed.

Based on the recommendation from Anna M. Gove Student Health Center, individuals may be asked to submit to a second step of the initial medical evaluation, a physical examination. The physical examination can be done by either the Anna M. Gove Student Health Center or the individual’s personal physician. The expense for this examination will be paid by the individual or his employer. Anna M. Gove Student Health Center does not accept any insurance. This examination may identify the need for vaccinations or immunizations. Once this step is completed satisfactorily, work with animals may begin.

4.2.3.5 Use of Respirators
Some individuals who work with animals may need to wear a respirator while they are working with them. They can self-identify or it can be determined as a result of the information supplied on the initial medical evaluation. If it is determined to be necessary for an individual to use a respirator when working with animals, the individual must complete the OSHA Respirator Medical Evaluation Questionnaire. This questionnaire is required to be completed by any paid UNCG employee, including graduate students. This form must be evaluated by the Anna M. Gove Student Health Center prior to the use of a respirator.

Once the Student Health Center has evaluated the OSHA Respirator Medical Evaluation Questionnaire, EHS will conduct a fit test and respiratory protection training. The fit test will allow EHS staff to determine what type will fit best for each
individual. After the fit test, EHS can provide the PI or respirator user with purchasing information. Only then can a respirator be used or purchased.

4.2.3.6 Renewal of Health Clearance
The Office of Research Integrity will send to all individuals who have been issued a medical clearance an annual follow-up medical questionnaire prior to the anniversary date of the last evaluation. Any changes to the work with animals that has occurred since the last medical clearance must be reported. The medical questionnaire will be evaluated by the Anna M. Gove Student Health Center for a nominal fee for UNCG faculty and staff. Students who are currently enrolled at UNCG will not be charged a fee. The Anna M. Gove Student Health Center will give the results of this evaluation to the ORI and the individual. Personal medical information generated by any of these exams will be kept confidential. If a physical examination is necessary, this information will remain between the employee and the physician. The employee can contact the physician who performs the examination with any questions regarding the results.

4.2.5 Principal Investigator Assurance
As part of completing the IACUC Protocol, the PI must sign a statement of assurance by which the investigator,

1. I certify that I am familiar with and assure compliance in this protocol with the legal standards of animal care and use established under the Federal and State laws and the policies on animal welfare of the National Institutes of Health and the University of North Carolina at Greensboro.
2. I assume responsibility for ensuring that all persons working with animals on this project are familiar with and are trained in relevant animal procedures and that they will comply with established laws and policies regarding animal care and use.
3. I certify that all individuals working with animals on this project will register with the University Occupational Health Clinic by completing and submitting the "Occupational Health Program Initial Health Screening" or the "Occupational Health Program Annual Screening for Continued Work with Animals" medical history questionnaire and I will follow the guidelines of the Animal Facility Manual as well as the Standard Operating Procedures of the UNCG Office of Research Integrity.
4. I certify the following: the research proposed herein is not unnecessarily duplicative of previously reported research; appropriate non-animal alternatives for this research do not exist; no alternatives to the potentially painful and/or distressful procedures conducted in this project exist. I have
indicated methods used to make these determinations in the appropriate section of this animal use application.

5. I will secure IACUC approval before changing procedures or personnel associated with this study (including adding personnel).

6. I assure that I and personnel under my direct supervision will use the animals acquired for the activity described herein solely for said purpose. I also certify that if live animals are shared with other PIs or are used in any procedure other than those described in this application, I will provide the details in the form of a written amendment to the original application prior to their use.

7. I acknowledge that veterinary care will be administered to moribund animals or animals experiencing more than momentary or slight pain or distress. Animal Facility staff or veterinary staff will attempt to contact me regarding the care of treatment of a moribund animal, but will institute treatment or euthanasia, as needed, if I cannot be reached.

8. I assure that I will notify the IACUC and the attending veterinarian regarding any unexpected study results that adversely impact the animals, including any unanticipated pain or distress, morbidity or mortality.

9. I agree if at any time any member of the research team or their immediate family members have financial interest in, receive personal compensation from, or hold a position in an industry sponsoring this study or otherwise have a personal conflict of interest, the Potential Conflict of Interest in Research form must be attached to this application.

10. I assure the IACUC and the University of North Carolina at Greensboro that the general procedures involving animals described in my grant application have been described in the animal use application and submitted to the IACUC for review.

11. I assure that I have read the "Euthanasia" link, available on the ORI website understand how it applies to animals in this animal use application.

12. If I use any biological, chemical or radiological hazards in animals in Animal Facility I will contact the ORI for information as to how to proceed.

13. I will follow the recommendations originating from veterinary consultation with specific emphasis on procedures expected to cause pain or distress. Such procedures will be restricted to the minimum time necessary to meet the objectives of the research. If an animal experiences severe or chronic pain or distress that cannot be relieved, it will be euthanatized at the end of the procedure, or if appropriate, during the procedure. In the event of unanticipated pain or distress, a signed retrospective report, detailing the circumstances of the event and referencing the appropriate IACUC protocol number, will be submitted to the IACUC with in seven (7) days of the event.
4.3 Approval Methods and Requirements
As of 08/12/2013 there is only one acceptable (compliant) method of IACUC Protocol review and approval. An IACUC Protocol that poses the potential for greater than transient and mild pain or distress will NOT be approved unless it receives approval from the Attending Veterinarian.

Routing and Review process for new Protocols:

1) As of 8/12/2013 all new IACUC protocols must have a scientific merit review (also called a departmental review) by a member of their department ahead of submission to the ORI. If there is no departmental representative, then one can be assigned by the IACUC Chair. If requested, ORI will route the application to departmental representative for a scientific merit review. The departmental reviewer may request changes from the
PI. Those changes will be addressed and returned to the departmental reviewer who will approve the changes. The departmental reviewer must sign off on the changes before the PI can submit.

2) Principal investigator submits IACUC application to the Office of Research Integrity (ORI). ORI checks for current occupational health certification and current CITI training and species specific CITI trainings.

3) The protocol will be then routed to the Attending Veterinarian (AV) for review. The AV may request changes from PI and this may be communicated through the staff of the ORI or directly to the PI from the AV and Animal Facility manager.

4) After the AV approves their requested changes, ORI add the protocol to the agenda for the next IACUC meeting.

5) Once a study is placed on the meeting agenda, ORI will assign two (2) members of the IACUC to act as Primary and Secondary reviewers. These reviewers will examine all aspects of the study and note any concerns they have with the protocol. At the IACUC meeting, the Primary reviewer will present the study to the committee. The Secondary will add any information he or she feels the Primary reviewer overlooked. These two reviewers will be assigned to the protocol for the life of the protocol, and will review any future amendments and annual renewals.

6) Amendments and annual renewals (formerly known as “annual reviews”) will be handled by a Designated Member Review (DMR). When an amendment is submitted to ORI and the IACUC, the chair of the IACUC, the Attending Veterinarian, and the Primary and Secondary reviewers will examine the submission. If all reviewers (Chair, Vet, Primary and Secondary) agree that the submission is acceptable as is, the ORI will approve the submission for the IACUC. Any of these reviewers (Chair, Vet, Primary and Secondary) may request the submission be reviewed by the Full Board Committee.

7) The Full Committee Review protocol will be put on the agenda for the next scheduled meeting. In order to get your new study reviewed at the next IACUC meeting, please allow at least two weeks of review time and make sure all requested changes are made at least ten (10) days ahead of the next meeting date. All committee members will be sent a complete copy of the protocol and any related supplemental documents for review prior to the meeting. Any IACUC member that has a conflict of interest will recuse themselves from the review of the protocol at the full board meeting. If the recused member’s absence affects quorum for a full board meeting, then the protocol will be rescheduled to be reviewed at the next meeting when quorum is present. All members must be present and a formal vote taken to approve, withhold or require modifications to secure approval with minor clarifications. When the outcome is “require modifications to secure approval”; the quorum of the full committee present may unanimously agree to review the resubmitted protocol by the DMR process or request to see the amended version at the next full committee meeting. If any DMR reviewer requests FCR then the revised protocol will be resubmitted back to the full committee at the next convened meeting when a quorum is present.

8) After the protocol is approved by the full committee review, it is sent to the Office of Research Integrity. This office sends an approval letter to the PI with copies to the Animal Facility Manager.
9) Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
   a. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.
   b. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure.
   c. The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
   d. Medical care for animals will be available and provided as necessary by a qualified veterinarian.
   e. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
   f. Methods of euthanasia used will be consistent with the current recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.

4.4 Stipulations for Additional Information

To assist IACUC members in making their decision on the need for a full-committee review, members are asked to report requests for clarifications or additional information to the ORI. The ORI or other designated IACUC member will communicate the nature of the request to the PI, in writing.

Investigator responses are reported back through the ORI or other designated IACUC member to the IACUC member(s) for review and consideration. Upon completion of their review, and if they desire a full-committee review, IACUC members notify the ORI or other designated IACUC member with their decision. Any IACUC member's request for clarifications, additional information and additional review time are honored.

Failure to supply the IACUC or ORI with the requested information within the IACUC-specified time frame can lead to suspension of all research studies for the PI.

4.5 Approval Status

There are three possible categories of approval:

1. Approved (as written)
2. Approved pending modifications to secure approval

   Modifications are either incorporated into a revised IACUC Protocol, or described in the body of the IACUC Approval Memo or described and agreed to in a written memo from the PI and attached to the IACUC Protocol. The research cannot begin nor animals procured until approval is granted.
3. Approval withheld

When the IACUC determines that a proposal has not adequately addressed all of the requirements of the PHS Policy and AWRs as applicable, the committee may withhold approval. This action may only be taken if the review is conducted using the full committee method of review.

As indicated above, a higher institutional authority may not administratively overrule an IACUC decision to withhold approval of a proposal.

4.5.1 IACUC Approval Number

Each IACUC Protocol is assigned an IACUC Approval Number only after full approval has been granted. The first two numbers represent the last digits of the calendar year in which the protocol was approved. The second set of digits represents the sequential order in which the IACUC Protocol was received. For example, the 13th IACUC Protocol submitted in calendar year 2007 is assigned the number 07-013.

An IACUC Approval Number is required to place animal orders. The corresponding IACUC Approval Number is required on cage cards. For a room housing animals all belonging to the same research program, the IACUC Approval Number can be clearly displayed on the animal room door or inside the animal room rather than on individual cage cards.

4.5.2 Approval Notification

When the IACUC approves an animal research protocol, ORI staff send the PI an approval letter indicating the dates of approval, and the IACUC protocol number with the Chair’s signature.

Approval Period

The IACUC approval to conduct a research program covers a period of three years. At a minimum, all animal research programs will be reviewed on an annual basis either as a "de novo" review or continuing review depending on how long the program has been active.

Programs that will continue beyond a 12-month period must be resubmitted to the IACUC for review and approval in advance of their expiration.

For first time submissions and 3rd year submissions, the PI must submit a completed “IACUC Animal Use Application” (the “IACUC Protocol”) for de novo review.

For protocol renewal in the first year and second year (annual renewals), the PI must submit an annual renewal through the ACAP system”.

Note: IACUC approval of a significant modification via the Annual Renewal does not change the original IACUC approval period.
4.5.3 IACUC Protocol Expiration Memo

At the date of expiration, no further use of the animals may occur. In addition, “no costs for activities with live vertebrate animals may be charged to NIH if there is not a valid Animal Welfare Assurance and Institutional Animal Care and Use Committee (IACUC) approval”

Approximately one month prior to the pending expiration of IACUC-approval to conduct a research program, the PI is notified in writing or is verbally advised to resubmit an “Annual Renewal” form for first and second year renewals or a new “IACUC Protocol” for 3rd year renewals.

4.5.3.1 Purpose of the Annual Renewal

The purpose of annual renewal is:

• to inform the IACUC of the current status of the animal activity and the number of animals used
• to ensure the activity continues to be conducted in compliance with all applicable federal laws and regulations, voluntary guidelines and institutional requirements
• to determine whether or not advances in animal alternatives (replacement, refinement and reduction) dictate consideration of changes to the research design.

4.5.3.2 Official Request for IACUC Protocol Termination

At any time, a PI can request the official “termination” of an IACUC approved program. For approved animal use activities that will not proceed, the IACUC encourages the PI to request termination prior to or at annual renewal or prior to or 3rd year “de novo” review.

4.6 IACUC Guidelines: General Animal Use and Specific Animal Techniques

The IACUC reserves the right to establish guidelines and positions on the humane conduct of animal use methods common to the field of biomedical research as well as other animal use issues (e.g. blood collection routes and frequency, physical methods of euthanasia, physical restraint, conduct of surgery, identification of the moribund condition). These guidelines will be based on sound scientific evidence and professional judgment and will meet or exceed the federal laws, regulations and voluntary guidelines for these procedures.

IACUC Guidelines are subject to IACUC revision and modification as deemed necessary to ensure the continued humane use of research animals.

4.7 IACUC Review and Approval of Minor, Significant, and Highly Significant Modifications

As an agent of the university, the IACUC is authorized to review and approve, require modification (in order to secure approval), or withhold approval of all proposed significant changes to on-going IACUC-approved animals in ongoing activities.

Amendments to currently approved protocols are submitted through ACAP (and certified by the PI). The PI must notify the IACUC via the ORI Amendment process. This form will be reported to the full committee at the next convened meeting. Highly significant changes to protocols cannot be handled via an Amendment and require submission of a new protocol.

Minor
PI must inform the IACUC via Amendment. This Submission should be sent to the ORI for review to ensure that the changes are in fact “minor” in nature. Once the desired change is deemed minor in nature, the ORI will note the change administratively in the corresponding IACUC file and database, approve the amendment, and the PI can proceed with his/her work.

A. If protocol requires non-survival surgery/euthanasia:
   1. Harvesting of additional tissues
   2. Taking of additional measures by currently approved procedures
   3. Longer duration (provided anesthesia is adequate)
   4. Additional surgical manipulations during non-survival procedures (provided that anesthesia is adequate)

B. Increase in number of animals by less than 5%

It is the IACUC’s responsibility, not the PI’s responsibility, to determine if a change is minor or significant in nature, and therefore does require IACUC review and approval prior to its initiation.

**Significant**
More than (3) significant changes other than items A 1-3 above in a (6) month period will require a new protocol. Additional guidance can be sought from the ORI and IACUC.

A. Demographic, personnel, or animal number changes
   1. Change or addition of funding agency
   2. Change in personnel
   3. Change in emergency contact person
   4. Increase in number of animals by 5 – 25%

B. If protocol requires non-survival surgery/euthanasia:
   1. Alteration in anesthesia
   2. Alteration in method of euthanasia

C. If protocol involves the survival of animals:
   1. Addition of minor surgery to an experiment that already involves anesthesia
   2. Alteration of surgical approach
   3. Alteration in choice of analgesics, anesthetics
   4. Alteration in schedule
   5. Additional sampling or minor surgeries provided that the additional procedures do not involve more distress than procedures already approved.

**Highly Significant**
Requires submission of new protocol.

1. Change in number of animals >25%
2. Change in experiment or project goal
3. Major change in species (e.g. mouse to lizard [change of order])
4. Change in surgical procedure (survival surgery)
5. The addition of a major survival surgical procedure
4.7.1 Proposing Highly Significant and/or Multiple Significant Modifications

If the nature and/or extent of the proposed significant modification(s) change the original IACUC-approved program substantially, and at the discretion of the IACUC, the IACUC may require the investigator to submit a new IACUC form.

Significant Modification Review and Approval Process

IACUC review and approval of proposed significant changes follow the same procedures for the review and approval of proposed animal use of the Application for Use of Animals in Research and Teaching. Depending on whether or not a request for full-committee review of the proposed modification is received, either the Full-Committee Review method or the Designated Member Review (DMR; no requests for full-committee review) will be implemented.

Significant Modifications - IACUC-Approval Period

If the IACUC approves an addendum (request for significant modifications) to an approved IACUC form, the 12-month approval period does not change but remains from the date of the IACUC approval of the original IACUC form.

4.7.2 Failure to Obtain IACUC Approval of Significant Modifications

If a research program is found to be inconsistent with the IACUC approved program—that is, if significant modifications have been initiated without prior IACUC review and approval—the IACUC has the authority to suspend the research. The Institutional Official, in consultation with the IACUC, must report the suspension to the appropriate regulatory agencies (e.g. OLAW, USDA).

5. IACUC-Approval of Protocols Originating from Non-UNCG Institutions Conducted at UNCG

No animal research activity can be initiated at UNCG until an “IACUC Application” has been reviewed and granted full-approval by the UNCG IACUC

5.1 Criteria for IACUC-approval of Protocols from non-UNCG Institutions

While “dual [IACUC] review” is not required by either the USDA or OLAW, if an animal use activity will be performed at UNCG (i.e. UNCG is the performance site), the UNCG IACUC requires its own review and full approval before the activity is initiated. The non-UNCG IACUC’s approval alone is not sufficient for initiating an animal research activity at UNCG.

If an animal use protocol originates from a non-UNCG institution required by law to have an Institutional Animal Care and Use Committee or its equivalent, written evidence of approval from the non-UNCG institution may also be required before the UNCG IACUC will grant full-approval.

The UNCG IACUC may also require additional information from the non-UNCG institution regarding the overall objectives of the research program and other information necessary to fully evaluate the proposal and to ensure that UNCG will remain in compliance with all applicable animal research laws, regulations and policies as well as its own institutional policies (e.g. consideration of alternatives, nonduplication, etc.).
5.1.1 Criteria for IACUC-approval of Protocols from UNCG and Conducted at non-UNCG institutions

The UNCG IACUC does NOT require its own review and approval of an animal use activity if the activity will be conducted at a non-UNCG institution (the performance site) and if the performance site has an established IACUC.

However, and at a minimum, the UNCG IACUC will require evidence that the IACUC at the performance site has reviewed and approved the protocol. In addition, the UNCG IACUC may also require the UNCG IACUC Chair and/or UNCG (consulting) veterinarian review the performance site’s approved protocol.

Criteria for IACUC-approval of Protocols from UNCG and performed and non-UNCG institutions WITHOUT Established Review and Approval Mechanisms (e.g. non-PHS Assured Institutions)

If the performance site does not have an established mechanism for the review and approval of animal activities (i.e. no IACUC in place), the UNCG IACUC will require the Principal Investigator at UNCG or the Principal Investigator at the performance site to complete the UNCG “Application for Use of Animals in Research and Teaching” or “IACUC Form”. The UNCG IACUC must review and approve the application before work can be initiated at the performance site.

5.1.2 Criteria for IACUC-approval of Protocols conducted at UNCG animal facility from non-UNCG institutions

The UNCG IACUC will review and approve any research conducted by faculty of non-UNCG institutions. In addition, the non-UNCG institutions must also have an animal use protocol approved by that site’s IACUC prior to being submitted to UNCG’s IACUC for the use of the animal facility. A UNCG faculty member must be listed on that protocol as a Principal Investigator and must act as a representative for the non-UNCG institution’s faculty and research staff while work is being conducted on the UNCG campus and, with that, follow all required responsibilities and guidelines of the UNCG IACUC Standard Operating procedures as well as the rules of the animal facility while listed on the protocol.

The non-UNCG institution must also adhere to the terms of any legal contracts between UNCG and that site. Personnel from any institution other than UNCG that perform work at UNCG are required to comply with any researcher prerequisites (training, health clearance) that are required of UNCG personnel.

5.1.2.1 Sub-granting of PHS Moneys to non-UNCG Institutions

If UNCG has been awarded PHS funds in support of an animal use activity, and these moneys will be sub-granted in part or in their entirety to a non-UNCG performance site, UNCG must comply with the following *:

1. UNCG must notify the NIH Grants Management Official (GMO) of its intention to sub-grant moneys to another, unrelated institution for the purpose of conducting the funded animal research activity. Notification can take place by phone or letter. The GMO must
ensure that the sub-granted institution was listed and approved as a performance site in the initial grant application.

2. If the sub-granted institution was not listed (and approved) in the initial grant application, the GMO must ensure that the activity has been granted IACUC approval and the GMO must contact OLAW to determine if the performance site has a current PHS Assurance on file.

A. If the performance site has a PHS Assurance and the activity has IACUC-approval, the GMO can grant the addition of the performance site to the grant.

B. If the performance site does not have a PHS Assurance, UNCG has two options:

1. UNCG must notify OLAW to request an amendment to the UNCG Assurance to include the performance site. A total renegotiation of the Assurance is usually not necessary. If OLAW agrees to add the performance site to the UNCG Assurance, the UNCG IACUC is obligated to include the performance site as a satellite facility and review its program and facilities as it does the UNCG program and facilities. As a covered component, all aspects of the approved UNCG Assurance must be seamlessly applicable to the performance site or;

2. The performance site must negotiate its own PHS Assurance with OLAW.

- Once IACUC-approval has been confirmed and the performance site is PHS-Assured (either as a component of the UNCG Assurance or as an independently PHS-Assured entity), the GMO can grant the addition of the performance site to the grant.
- Once permission is granted, the animal activity can be initiated.

When necessary, UNCG IACUC/ORI will also seek out direct guidance from the Grants Manager at the specific funding institution on the expectations and requirements for adding a performance site to an existing grant. While the grants policy covers all NIH institutes, there may also be some institute-specific procedures, such as an Institutional Assurance from NIH. As a consequence, consultation in advance of seeking permission from the GMO is advised.

5.2 Criteria for IACUC-approval of Programs which Terminate in the Transfer of Animals to otherwise Unaffiliated Institutions

If an animal research activity terminates in the transfer of research animals to an otherwise unaffiliated institution, the UNCG IACUC may require the recipient facility to provide written assurance that high quality animal care and use standards are established and observed, and that the non-UNCG institution meets all applicable federal, state and local regulations at the recipient facility.

5.3 The University Animal Transfer Form

In order to help ensure the humane transfer and receipt of animals from UNCG, and prior to transportation of animals to outside institutions, intended recipients are requested to complete an animal transfer form. (Appendix: UNCG Animal Transfer Form)
The animal transfer form requests specific information about Transfer Destination, Acquisitioner Information, and Attending Veterinarian. It also includes an assurance statement that must be signed and dated:

Assurance: I hereby assure that provisions will be in place for the humane receipt and housing of animals at the time of their arrival. I assure that high quality animal care and use standards are established and observed at my institution, and meet all applicable animal welfare laws and regulations.

5.4 Intra-campus Transfer of animals
In order to assist in the documentation of animals on campus, researchers must complete an “Animal Transfer Form” when they wish to transfer animals from one protocol to another. This form is available from the Manager of the Animal Facility and must be submitted via ACAP (as an attachment to the most current approved submission) to the ORI and IACUC. See 6.5 UNCG’s Lab Animal Resources Protocol.

6. Animal Procurement, Animal Usage and Related-Issues
All research animals on UNCG protocol or in other areas outside the centralized animal facilities including investigator laboratories must be associated with a current Application for Use of Animals in Research and Teaching or the “IACUC Form” approval number.

Criteria for Placing Animal Orders
Animal orders can be placed ONLY if the corresponding IACUC Submission has been granted IACUC approval. The animal order must have a corresponding and current IACUC-approval number (assigned at the time of IACUC-approval).

The number of animals ordered must not exceed the number designated and/or approved for use in the IACUC Form. The total number of USDA-regulated animals may not exceed the total number of animals approved for use by the IACUC for the 1-, 2- and 3- year periods indicated on the approved IACUC Form. The total number of unregulated species may not exceed 5 – 25% (more than 25% will require a new protocol) the total approved for use by the IACUC for the 1-, 2- and 3-year periods.

Animal Vendor Source
Animals may be ordered only from vendor sources approved by the Attending Veterinarian. As a rule, animals are not accepted from non-commercial sources. However, if such an arrangement is needed, the non-commercial source (e.g. another research institution in support of collaborative projects or special strain unavailable from licensed animal vendors) will be required to provide a health status report supporting the appropriate health status before animals are shipped and accepted. The quarantine program is initiated upon arrival of animals for a specified period of time determined by the Animal Facility Manager.

6.1 Biologic Materials
Biologic materials that are potential sources of murine viruses (e.g. transplantable tumors, hybridomas, cell lines, other biologic materials) are evaluated prior to their introduction into animal research programs and handled in ways to prevent transmission to animal colonies.
6.2 Display of the IACUC-Approval Number
To ensure that animals housed at UNCG can be readily associated with their corresponding research program, the IACUC-approval number must be displayed on cage identification cards.

6.3 Criteria for Initiating Research on Received Animals
Animal orders cannot be placed and research cannot be initiated until the corresponding IACUC Submission has been granted full IACUC-approval. Only the Animal Facility Manager has the authority to place animal orders.

6.3.1 Tracking Animal Use and Total Animal Numbers Used
The Animal Facility Manager will monitor and track the number of animals available in order to ensure that the total number of animal approved for use and designated in the IACUC Submission is not exceeded.

6.3.2 Exceeding Animal Numbers Approved for Use
Investigators who approach the total number of animals approved for use during the 1-, 2- and 3-year periods (indicated in the approved IACUC Form) and who expect to exceed this number must submit to the IACUC a written justification for additional animals as well as a revised estimate of the total number of animals to be used during the 1-, 2- and 3-year periods. Only upon IACUC-approval can additional animal (up to 25% (more than 25% will require a new protocol) of initial number approved by IACUC) orders be placed.

6.3.3 Retention of Research Animals under Expired IACUC-Approval Numbers
If animals remain in the animal facility under expired IACUC-approved programs that will not be renewed, the Animal Facility Manager will make every effort to reassign these animals to current IACUC-approved programs. All internal transfers will be documented, tracked and accounted for in animal usage records by the principal investigator. Those animals for which research programs cannot be identified will be euthanized prior to the expiration of funded projects.

6.4 Transfer of Animals to other IACUC-Approved Programs
The IACUC maintains that it is acceptable under certain circumstances to make internal transfers of animals to other IACUC-approved research programs. In particular, internal transfers of animals are encouraged if the animals cannot be used in their own designated IACUC-approved program.

6.4.1 Criteria for Internal Transfers
Internal transfers will be permitted only if the following criteria are met:

- transfers are made only to current IACUC-approved programs
- transfers are be documented including the date of transfer and the corresponding IACUC-approval numbers (transferred from, transferred to)
- transfers are made only to those programs that have not yet met and will not exceed (upon receipt of the transferred animals) the total number of animals approved for use
- transfers are tracked and accounted for in animal usage records
• when transferring USDA regulated species that have had a major surgery investigators should follow guidance at http://www.aphis.usda.gov/animal_welfare/downloads/policy/policy14.pdf

6.4.2 Animal Usage Record Keeping Requirements

It is necessary to maintain accurate and current animal use records. Animal use records include the documentation of the acquisition of animals (including their receipt through commercial or non-commercial vendors, through transfers from other in-house research programs and through in-house breeding programs), documentation of their use as designated by an IACUC-approval number including the associated pain category assignment, and documentation of animal disposition.

If animals are acquired for research purposes and are not entered into the program, but are euthanized or transferred outside of UNCG without research use, these animal numbers must be accurately accounted for as well.

6.4.3 Animal Usage Record Keeping - Responsible Parties

The principal investigator for each IACUC-approved program is responsible for maintaining accurate animal use records, which are verified by the Animal Facility staff. This responsibility also includes reporting animal usage for each IACUC-approved program to the IACUC on an annual basis and reporting annual animal use if and when required by regulatory agencies (e.g. OLAW, USDA).

Failure to consistently maintain accurate records could lead to issues of protocol non-compliance and be cause for IACUC review and/or sanctions.

6.4.4 Animal Usage Records

Animal usage records will include the following:

1. Total number of animals used during the 1-, 2- and 3-year approval periods, including animals euthanized prior to weaning.

2. Total number of animals used in painful or distressful procedures with or without the use of pain relieving agents
   a. justification for withholding pain relieving agents
   b. a brief description of the research protocol if pain-relief was withheld

6.5 UNCG’s Lab Animal Resources Protocol (LARP)

UNCG has established a Lab Animal Resources Protocol (LARP) to provide a mechanism for holding animals not on a study or not currently assigned to UNCG protocols.

All animals maintained by the University of North Carolina at Greensboro must be covered by an active, approved IACUC protocol. The IACUC has the responsibility to ensure all animal use activity meets federal law, Public Health Service policy, and AAALAC accreditation expectations.
LARP

1. Situations which may result in the use of this protocol might include:
   a. Animals to be used for training purposes
   b. Animals ordered without an approved protocol (non-compliance situation)
   c. Animals originating from inactive (or terminated) protocols.
   d. Animals on a protocol under investigation for potential issues of noncompliance where the welfare or well-being of the animals is in question.
   e. Investigators without an approved UNCG protocol having animals that may require immediate housing at UNCG (new faculty).
   f. Investigators that are leaving UNCG and do not have the necessary approvals for transfer to the new institution.

2. Requests to place animals on the LARP will be generated by the Animal Facilities Manager, PI, the IACUC, the ORI Director, or the AV (or designee).

3. An investigator requesting the use of the LARP must complete the “Lab Animal Resources Protocol Request Form” and submit to the Animal Facilities Manager.

4. Transfer Required Due to Termination of Approved Protocol: IACUC- and ORI-authorized transfers from expiring protocols will be generated through currently produced monthly reports: Protocol Expiration Memo and New Numbers for Expiring Protocols. These reports will be generated and sent to Animal Facilities within two (2) business days after the IACUC Full Committee meeting. These reports are the authorizing source documents for Animal Facilities staff to transfer animals to the LARP.

5. Transfer Required Due to Non-Compliant / Adverse Event: The IACUC Chair, the ORI Director, or the Attending Veterinarian are authorized to initiate the transfer of animals from an active protocol to the LARP. These actions will be reported to the IACUC at the next regularly scheduled meeting.

6. Transfer due to abandonment: The PI of an approved research protocol may elect to transfer animals to the LARP. Once the transfer has been accepted by the Animal Facilities Manager, these animals are considered “Abandoned by Researcher” and may be transferred to other protocols in line with the SOPs of UNCG and as the Animal Facilities Manager sees fit. This transfer may be acceptable in the following situations:
   a. Extra animals were inadvertently shipped from the Procurement center. If they are not needed for the approved protocol, Animal Facilities may allow transfer of the surplus into the LARP.
   b. Non-experimental animals alive at the cessation of a protocol may be allowed by the Animal Facilities Manager to be transferred.

7. Animal Facilities will transfer animals within three (3) business days of receipt of transfer request from the PI or monthly reports from IACUC and ORI.

8. Management of Animals on the LARP (what can be done):
   a. Breeding performed to maintain viability of specific lines may occur under this protocol. Expansion colony breeding is not authorized. Animal Facilities will perform all procedures necessary to maintain colony viability.
b. Feeding, sanitation, and environmental enrichment will be provided according to the approved protocol.
c. Animal Facilities may transfer animals from the LARP to other IACUC approved studies, provided such animals are Abandoned by Researcher. Appropriate transfer forms must be completed, and semiannual transfer list documenting all transfers to and from the LARP in the most current period must be submitted to the ORI.
d. When ordering new animals, PIs will be notified by the Animal Facilities Manager of available, relevant animals currently on the LARP. Also, when animals are transferred to this protocol, the Animal Facilities Manager will notify any PI that may have a need for these available animals. When applicable, a PI may make a request to the Operations Manager to transfer animals off of the LARP to an approved protocol.

These animals may then be used to practice approved procedures or for actual use in the protocol and all request to use animals on this protocol must be approved via an amendment to the ORI and IACUC. Any animal acquired from the LARP will count toward the PI's number of approved animals. No animals being held temporarily under an investigation of noncompliance (i.e. “in holding”) can be used for any procedure until the investigation is complete and the holding status on the animals has changed.

9. Animal Facilities must be notified of any pre-existing conditions of note prior to transfer of animals onto the LARP (for PI-initiated actions); and will coordinate with the PI concerning any special conditions when the transfer request is initiated by the IACUC or ORI. Examples include but are not limited to:
   a. Existing surgical implants.
   b. Zoonotic disease.
   c. Special dietary needs.
   d. Past surgical history.
   e. Viral vectors.
   f. Poor fecundity.

10. Fees: Per diem, procedure, or the fees for support of the animals on any protocol in holding for a PI will be charged to the investigator (or department) while their animals are “in holding”. Animal Facilities may place a surcharge for animals on a holding protocol. The Animal Facilities Manager may waive this surcharge as appropriate.

   NOTE: Federal grant funds may NOT be used for support of any animals in a holding protocol status due to non-compliance or failure to obtain IACUC approval for a 3 year replacement protocol.
   NOTE: New faculty transfers to UNCG may use federal funds for support of animals on a holding protocol, until such time that a protocol is approved.

11. A copy of the form to request transfer to the holding protocol by principal investigators is located on the ORI website.

7. Veterinary Medical Program
The University of North Carolina at Greensboro UNCG Attending Veterinarian is responsible for developing and implementing the Veterinary Care Program. The Attending Veterinarian for UNCG has expertise in the areas of laboratory animal medicine and science and direct animal care and use.
program authority and responsibility for activities involving animals. The Attending Veterinarian is also the appointed Doctor of Veterinary Medicine on the UNCG IACUC.

Based on UNCG’s programmatic goals and relatively small size of the animal program, the services of the Attending Veterinarian are provided on a consultative basis. Under this arrangement, other qualified and authorized individuals on the Attending Veterinarian’s behalf conduct certain components of the Veterinary Care Program such as daily monitoring of animal health and behavior. The criteria for selection of Attending Veterinarian designees includes, at a minimum, training and demonstrated ability to conduct the designated activities. Together, the Attending Veterinarian and these delegated individuals develop, implement and re-evaluate on a continuing basis those mechanisms necessary to ensure the continued well-being of research animals maintained at UNCG.

These mechanisms include a schedule of direct and frequent communication to ensure that timely and accurate information is conveyed to the Attending Veterinarian regarding identified animal health, behavior, and well-being deviations or concerns. They also include the provision of back-up veterinary support from other qualified and authorized individuals in the absence of the Attending Veterinarian.

In addition, an "emergency" notification plan has been established in the event of an animal health problem necessitating direct and/or immediate veterinary attention or guidance. In the event of a medical emergency necessitating direct and/or immediate veterinary attention or guidance, an Emergency Contact list is posted in the animal facility, which lists contact information for key animal facility personnel and the Attending Veterinarian.

7.1 Overview of Animal Care and Use Facility Personnel Training

Individuals hired into the institution to work in the Animal Facility in any animal care and use activities often possess prior specialized training and experience and/or certification in the field of animal care and/or use. They may also maintain national membership and/or certification in the American Association of Laboratory Animal Science (AALAS), AALAS Certification Registry, an organization active in public education in the importance of humane animal research and agricultural animal food production.

UNCG animal care and use personnel may also be appointed to the IACUC as non-voting members. In this capacity, they work very closely with the committee by overseeing the majority of the administrative functions. As IACUC members, these individuals attend IACUC meetings and act as sources of information to the IACUC in the review of animal use proposals and the conduct of program reviews and facility inspections. By virtue of their IACUC appointments and IACUC responsibilities, they receive the same initial and continuing education as IACUC members including the verbal updates and hard copy materials that are intended to train and educate committee members with regard to the humane care and use of animals and the current animal welfare laws and regulations.

The IACUC may also participate in training new animal care and use employees, who are not appointed to the IACUC in issues related to IACUC activities and animal care and use responsibilities. These individuals are encouraged to attend IACUC meetings and inspections or program reviews.
Other instructional mechanisms for continued training and education of animal care and use personal may include proficiency evaluations, individual (one-on-one) instruction provided by the Attending Veterinarian or other qualified and experienced persons, the provision of established guidelines, regulations and other self-instructional materials and institutional and/or IACUC handbooks and materials containing basic general information regarding animal care and use issues and occupational health.

7.2 Preventive Medicine
Quarantine, Stabilization, and Separation

Receiving and Initial Evaluation Procedures
Upon receipt, all animals are checked for order specifications (e.g. species/strain, sex, age, weight, health status, number) to ensure that the shipment received is as ordered. During removal from their shipping cartons and placement into their cages, newly received animals are examined for injury, signs of dehydration, heat exhaustion, illness, abnormal behavior, etc.

In consultation with the Attending Veterinarian and depending on the nature of the problem and/or the potential risk to other colony animals, newly received animals with suspected medical problems may be treated and retained or euthanized.

7.2.1 Quarantine and Isolation Facilities and Procedures for Purpose Bred Animals
The Quarantine/Isolation area is used when so indicated. Animals are housed in microisolators on shelving units. The Quarantine room is made up of four cubicles, each having its own air supply and exhaust. The Quarantine room airflow is negative to the animal facility to prevent the potential for contamination. The general Animal Facility housing areas consists of four animal holding rooms. Each room has its own air supply and exhaust. Animals are housed in microisolators on ventilated racks.

A sentinel program has been established. Sentinel animals are evaluated every 3-6 months to establish the health status of the animal colony.

7.2.2 Periods for Physiologic, Psychological, and Nutritional Acclimation
With the possible exception of animals designated for acute non-survival studies, newly received animals by the Animal Facility are closely observed during a minimum 7 - 14 day acclimation period for physiologic, psychological, and nutritional stabilization. The length of time depends on the type and duration of animal transportation and the intended use of the animals. The personnel of the Animal Facility, in consultation with the Attending Veterinarian, and depending on the nature of the problem and/or the potential risk to other colony animals, animals with suspected medical problems during the acclimation period might be treated and retained or euthanized.

Animals designated for acute non-survival studies (e.g. tissue collection, diagnostic purposes/vendor screen) may be used prior to completion of the acclimation period.

7.2.3 Program for Separation of Animals by Species, Source, and Health Status
Animals are housed in rooms with animals of the same species only. Animals from the same shipment are housed individually or in groups in microisolators designated animal rooms.
Since only animals with comparable health status are acquired and only from approved reputable vendors, animals from different sources may be housed in the same animal room.

7.3 Surveillance, Diagnosis, Treatment, and Control of Disease Program

7.3.1 Daily Observation of Animals and Responsible Personnel
Animal Facility personnel conduct daily checks of animals. If needed, and based on professional judgment and in consultation with the Attending Veterinarian, more frequent observations of animals are conducted as in the cases of post-operative recovery, anticipated delivery of pups, post-partum health checks, pup well-being, etc. Additionally the Principal Investigator can request more frequent observations of their animals by contacting the Animal Facility Manager.

Individuals responsible for conducting animal care checks are trained to recognize signs of illness, injury, and/or abnormal behavior.

7.3.2 Emergency Notification
An Emergency Contact list is posted in the animal facility, which lists contact information for key Animal Facility personnel and the Attending Veterinarian.

7.3.3 Medical Records - Maintenance Procedures
Animal Facility personnel are responsible for maintaining all animal health and medical records on file in the Animal Facility Manager's office. These reports include:

- Vendor health screen reports that accompany all animal shipments
- Diagnostic reports generated from the quarterly sentinel program
- Results of other diagnostic evaluations which may be conducted in the event of a disease investigation or suspected illness warranting diagnostic evaluation
- Weekly "Colony Population, Animal Health and Facility Environment" Reports
- Medical records generated in the event of a sick or injured animal, including date and nature of illness or injury, on-going accounts of actions taken (e.g. administration of medical treatment) and the description of the animal's progress. (Medical records may also include information about experimental procedures.)
- Records of animal deaths

7.3.4 Sentinel Program - Quarterly Health Monitoring:
- The Sentinel Program is a primary means for ensuring the continued health quality of research animals maintained in the animal colony at the facility. On a quarterly basis or more often if needed, sentinels from the animal colony are submitted for a comprehensive diagnostic and health evaluation screen to determine the health of the research animal colony. The sentinel program is conducted as approved by the UNCG IACUC. The housing of sentinel animals, in equivalent macro- and micro-environments, as well as their direct exposure to fomite-contaminated bedding from these other, non-sentinel animals, enable monitoring the research animal colony for exposure to common murine pathogens.
- Typically, one to two sentinels are housed per cage, one cage per side of rack, and positioned on the lowest shelf of an animal rack housing other boxes of research
animals. Cages are changed once a week. To ensure direct contact with fomites to increase the chances of pathogen transmission, small amounts of soiled bedding from every cage of other research rodents housed on the same rack are introduced into the sentinel cages in-between cage changes.

- The design of the sentinel program may be modified as deemed necessary to meet the needs of the program and to ensure high quality monitoring of the health status of the research animals. The sentinel program is reviewed and approved by the IACUC on an annual continuing review and a triennial de novo review basis.
- After 3 months within the facility, sentinels are transported to a reputable animal diagnostic laboratory for either a “comprehensive” evaluation or diagnostic testing.
- The "comprehensive" battery includes:
  - **Pre-Necropsy Examination:** Hair Coat/Skin, Skeletal Palpation, Nasal Discharge, Ocular Discharge, Diarrhea, Hydration, Body Fat, Ears
  - **Gross Necropsy Pathology:** Respiratory System, Digestive System, Musculoskeletal System, Urinary System, Genital System, Thymus, Spleen, Lymph Nodes, Adrenal Gland, Thyroid, Middle Ear, Eye
  - **Histopathologic Pathology** (on representative tissue samples if evidence of lesions or disease): Lung, Cecum, Small Intestine, Liver, Colon
  - **Parasitology:** Ecto-parasites (pelt examination), Endo-parasites (fecal-floatation, cellophane tape test)
  - **Mouse Serology:** Mouse Hepatitis Virus, REO3, Minute Virus of Mice, Lymphocytic Choriomeningitis Virus, Ecrtromelia Virus, MCMV, Polyoma, Sendai Virus, Pneumonia Virus of Mice, EDIM, GDVII, K-Virus, MPUL, MAV, HANT, ECUN, MTLV, CARB, MPV NS1 and MPV VP2
  - **Rat Serology:** Sendai, PVM, SDAV, KRV, H-1, REO, MPUL, RPV, TMEV, LCMV, MAV, HTN, ECUN, CARB
  - **Extra testing includes:** Helicobacter (H. species, H. hepaticus, H. bilis)
  - **In addition, all sentinels are tested for Helicobacter ((H. species, H. hepaticus, H. bilis)).**

### 7.3.4.1 Disease Investigations
- In the event of a suspected illness, and in consultation with the Attending Veterinarian, representative animals and/or their tissues/products are submitted to reputable diagnostic facilities for evaluation.

### 7.3.4.2 Diagnostic Reports
- Diagnostic reports are submitted to the Attending Veterinarian or authorized designee for review, evaluation and action plan development. Diagnostic reports are maintained in the animal colony medical health records.

### 7.3.4.3 Diagnostic laboratory facilities, equipment and commercial services
- UNCG relies exclusively on reputable commercial sources for animal health support services. UNCG submits animals, animal tissues/products and/or cell lines to reputable
contract research animal diagnostic facilities. There is no in-house support for diagnostic services including serology, necropsy, pathology, and radiology.

7.3.4.4 Annual Diagnostic Frequency
- The number of sentinels submitted for diagnostic services and animal health evaluation per year varies based on the health status of the colony, average daily census, and other factors.

7.4 Study Records

The Principal Investigator and corresponding IACUC-approved animal use personnel are responsible for maintaining animal records associated with an animal use activity. These records include but are not limited to an on-going account of animal procedures performed, the nature of any animal illness or injury and corresponding actions, the Controlled Drugs Log-Book (if applicable), etc.

Failure to consistently maintain accurate records could lead to issues of protocol non-compliance and be cause for IACUC review and/or sanctions.

7.5 Surgery

Oversight of the Surgical Program; Responsible Individuals

Surgical monitoring is the responsibility of the Attending Veterinarian or the principal investigator in consultation with the Attending Veterinarian. Other individuals who have been trained and deemed proficient and have been reviewed and approved by the IACUC may also conduct specialized surgical techniques including monitoring associated with approved animal use activities.

All surgical procedures are developed in consultation with, reviewed, approved and authorized by the Attending Veterinarian and approved by the IACUC before initiation. The IACUC can exercise its authority to withhold approval of a proposed surgical procedure, require a surgical proficiency evaluation by the Attending Veterinarian or other qualified individual as a requirement for approval, or require the Attending Veterinarian to participate in or conduct the surgical manipulation.

7.5.1 Pre-surgical Planning

Processes Used to Assure Adequate Pre-surgical Planning

During the Animal Use Proposal review process and prior to the initiation of any surgical procedure, appropriate attention to pre-surgical planning, personnel training, aseptic and surgical technique, animal well-being, and animal physiologic status during all phases of a protocol is assured.

Appropriate pre-surgical planning involves active consultation of the principal investigator (and other members of the surgical, research and animal care team, if applicable) with the Attending Veterinarian. The Attending Veterinarian provides necessary guidance and direction in the development of all phases of the surgical design, and if necessary, direct supervision or training, to ensure all aspects will be conducted appropriately. Consultations take places either prior to the submission of the IACUC Submission to the IACUC or during
the IACUC review and approval process itself. IACUC approval to initiate any animal use proposal is not granted until the Attending Veterinarian has signed the "Attending Veterinarian Review" section of the IACUC Form, which states:

"As Attending Veterinarian, I have reviewed the proposed animal use procedures and have found them appropriate for this protocol."

In addition, and during its review of the "Assigned Responsibilities: Laboratory Personnel" section of the IACUC Form, the IACUC:

- Reviews the list of all program participants (including temporary employees, etc.) and their assigned responsibilities.
- Considers the investigator's response to "Are all individuals active in this research program experienced or trained to perform their assigned animal use procedures"?
- Considers the investigator's account of the provisions for training, if personnel are unqualified or untrained.

In addition, the IACUC considers the principal investigator's assurance statement in the IACUC form, which includes the statement:

"The laboratory personnel listed in this Submission will have sufficient education, training, and/or experience to appropriately perform their assigned animal care and use activities."

and

"I will obtain veterinary consultation prior to the initiation of this research, with specific emphasis on procedures expected to cause pain or distress."

7.5.2 Surgical Training Program

Only those individuals who are trained, qualified, proficient and approved by the IACUC may perform surgical procedures. Those with surgical proficiency may also provide training to inexperienced or inadequately experienced individuals.

7.5.3 Major and Minor Procedures

Criteria for Differentiation of Major and Minor Procedures

Surgery can be major or minor in nature.

**Major surgery:** any surgical manipulation that "...penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic function." (Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Academy Press, Washington, D.C., 1996) and "...any surgical intervention that penetrates and exposes a body cavity or any procedure which produces permanent impairment of physical or physiological functions" (Animal Welfare, 9CFR Part 1 Section 1.1).
Examples of major surgery are laparotomy, thoracotomy, craniotomy, joint replacement, ovariectomy, embryo transfer and limb amputation.

**Minor surgery:** any surgical manipulation that "$\ldots$does not expose a body cavity and causes little or no physical impairment" (Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Academy Press, Washington, D.C., 1996)

Examples of minor surgery include peripheral vessel exposure and cannulation, dermal incision, superficial biopsies and suturing etc.

Surgery can be broken down further into aseptic or sterile versus clean surgery:

- **Aseptic surgery:** an aseptic field is created at the surgical site and involves preparing the patient, surgical team and all surgical instruments to prevent introduction of microorganisms into the patient. Aseptic technique is required for all survival surgeries.
- **Clean surgery:** the surgical site is cleaned with a minimum of 70% alcohol and instruments, gloves, and associated equipment are clean but not necessarily sterile. Clean surgery is only acceptable for non-survival surgeries.

The required surgical facility is dependent upon both the nature of the surgical procedure (minor or major) and the species of animal.

Dedicated facilities are required for the conduct of major surgeries in non-rodent, mammalian species. They are not required for rodent surgery but rodent surgery must be conducted aseptically in a portion of a room dedicated to the conduct of surgery and provided it is the only ongoing activity in the room at the time of the procedure.

- **Dedicated facilities:** an area specifically equipped and exclusively dedicated to the conduct of surgery and operated under aseptic conditions.

Surgical procedures in animal research fall into one of two categories:

- **Non-survival surgeries:** animals are euthanized prior to anesthetic recovery
- **Survival surgery:** animals will recover from anesthesia

In all survival surgeries, post-operative analgesia and care must be considered.

Surgical procedures performed at UNCG may include:

- embryo (blastocysts) transfer (a major survival surgery)
- vasectomy (a minor survival surgery which may also be conducted by the vendor facility prior to shipment to UNCG
- C-section delivery of chimeras from euthanized mothers (a minor survival surgery with respect to pups)
7.5.4 Practices Employed During Non-survival Surgeries

Non-survival surgery must meet at a minimum the definition of "clean surgery". The procedure must be preceded by the administration of appropriate anesthetics that will be maintained to ensure unconsciousness throughout the procedure and the subsequent euthanasia. The surgical site must be cleaned with a minimum of 70% alcohol and instruments. Gloves, equipment, instruments and surrounding area must be clean but not necessarily sterile. Clean surgery is only acceptable for non-survival surgeries of relatively short-duration.

7.5.4.1 Aseptic Procedures

Procedures and Equipment Used to Assure Aseptic Surgical Technique

Patient Preparation

Patient preparation is conducted in an area within the surgical hood away from the area in the surgical hood designated for performing the aseptic surgery.

Anesthesia is induced. Hair is removed from the area about the incision site. An adequate area is removed of hair to ensure that instruments will have no contact with the pelage during surgery. This is particularly important since sterile drapes are not used and the sterile field is restricted to the area of skin surrounding the incision.

Immediately prior to surgery, the surgical site is thoroughly cleansed and disinfected with surgical scrub (e.g. Betadine, Chlorhexidine) following manufacturer’s instructions. 70% alcohol solution may be substituted for the final iodine solution and is allowed to dry in place. To prevent prolonged recovery, irreversible hypothermia and/or death, drenching the animal with excess fluid is avoided. Caution is exercised to prevent subsequent contamination of the disinfected area.

7.5.4.2 Surgeon Preparation

The surgical garb includes clean surgical scrubs, surgical mask, bonnet, booties and sterile gloves. A sterile surgical gown may also be worn for rodent aseptic surgery. Non-rodent aseptic surgery requires sterile surgical gown. Surgical garb that becomes grossly contaminated is changed between animals.

Surgical procedures are conducted under a hood located within the injection suites/procedures rooms within the barrier facility. Entry and garbing procedures into the barrier follow very specific protocol. As such, the surgeon than washes his/her hands thoroughly with microbicidal soap, dries them with a clean towel when entering the surgical area. The surgeon dons mask, bonnet, and sterile gloves.

After patient preparation, surgical stage preparation and prior to initiating the actual surgery, the surgeon removes and disposes of his/her gloves and replaces them with sterile gloves. Sterile surgical gloves are carefully donned in a manner that prevents contamination of their exterior surfaces. Gloves are changed if they become ripped or
inadvertently contaminated by contact outside the aseptic field and between animals. Gloves are changed between animals during the conduct of multiple consecutive surgeries.

7.5.5 Equipment Preparation

Prior to introducing surgical support equipment or any materials that will be used during the conduct of surgery, the interior surfaces of the surgical hood are removed of any equipment or supplies and disinfected. The stage of the microscope, used during the conduct of embryo transfers, is wiped with 70% ethanol.

7.5.5.1 Methods Used to Sterilize Instruments and Protective Clothing

Instruments
The conduct of aseptic surgery includes the provision of a sterile field at the surgical site. This provision necessitates the preparation of the patient, surgical team and all surgical instruments to prevent introduction of microorganisms into the patient. Aseptic technique is required for all survival surgeries.

All surgical instruments are either purchased pre-sterilized or sterilized prior to use: steam (autoclave) or chemical methods (e.g. liquid sterilants). Use of quaternary ammonium compounds and alcohol for the purpose of sterilization are not considered acceptable. If sterilized at the facility, surgical instruments required for the procedure are washed with an antibacterial soap, dried, assembled into pack(s), wrapped, and autoclaved prior to surgery. Sterilization tape indicators positioned on the outside of packs are used to ensure sterilization.

If consecutive surgeries on a group of animals are performed, one pack of instruments may be used for more than one animal provided the instruments do not become contaminated during surgery and are properly disinfected between animals (e.g. hot bead sterilizer followed by adequate cooling, immersion in liquid sterilants or disinfectant - Betadine, Povidone - followed by a sterile saline rinse or blotting to remove the solution).

If the surgical procedure involves a significant potential for instrument contamination between patients (e.g. penetration of the gastrointestinal tract, presence of infected wounds), only one surgery is conducted per sterile set of instruments. Any fluid, instrument, material or device that contacts the internal environment of the animal is sterilized before use in another animal.

Sterile, prepackaged sutures/staples (available commercially) may be used for incision closure. Precut non-sterile silk may be included in instrument packs, steam sterilized (autoclaved) and discarded if not used. Surgical staples or sterilized wound clips may be used as alternatives to sutures.

Disposable sterile or autoclaved cloth drapes are not used in rodent survival surgery. Drapes may be used for wrapping surgical instrument packs or for creating a sterile field.

Protective Clothing
The surgical garb includes a clean surgical scrubs, surgical mask, bonnet and booties. A surgical gown may also be worn. Sterile surgical gloves are worn during aseptic surgery and are purchased pre-sterilized.

7.5.6 Surgical Facility Use

Approximate Number of Surgical Procedures

The approximate range of non-survival surgeries that may be performed over a one-year period is based upon IACUC approved protocols for Non-survival procedures.

The approximate range of survival surgeries, which may be performed over a one-year period, is based upon the IACUC approved protocol for survival procedures.

All surgical procedures are conducted under a positive pressure hood located within the procedure room.

7.5.6.1 Surgical Preparation and Approach

In preparation for surgery, all non-related activities within the hood and within the room are stopped. The interior surfaces of the hood are disinfected with disinfectant and wiped down with paper towels.

Using embryo transfer as an example, a mouse cage is introduced and positioned within the hood. An absorbent paper/cloth is positioned on the hood surface just in front of the cage. An animal is removed momentarily for administration of anesthesia and returned to the cage.

The microscope and fiber optic lamp are in the hood. The stage of the scope is wiped down with 70% ethanol.

Once anesthetized, the animal is removed from its cage and positioned (ventral recumbency) on the absorbent paper/cloth. The area of hair overlying the surgical site is shaved followed by a thorough cleansing and disinfecting of the surgical site with surgical scrub (e.g. Betadine, Povidone, DuraPrep). The final iodine solution may be substituted with a 70% alcohol solution, which is allowed to dry in place. Drenching the animal with excess fluid is avoided to prevent prolonged recovery, irreversible hypothermia and/or death.

The hood surfaces and patient preparation area are sprayed with 70% ethanol exercising caution not to expose the patient. The patient is positioned in a sterile petri dish for easy transport between center hood and microscope stage. Sterile instrument pack including instruments and closure materials are introduced and opened.

Used gloves are removed. Sterile gloves are donned and the surgical procedure is initiated and performed. A single suture is used to close the body wall incision. Wound clips are used to close the skin incision. (The surgery takes approximately 8 - 10 minutes.) The animal is returned to its cage and monitored frequently during anesthetic recovery. The underlying heating pad is used to prevent hypothermia. The mouse is anesthetized for an approximate 40-minute total period. After full anesthetic recovery, the animal is returned
to its home cage for post-operative recovery. It is observed and evaluated at least 1 time per day. Analgesia is administered, if needed. Wound clips may be removed 3-5 days post-surgery or when incision is sufficiently healed, however this approach may not be acceptable in this particular procedure and therefore not always followed. Specifically as it pertains to embryo recipients, skin closure clips may remain in place until after delivery of pups. Based on the experience with this specific procedure, the ensuing pregnancy and its associated abdominal distention can cause progressive pulling and tension at the incision site and may compromise healing. As such, removal of clips during the standard 3-5 day post-surgery period may significantly increase the potential for a break or rupture in the surgical incision. Decisions to remove or not to remove wound clips are made on a case-by-case basis.

7.5.6.2 Postsurgical Actions

Postsurgical Care

Animal facility personnel are responsible for overseeing and providing care during the postsurgical period. After anesthetic recovery, the animal is returned to its home cage for post-operative recovery and observed and evaluated at least 1 time per day. Analgesia is administered, if needed.

During the post-surgical period, special attention is given to the basic biologic functions, feed intake, urine and feces output, behavioral signs of postoperative pain (i.e. deviations from normal behavior), monitoring for postsurgical infections, monitoring of the surgical incision, and timely * removal of skin sutures, clips, or staples.

For uneventful post-operative recovery, all observations and actions taken, including the administration of analgesics, are recorded in the principal investigator’s study records as well as the Facility Manager’s animal medical records (generated in the event of a sick or injured animal, including date and nature of illness or injury, on-going accounts of actions taken and the description of the animal’s progress). Medical records may also include information about experimental procedures. In addition, all eventful post-operative recoveries will be brought to the attention of the Attending Veterinarian. Depending on the nature and severity of the problem, the Attending Veterinarian will be notified immediately or in the weekly “Colony Population, Animal Health and Facility Environment” report.

7.5.6.3 Rodent Survival and Non-Survival Procedures

7.5.6.3.1 Locations of Rodent Survival and Non-Survival Procedures

The injection suites/procedure rooms within the barrier facility are used for survival rodent surgeries. All surgical manipulations are performed under a positive pressure hood located within the injection suite. During the conduct of surgery, no unrelated activities are permitted within this room.

Survival procedures performed in the surgical hood include embryo transfer (survival surgery) and C-section delivery of pups (from euthanized mothers).
Tissue collection on euthanized animals may also be performed in the surgical hood
including embryo collection and uterus collection (for processing of Mouse Embryonic
Fibroblasts).

At a minimum, all survival surgical procedures are performed in a disinfected hood, with
adequate preparation of the surgical site, including hair removal and skin disinfection, use
of sterile instruments and closure materials, use of sterile gloves, and face mask.

7.5.6.3.2 Summary of Performance Sequence
In general*, the sequence of events for aseptic rodent surgery conducted by an unassisted
person garbed for surgery is:

1. Anesthetize animal
2. Remove hair/fur from and cleanse and disinfect incision site
3. Move patient to aseptic surgical space and position appropriately
4. Don surgical mask and bonnet *
5. Open sterile pack(s), including instruments, drapes, suture material, etc.
6. Wash and dry hands *
7. Don sterile surgical gloves
8. Incise skin
9. Complete surgical procedure
10. Close skin
11. Disinfect used instruments between patients; e.g. cold sterilizing solution or hot bead
    unit
12. Move patient to recovery area
13. Initiate post-operative recovery monitoring and care

* Surgical procedures are conducted under a hood located in the injection suites/procedure
rooms. Hands are washed thoroughly with microbicidal soap and dried with a clean towel
prior to starting surgery.

7.5.6.4 Pain, Distress, Analgesia, and Anesthesia

7.5.6.4.1 Assessment and Assignment of Pain and Distress Levels
The IACUC classifies the corresponding level of pain and distress anticipated in a given
animal use activity during the Animal Use Proposal review and approval process. In the
IACUC Submission, the principal investigator is requested to assign research animals to one
or more of the following categories:

Category C: animals will not experience greater than momentary or transient pain or
distress such as that produced by routine injections or venipuncture.

Category D: animals may experience greater than momentary or transient pain or distress
but will receive anesthetics, analgesics or tranquilizers to prevent, alleviate and/or
minimize pain or distress.
Category E: animals may experience greater than momentary or transient pain or distress and will not receive anesthetics, analgesics or tranquilizers.

If any portion of the research animals is assigned to Category E, the principal investigator must also address the following:

- Describe the nature of the pain and/or distress and the measures to be taken to minimize the pain and/or distress:
- Provide scientific justification for withholding pain-relieving agents. Include literature references if available.

During the IACUC Submission review and approval process, the IACUC including the Attending Veterinarian reserves the right to reassign animals as they deem appropriate to one or more of the three defined pain/distress categories if they agree that reassignment is necessary to accurately reflect the anticipated distribution of research animals between pain/distress categories.

The IACUC also reserves the right to require the observation of the procedure or procedure outcome (conducted on a limited basis) by the Attending Veterinarian and/or representative IACUC members or other qualified and authorized individual to assess the pain/distress levels of animals on study before granting full-approval.

7.5.6.4.2 Guidelines for ensuring unnecessary pain or distress is avoided

The IACUC maintains that anesthetic, analgesic, or tranquilizing agents should be administered for any procedure with the potential for causing more than minimal and/or transient pain or distress to the animal. For proposals that have significant potential for causing more than slight and momentary pain and distress, investigators are required to

- provide scientific justification for withholding pain relieving agents if applicable
- describe the degree and duration of pain/distress
- provide assurance that the painful procedure will continue only for the period of time necessary
- clearly establish the steps to monitor and to respond to animals in pain
- develop all painful or potentially painful procedures in consultation with the Attending Veterinarian

The IACUC requires that all potentially painful or distressful procedures including those which utilize anesthetics, analgesics and tranquilizers to prevent, minimize or alleviate pain and distress be developed in consultation with the Attending Veterinarian or his/her designee.

The IACUC also requires the Principal investigator to sign the IACUC Submission Principal Investigator's Assurance Statement, which includes the following assurance:

"I have engaged in veterinary consultation with specific emphasis on procedures expected to cause pain or distress. Such procedures will be restricted to the minimum time necessary to meet the objectives of the research. If an animal experiences severe or chronic pain or
distress that cannot be relieved, it will be euthanatized at the end of the procedure, or if appropriate, during the procedure. In the event of unanticipated pain or distress, a signed retrospective report, detailing the circumstances of the event and referencing the appropriate AUA number, will be submitted to the IACUC in a timely fashion.”

In addition, the availability of alternatives must also be addressed in animal research programs which have the potential for causing greater than slight or momentary pain (i.e. pain or distress greater than that caused by routine injections or venipuncture) even in those programs which incorporate the use of pain relieving agents to prevent or minimize pain.

The IACUC maintains that the use of pain relieving agents to prevent or minimize pain does not negate the PI’s responsibility to consider alternatives to these procedures and list the sources, date of literature search and key words (if applicable) used.

**7.5.6.4.3 Anesthetics and Analgesics Used**

- **Mice**: Avertin, 30 mg/gm (ip); Children’s Tylenol, 1.25 ml per 200 ml of water (po)
- **Rats**: Avertin 0.5 - 0.6 mg/gm (ip); Children’s Tylenol - 1.25 ml per 200 ml of water (po)

**Veterinarian Consultation**

All potentially painful or distressful procedures including those which utilize anesthetics, analgesics and tranquilizers to prevent, minimize or alleviate pain and distress must be developed in consultation with the Attending Veterinarian or his/her designee.

In addition, the Attending Veterinarian is a full-voting member of the IACUC. The IACUC will not approved any IACUC Submission until it they are assured that the Attending Veterinarian has reviewed the document.

**Training and Experience of Individuals in the Recognition of Pain and Distress**

Individuals responsible for assessing pain and distress are trained and experienced to recognize normal animal behavior related to states of comfort or homeostasis as well as to recognize clinical signs indicative of pain and distress in the specific species. While species-specific behavioral manifestations of pain or distress are used as indicators if and when they are present or apparent, these individuals rely heavily on careful and frequent observation of animals for deviations from physiological and behavioral homeostasis. Deviations from the norm are considered probable warning that an animal may be experiencing some degree of pain or distress, and further evaluation is warranted.

If a possible problem is identified, the Attending Veterinarian is notified and informed. Depending on the nature and severity of the problem, the Attending Veterinarian may recommend appropriate non-pharmacologic or pharmacologic interventions, as necessary.

Those individuals responsible for pain-relieving agent administration (post-surgical care) are listed in the corresponding IACUC-approved IACUC.
7.5.6.5 Anesthesia Machine/Vaporizer Calibration and Maintenance Guidelines

The purpose of this document is to provide guidelines regarding recommended scheduling for anesthesia machine/vaporizer calibration and maintenance. All users are advised to follow the manufacturer’s recommendations if they differ from this document.

Anesthesia machines and vaporizers must be in good working condition to reduce anesthetic gas leaks, to ensure the best performance of scavenging equipment, and provide the appropriate percentage of anesthetic delivery. Personnel must be trained in the proper use of anesthetic machines and vaporizers prior to operation. Each piece of equipment involved in the delivery of inhalant anesthetics must be evaluated regularly to assure its proper function and integrity.

NOTE: All anesthesia machines must be available for inspection during IACUC Semi-Annual inspections for verification of proper service and maintenance.

Guidelines

7.5.6.5.1 Vaporizer Service:

Accuracy of anesthetic agent delivery must be verified annually or any time the vaporizer has not been in service for more than a year. If the verified delivery is +/- 15% out of calibration, the unit should be serviced by an authorized service center.

All anesthetic vaporizers should be serviced by qualified personnel (authorized service center) as recommended by the manufacturer. Manufacturer recommendations range from one to three years depending on the model.

Discoloration (yellowish-brown) in the “Fill” sight glass of a vaporizer is an indication of need for service by an authorized service center.

7.5.6.5.2 Waste Gas Scavenging Systems:

Anesthetic machines must have an effective mechanism of waste gas scavenging because waste anesthetic gases may adversely affect liver, kidney, or the central nervous system of chronically exposed personnel and animals. Scavenging systems may be active or passive and could include the use of an absorber. Charcoal canisters (e.g. F/AIR, BREATHE FRESH) may be used to absorb halogenated waste gases, but not nitrous oxide. Manufacturer's guidelines must be followed and usage must be documented either with a log indicating the hours used or weight of the canister (pre and post use) which must be indicated on the side of the canister.

7.5.6.5.3 Fume hood:

Open drop anesthesia techniques must be conducted in a fume hood that has been tested and certified by Physical Plant.

7.5.6.5.4 Documentation:

Vaporizers must have documentation of a date of delivery test with the initials for the person who performed the test and the test results. Vaporizers must have a certificate of the calibration date affixed after each service.
Services available:
Following are a list of services available through private industry. The Animal Facility will coordinate and maintain Animal Facility owned anesthesia machines. Researchers that own their own anesthesia machine are responsible for arranging and covering the costs for service.

Absolute Anesthesia
Mitch Madison
434-277-9360

7.5.7 Use of Expired Medical Materials and Non-Pharmaceutical-Grade Compounds in Research

7.5.7.1 Pharmaceutical-Grade Chemical Use:
All compounds/substances/chemicals introduced into animals should be pharmaceutical grade to prevent contamination, infection or damage and to support research outcomes.

The use of pharmaceutical-grade substances in laboratory animals ensures that the substances administered meet established documentable standards of purity and composition. This in turn helps ensure research animal health and welfare, as well as the validity of experimental results. The use of lower grade substances/compounds with undefined or higher levels of impurities or poorly formulated non-commercial preparations can introduce unwanted experimental variables or even toxic effects, and so should be avoided if at all possible. Although pharmaceutical grade substances should be used in experimental animals whenever possible, the use of non-pharmaceutical-grade substances in experimental animals is an acceptable practice under certain circumstances. For example, in the case of new investigational compounds, they would be the only grade and formulation available. The NIH Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture (USDA) both have determined that the use of non-pharmaceutical-grade substances should be based on (1) scientific necessity, (2) non-availability of an acceptable veterinary or human pharmaceutical-grade compound, and (3) specific review and approval by the institutional IACUC. Cost savings alone is not considered an adequate justification for the use of non-pharmaceutical-grade substances in laboratory animals. OLAW has also stated that while the possible implications of the use of non-pharmaceutical grade substances in non-survival studies appears less evident, the scientific issues remain the same and professional judgment, as outlined above, must still apply. It is important to understand that this guideline pertains to all components, both active and inactive, contained in the preparation to be administered. Therefore, the vehicle used to facilitate administration of a compound is as important of a consideration as the active compound in the preparation.

Pharmaceutical grade compound: Drug, biologic, reagent, etc. which is approved by the FDA or for which a chemical purity standard has been written/established by USP/NF, BP
**Analytical grade bulk chemical**: ~99% purity; Certificate of Analysis is usually available

**Non-availability**: Not commercially available from an active US vendor; includes formulations supplied as tablet, capsule, injectable, etc.

**New investigational compound**: Supplied by its manufacturer for testing in an experimental setting only and for this reason would not have chemical purity standards established; by default is considered a non-pharmaceutical grade compound

**USP/NF**: United States Pharmacopeia/National Formulary

**BP**: British Pharmacopeia

**FDA**: Food and Drug Administration; FDA approved compounds are manufactured using USP/NF compounds

### 7.5.7.2 Non-Pharmaceutical Grade Chemical Use:

This policy provides a definitive position on the use of non-pharmaceutical grade substances in the UNCG Animal Care & Use Program. The policy is consistent with the guidance from the NIH/ILAR Guide for the Care and Use of Animals, the corresponding Position Statement from AAALAC, International, and the NIH/Office of Laboratory Animal Welfare’s Position Statement.

1. When selecting compounds the following order of choice should be applied:
   a. FDA-approved veterinary or human pharmaceutical substances;
   b. FDA-approved veterinary or human pharmaceutical substances used to compound a needed dosage form;
   c. USP/NF or BP pharmaceutical grade substance used in a needed dosage form (also includes compounded products from sources such as compounding pharmacies);
   d. Analytical grade bulk chemical used to compound a needed dosage form (requires justification);

2. Other grades and sources of substances (requires justification).

**NOTE**: For new investigational drugs the grade and formulation is not optional, but the investigator and IACUC can verify health and safety issues described above.

3. For a majority of common substances used in laboratory animal research, pharmaceutical grade (USP or NF grade) substances are available and should be used. Examples of common substances that are available in USP or NF grades include:
   - Saline
   - DMSO
   - Corn oil
   - Tamoxifen
   - Tetracycline
   - Analgesics (e.g., buprenorphine)
   - Anesthetics (e.g. ketamine)
   - Euthanasia reagents (e.g. Euthasol)

4. **When a non-pharmaceutical grade substance is proposed**: When developing and reviewing a proposal to use non-pharmaceutical grade substances, the investigator and IACUC should consider animal welfare and scientific issues related to the use of the
substances, including potential for contamination, safety, efficacy, and the inadvertent introduction of confounding research variables. **For all non-pharmaceutical grade substances used in animals, the IACUC shall consider the grade/purity being proposed, the formulation of the final product, and issues such as sterility, pyrogenicity, stability, pH, osmolality, site/route of administration, pharmacokinetics, physiological compatibility, and quality control.** The IACUC may use a variety of administrative methods to review and approve the use of such agents. For example, the IACUC may establish acceptable scientific criteria within the institution, rather than on a case-by-case basis. The use of non-pharmaceutical-grade compounds in laboratory animals shall be clearly delineated and justified in the protocol document and/or covered by an IACUC policy developed for their use.

5. **Examples for use of Non-Pharmaceutical-Grade Substances:** It would be reasonable for the IACUC to review and the Committee may approve the use of non-pharmaceutical-grade substances in the following situations:
   a. If no equivalent veterinary or human drug is available for experimental use, then the highest-grade equivalent chemical reagent should be used and formulated aseptically and with a non-toxic vehicle as appropriate for the route of administration.
   b. Although an equivalent veterinary or human drug is available for experimental use, the chemical-grade reagent is required to replicate methods from previous studies because results are directly compared to those of replicated studies.
   c. Although an equivalent veterinary or human drug is available, dilution or change in formulation is required.
      - If adulteration by dilution, addition, or other change in formulation is required, there may be no additional advantage to be gained by using the USP formulation.
      - Use of the highest-grade reagent may have the advantage of single-stage formulation and also result in purity that is equal to or higher than the human or veterinary drug.
      - Professional judgment should be used to determine the appropriate test material and to ensure use of an agent with the least likelihood for causing adverse effects.
   d. The available human or veterinary drug is not concentrated enough to meet experimental requirements.
   e. The available human or veterinary drug does not meet the non-toxic vehicle requirements for the specified route of injection.

7.6 Euthanasia

*AVMA Guidelines for Euthanasia of Animals: 2013 Edition*

**Euthanasia Secondary Methods by Species**

7.6.1 CO2 inhalation:

- Specifically designated rats or mice for which the study endpoint is euthanasia in the approved IACUC Submission
Rats and mice housed at UNCG that present with health problems necessitating euthanasia and for which this euthanasia method will not compromise research results (as supported by scientific justification in the approved IACUC Submission).

This form of euthanasia may not be appropriate for neonates.

AVMA Guidelines recommend:

- General recommendations—Carbon dioxide is acceptable with conditions for euthanasia in those species where aversion or distress can be minimized. Carbon dioxide exposure using a gradual fill method is less likely to cause pain due to nociceptor activation by carbonic acid prior to onset of unconsciousness; a displacement rate from 10% to 30% of the chamber volume/min is recommended.25,152,193,195 Whenever gradual displacement methods are used, CO2 flow should be maintained for at least 1 minute after respiratory arrest.153 If animals need to be combined, they should be of the same species and, if needed, restrained so that they will not hurt themselves or others. Immature animals must be exposed to high concentrations of CO2 for an extended period of time to ensure death. Oxygen administered together with CO2 appears to provide little advantage and is not recommended for euthanasia.
- The practice of immersion, where conscious animals are placed directly into a container prefilled with 100% CO2, is unacceptable. A 2-step process, where animals are first rendered unconscious and then immersed into 100% CO2, is preferred when gradual displacement methods cannot be used. Immersion of poultry in lesser concentrations is acceptable with conditions as it does not appear to be distressing.
- Carbon dioxide and CO2 gas mixtures must be supplied in a precisely regulated and purified form without contaminants or adulterants, typically from a commercially supplied cylinder or tank. The direct application of products of combustion or sublimation is not acceptable due to unreliable or undesirable composition and/or displacement rate. As gas displacement rate is critical to the humane application of CO2, an appropriate pressure-reducing regulator and flow meter or equivalent equipment with demonstrated capability for generating the recommended displacement rates for the size container being utilized is absolutely necessary.

7.6.2 Cervical Dislocation without anesthesia:

- Specifically designated research mice for which the study endpoint is euthanasia and for which the unacceptability or unavailability of satisfactory alternative euthanasia methods is supported by scientific justification in the approved IACUC Submission.

7.6.3 Cervical Dislocation with anesthesia:

- Specifically designated rat embryo donors; cervical dislocation will be performed immediately after embryo harvest and prior to anesthetic recovery.

7.6.4 Training and Experience in Euthanasia Methods

Only individuals who are trained and skilled to perform euthanasia and to recognize cessation of vital signs in the particular species are authorized to carry out euthanasia. Those individuals responsible for the conduct of euthanasia are listed in the corresponding IACUC-approved IACUC Submission.
7.7 Breeding Colonies

The Facility staff will perform daily checks in rooms housing rodents used in breeding protocols. Special housing/husbandry requirements should be communicated to the Operations Manager in writing (memo or email). It is the investigator's responsibility to monitor and record new births, determine wean dates, and wean animals. The date of birth for all litters must be written on the cage card. In order to avoid overcrowded cages, weaning must take place as outlined below. If cages are needed for weaning, the investigator can set up the cages or request the Facility staff have them placed in the animal room.

It is the investigator's responsibility to ensure that management of a colony complies with guidelines. To ensure compliance, the Facility staff will place a card on cages that exceed cage densities described below signifying that the investigator has two days to take corrective action. If there is no action within this time, the Facility staff will correct the cage density and assess a service charge on a per cage basis. The Facility staff assumes no liability whatsoever in the maintenance of research data on the affected animals’ cage card. Animal Facilities will notify the IACUC of any breeding colonies with inordinate numbers of cages requiring Facility staff action.

7.7.1 Mice

The standard mouse cages used at UNCG provide approximately 67 square inches of floor space and are permitted to contain no more than the following numbers of animals:

- When a litter is born, there can be no more than 3 adults in the cage.
- The following variations are allowed when the litter is 14 days old:
  - a maximum of 3 adults (2 females and 1 male or 3 females) and up to a total of nine pups (less than or equal to 10 grams each),
  - two adults (1 female and 1 male or 2 females) and up to a total of 11 pups (less than or equal to 10 grams each), or
  - One adult (one female) and no more than 14 pups (less than or equal to 10 grams each).
- When pups attain a weight of 10 grams or more or reach 21 days of age, they must be weaned promptly. All weaned animals must be housed in compliance with the Guide space requirements, as outlined on the following page.

The Guide's Requirement of Mice Post Weaning

Standard mouse cage: 7⅝”W x 11⅝”D x 5”H

<table>
<thead>
<tr>
<th>Weight</th>
<th># per cage</th>
<th>Floor Area per Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 grams</td>
<td>11</td>
<td>6 sq. inch space required</td>
</tr>
<tr>
<td>10-15 grams</td>
<td>8</td>
<td>8 sq. inch space required</td>
</tr>
<tr>
<td>16-25 grams</td>
<td>5</td>
<td>12 sq. inch space required</td>
</tr>
<tr>
<td>&gt; 25 grams</td>
<td>4</td>
<td>&gt; 15 sq. inch space required</td>
</tr>
</tbody>
</table>
7.7.2 Rats

The standard rat cages used at UNCG provide ~143 square inches of floor space and are permitted to house one breeding pair per cage. Litters are to be weaned at 21 days of age.

**The Guide’s Requirement of Rats Post Weaning**

Standard Rat Cage: 10½”W x 19”D x 8”H
143 square inches of floor space

<table>
<thead>
<tr>
<th>Weight</th>
<th># per cage</th>
<th>Floor Area per Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 grams</td>
<td>8</td>
<td>17 sq. inch space required</td>
</tr>
<tr>
<td>100-200 grams</td>
<td>6</td>
<td>23 sq. inch space required</td>
</tr>
<tr>
<td>201-300 grams</td>
<td>4</td>
<td>29 sq. inch space required</td>
</tr>
<tr>
<td>301-400 grams</td>
<td>3</td>
<td>40 sq. inch space required</td>
</tr>
<tr>
<td>401-500 grams</td>
<td>2</td>
<td>60 sq. inch space required</td>
</tr>
<tr>
<td>&gt; 500 grams</td>
<td>1</td>
<td>&gt;70 sq. inch space required</td>
</tr>
</tbody>
</table>

**Note:** Under no circumstances are two or more females of either species allowed to occupy the same cage with their litters or have a new litter before the previous litter has been weaned.

8. Post –Approval Monitoring Program (PAM)

According to the Guide for the Care and Use of Laboratory Animals (8th edition), the Institutional Animal Care and Use Committee (IACUC) is charged with the responsibility to oversee and evaluate the University’s animal program, procedures, and facilities to ensure that they are consistent with the recommendations in the Guide, the regulations of the Animal Welfare Act, and the Public Health Service Policy of Humane Care and Use of Laboratory Animals.

The goal of the post approval monitoring process at UNCG is to review active protocols to ensure research is being conducted in accordance with what is written and approved by the IACUC. The protocols will be selected randomly or as a result of a request by the IACUC, veterinary staff, or animal care personnel. The laboratory will visited by the ORI Research Integrity Coordinator, often with the IACUC Chair or veterinarian. Procedures on the selected protocol are observed and any drift away from the protocol is noted. The investigator then has the opportunity to correct any deviations by improving techniques or by submitting an amendment to the protocol.
The visit is as informal as possible and is an opportunity for the investigators to request any help they may need. Findings are reported at the next IACUC meeting. The report of the visit and any follow up visits are filed in the investigators IACUC protocol file. The laboratories receive a brief follow up visit after the first to document that any deficiencies highlighted in the first visit have been rectified.

The UNCG IACUC has historically performed post approval monitoring on a regular basis, based on the eyes and ears of the research staff, and the Animal Facility, and through the required semiannual program and facility inspections required by our assurance with PHS policy. In addition, the IACUC requires annual reviews of all IACUC protocols, which is a time for animal numbers to be updated and verified as well as an opportunity for the PI to submit any modifications or interim findings as a report to the IACUC.

The goal of this new program is to enhance the education of the researchers who are entering the facility and working with animals. At this time, post approval monitoring is based on a “just-cause” process, the ORI, in conjunction with the IACUC, IACUC Chair, attending veterinarian and the staff of the Animal Facility, but in the near future, the ORI will be conducting random audits of research studies as the online system we have adopted will allow for record-keeping that is in line with successful post approval monitoring.

8.1 IACUC Procedures for the Investigation of Animal Care and Use Concerns

As an agent of the university, the IACUC has the authority and the responsibility to review, and if warranted, investigate all animal welfare concerns. In keeping with this charge, the IACUC has developed and established reporting procedures whereby laboratory and research facility employees as well as other employees and members of the public can voice animal welfare concerns or alleged violations to federal, state or institutional animal welfare regulations or IACUC policies to a group with the responsibility and authority to make appropriate changes (the IACUC).

The IACUC will address all animal welfare concerns raised by employees and from the public, including those concerns not specifically directed to the IACUC.

8.1.1 Employee Voiced Animal Welfare Concerns

If any employee of the university wants to voice an animal welfare concern or an alleged animal welfare violation that individual is directed to contact the IACUC Chair, Director of the Office of Research Integrity, Attending Veterinarian, or the Manager of the Animal Facility who will in turn bring the concern to the attention of the full-committee.

8.2 Procedures for the Review and Reporting of Animal Welfare Concerns

The procedures for voicing animal welfare concerns should be available to all personnel along with the university's "Policy on Animal Care and Use" and in the Animal Facility manual that is distributed to all individuals that use the facility. Concerns may be addressed by submitting the concern on-line using the comments and concerns section of the Office of Research Integrity website.
8.2.1 Public Voiced Animal Welfare Concerns

In the event university administrative personnel receive a concern from the public (via phone or by written communication); they will direct the call to the attention of the Director of the Office of Research Integrity (ORI) or IACUC Chair and Attending Veterinarian.

Alternatively, if a concern is received, the administrative personnel may document the date and time the concern was received, obtain details about the concern, establish whether or not the caller wants to remain anonymous, obtain a mutually acceptable method for contacting the caller if a review of the IACUC responses and actions is desired, and assure the caller that the complaint will be forwarded to the IACUC for review.

In this latter case, and if confidentiality is requested, the personnel will forward the details of the complaint to the ORI Director or IACUC Chair without identifying the caller.

If the complaint involves sick or injured animals, the Animal Facility Manager and Attending Veterinarian personnel will be immediately notified.

8.3 Personnel Training in the Handling, Notification and Documentation of Public Animal Welfare Concerns

Training is provided to appropriate personnel in the IACUC-established procedures for handling animal welfare concerns from the public and bringing these concerns to the immediate attention of the IACUC.

In addition, personnel will use an “Animal Welfare Response Form” for documenting and handling the receipt of public animal welfare. This form prompts personnel to request and document the required information and to notify appropriate individuals, if and when, an animal welfare concern from the public is received. Copies of the form are maintained in a readily accessible location for use by trained administrative personnel.

8.3.1 Animal Welfare Concerns and Guaranteed Anonymity

Regardless of the origin of the concern, all individuals voicing concerns are absolutely assured anonymity if confidentiality is requested. No university employee or IACUC member shall be discriminated against or be subject to any reprisal for reporting suspected violations of any regulation or standards or animal welfare concerns. However, before the IACUC can make a reasonable evaluation of the concern and investigate the concern (if warranted), these individuals must be willing to provide a specified minimum amount of information.

8.3.2 Review, Investigation and Documentation of Animal Welfare Concerns

The IACUC will review, and if deemed necessary, investigate and resolve the concern. The Vice Provost for Research will be invited to the meeting whom may choose to invite a representative from the Institutional Public Relation Office. The nature of the concern and the steps taken to review, and if warranted, investigate, and resolve the concern will be documented in the IACUC meeting minutes. If appropriate, the IACUC Chair will appoint a subcommittee to investigate alleged violations, notify proper personnel and forward final reports of investigations to the full-committee. If follow-up was requested, the IACUC Chair will implement necessary steps to
ensure that the individual lodging the complaint or concern is contacted and briefed on the IACUC actions.

The IACUC documentation of the review and investigation will be finalized within reasonable time frame upon receipt of the complaint if possible. The documentation will include:

1. Date and time(s) the complaint was received (by the administrative personnel and/or IACUC member).
2. Nature of the complaint.
3. Names of persons involved with the review and investigation.
4. Results of the review and investigation.
5. Conclusions.
6. Appropriate corrective actions.
7. Actions taken to inform the individual lodging the complaint of the IACUC actions, if requested.

This documentation will be forwarded to the Institutional Official for review and maintained for at least 3 years from the date of the report. If corrective action includes a suspension in animal activities or a serious deviation or deficiency, the Institutional Official in consultation with the IACUC will report the incident to the appropriate regulatory agencies.

8.4 ORI policy on investigation of animal use concern and/or potential issue of noncompliance

In the normal course of administration, the PI is often asked to provide additional information to the IACUC, IACUC Chair, or ORI for clarity or additional information. Researchers are expected to provide this information in a timely manner.

When requests are made for information involving potential non-compliance, these requests will include specific dates when the responses from the PI are due.

Once the PI is made aware of an investigation on an animal use protocol that may have jeopardized the health and well-being of the animal, the PI should cease from any further work with animals until further notice from the Chair or the IACUC.

The nature of the information required will vary depending on the circumstances, but often involves:
1) Interviewing complainants (if known), any persons against whom allegations were directed, and any pertinent program officials;
2) Observing the animals and their housing and experimental environment;
3) Reviewing any pertinent records (e.g., animal health records, protocol, and other documents).

If the PI does not respond within the specified time, the IACUC Chair may elect to label the lack of response non-compliance and/or take appropriate actions including but not limited to:
- “Pausing” the research, temporarily limiting PI interaction with research animals to basic husbandry
- Notifying the PI’s department head of the delay
- Notifying the ORI of the PI’s delay
- Notifying the Animal Facility Manager

A PI may request additional time if there are exceptional circumstances (e.g., the PI is out of the country), but these requests must be submitted before the due date and are subject to approval by the IACUC Chair.

If the IACUC determines that further investigation is required, the Chair, an individual appointed by the Chair, or the subcommittee appointed by the Chair, will conduct the investigation and report back to the IACUC. Members of the investigating subcommittee will be chosen to avoid actual or perceived conflicts of interest. The matter then will go to the full board of the IACUC for further review.

Emergency meetings may be necessary in these cases to ensure prompt consideration of concerns.

Continuing noncompliance encompasses multiple infractions by the same investigator or their research team. These infractions could be serious in nature or when independently evaluated could be categorized as non-serious. However, the infractions have happened on multiple occasions may be considered serious and reportable.

8.5 Consequences of Noncompliance with IACUC Protocol, Policies, Procedures, or Decisions

The IACUC shall review all reports from the investigation or initial report (in cases where further investigation was not required) and any information provided by the PI before reaching a decision. After evaluating these materials, the IACUC may request additional information and/or take action with respect to the investigation, including but not limited to the following:

- Dismissal of the complaint/concern;
- Requirement of submission and approval of a protocol amendment, or placement of specific additional conditions or stipulations on the protocol
- Imposition of specific remedial education and training for the PI and/or other personnel listed under the protocol
- Monitoring research, testing, or training that involves animals
- Temporary revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals, pending compliance with specific, IACUC-mandated conditions
- Issuing letters of reprimand
- Restricting research practices, such as limiting the PI to conduct studies with certain procedures, or conduct research under supervision
• Suspension of approval for one or more of the PI’s studies and establishment of conditions for reinstatement
• Termination of approval for one or more of the PI’s studies
• Permanent revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals
• Recommending to the Institutional Official that institutional (e.g., reassignment, suspension or termination of employment) sanctions be imposed.

The IACUC will notify the PI in writing of any action taken by the IACUC and the reasons for that action. In addition, the IACUC will notify, as it deems appropriate:

• Other investigators involved in the animal care and use activities at issue
• The PI’s department head (and any additional department heads where the PI holds multiple professional appointments)
• Any additional departments involved in the research
• The Institutional Official (who will contact any additional institutional authorities) and other pertinent program officials as required (such as appropriate supervisory and management staff, the public affairs office, the compliance office, the office of the general counsel)
• Any funding, regulatory or accreditation agencies, as required.

The PI may elect to respond in writing to the final report to the Chair of the IACUC if he/she would like to appeal the IACUC decision or present further information related to the incident.

8.5.1 Suspension of Protocol
As indicated above, the IACUC is empowered to suspend a protocol if it finds violations of the PHS Policy, Guide, Assurance, or Animal Welfare Regulations. Suspension may occur only after review of the matter at a convened meeting of a quorum of the IACUC, and with a vote for suspension from a majority of the quorum present. In addition, the PI may (and in appropriate cases will be encouraged to) agree to voluntarily suspend his/her protocol pending review by the IACUC.

If the IACUC suspends an activity involving animals, the Institutional Official, in consultation with the IACUC, shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OLAW and any federal agency funding that activity. At the time of suspension of a protocol, the IACUC will vote on terms for reactivation of the protocol. The IACUC may vote for the IACUC Chair to be empowered to reactivate the protocol at his/her discretion or it can vote that the Committee itself must approve reactivation. Protocols will be reactivated only after violations have been corrected.

8.6 Reports to outside agencies of Noncompliance and Animal Activity Suspensions

8.6.1 IACUC Suspension of On-Going Animal Activities
As an agent of the university, the UNCG IACUC is authorized to suspend any and all animal activities due to noncompliance, report suspensions to the Institutional Official, and through the Institutional Official, notify OLAW, the USDA if a regulated species is involved and any other
required regulatory agency including corresponding federal funding agencies. The IACUC is authorized to suspend any and all animal activities that are not in compliance with applicable animal welfare laws and regulations or university policies including, but is not limited to, the PHS Policy and UNCG PHS Assurance, the Animal Welfare Act and USDA Animal Welfare Regulations and Standards (if applicable), the Guide for the Care and Use of Laboratory Animals, the UNCG’s Animal Care and Use Policy, and UNCG IACUC policies.

Non-Compliance is defined as

1) Activity that endangers the health and well-being of animals
2) Violations of the AWA that are grossly inconsistent with PHS Policy or are serious deviations from the provisions of the Guide
3) Serious deviation from accepted practices

Non-serious issues of noncompliance do not need to be reported to OLAW or USDA but do need to be documented and managed by the IACUC. Examples of non-serious issues of noncompliance can be found in the attached document entitled “Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals” page 5 (Examples of situations not normally required to be reported).

Serious issues of noncompliance must be reported to OLAW. Examples of serious noncompliance can be found in the appendices (1) of this document entitled “Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals” page 56 (Examples of reportable situations) Serious issues of noncompliance discovered at the time of the semi-annual IACUC inspection and program review and not corrected by the date specified by the Committee must be reported to the USDA within 15 days of the specified date of correction if regulated species are involved (see Appendix 2)

The IACUC will file a report to OLAW in the event of:

• A serious deviation that is or may be a threat to the health or safety of the animals or continuing noncompliance with PHS Policy
• A serious deviation from the Guide for the Care and Use of Laboratory Animals
• An IACUC suspension of an animal protocol

The IACUC will file a report to the USDA in the event of:

• A failure to adhere to an IACUC plan and schedule for corrective action of an identified deficiency or departure discovered during a semiannual inspection that results in a significant deficiency remaining uncorrected.

In order to ensure prompt reporting of the noncompliance or suspension to the appropriate regulatory agency(ies), the Institutional Official, in consultation with the IACUC, will

• Verbally notify the appropriate regulatory agency(ies), then follow up with a written report from the IACUC, signed by the Institutional Official, and delivered to: Office of Laboratory Animal Welfare, National Institutes of Health, 6705 Rockledge Drive, Rockledge 1, Suite 360
9. Semi-Annual Facility Inspection
As an agent of the university, the IACUC is authorized to inspect and evaluate all animal facilities
and animal study areas or satellite facilities at least once every six months.

The IACUC must conduct a Semi-Annual Program Evaluation of the Institutional Animal Care and
Use Program. This Program Evaluation consists of two components:

1. A Facility Inspection component
2. A Program Review component

Both components must be conducted at least semi-annually and the corresponding reports of these
evaluations must be written and submitted to the Institutional Official at least semi-annually.

The IACUC inspects and evaluates all animal facilities and animal study areas (and satellite facilities,
if applicable) at least once every six months. Inspection teams include at least two voting members
of the IACUC.

9.1 Standards for Facility Inspection
The IACUC utilizes the following standards for program review and evaluation (if applicable):

1. The U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in
   Testing, Research, and Training, Interagency Research Animal Committee, 1985
2. The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals, NIH,
   Amended 2003
3. The UNCG Animal Welfare Assurance (PHS)
   Animal Resources, Commission on Life Sciences, National Research Council, March 2011
5. 2013 AVMA Guidelines on Euthanasia, American Veterinary Medical Association
6. The Animal Welfare Act and all pertinent laws and regulations of the United States Department
   of Agriculture (7 U.S.C. 2131 et seq. and 9 CFR Subchapter A, Parts 1-3)
7. State and Local Research Animal Welfare Laws and Regulations
The IACUC inspects all animal facilities, animal study areas (and satellite facilities, if applicable) and surgery areas at least once every six months.

9.2 Required Areas of Inspection*

Animal facilities include all of the areas within both animal facilities including buildings, rooms, areas, enclosures, vehicles, holding areas, animal care support areas (e.g. anterooms, cage wash facilities, feed/bedding storage areas, implement storage areas, etc.), animal use support areas (e.g. procedure rooms, surgeon and patient preparation areas, surgery and recovery areas, euthanasia and necropsy areas, pharmacy, etc.) and personnel preparation areas (e.g. change facilities, locker areas, showers/rest rooms, etc.).

Animal study areas or satellite facilities are defined as rooms or containment areas outside the central or core animal facility where USDA-regulated animals are housed for periods greater than twelve (12) consecutive hours or where unregulated animals are housed for periods greater than twenty-four (24) hours.

Surgery areas include all areas within or outside of the central or core animal facilities where any form of surgery is performed including non-survival or survival surgery, minor or major surgery, and regardless of whether or not the animal is USDA-regulated or non-regulated, and regardless of the time period held.

*The IACUC remains responsible for all animal activities and the areas where they are conducted even if they do not meet the criteria of “animal facilities”, “animal study areas or satellite facilities” or “surgery areas”. For these areas, the IACUC can inspect on a less frequent basis than semi-annually and/or designate at least one trained and qualified individuals to conduct inspections on the IACUC’s behalf as long as the IACUC remains responsible for the recommendations and report to the Institutional Official.

9.2.1 Inspection Participants

While every IACUC member is not required to participate in the facility inspection, no member can be denied participation. All voting IACUC members must be given the opportunity to participate.

For areas that involve USDA-regulated animals, the IACUC may appoint inspection teams consisting of at least two voting members to conduct the facility inspection on behalf of the IACUC.

For areas that involve non-regulated species, the IACUC may designate at least one trained and qualified individual to conduct inspections on the IACUC’s behalf as long as the IACUC remains responsible for the recommendations and report to the Institutional Official.
In addition, consultants may be invited to participate in facility inspections but cannot vote unless they are official appointed voting members of the IACUC.

Regardless of its approach, the IACUC remains responsible for the recommendations and report to the Institutional Official.

9.2.2 Facility Inspection Preparation
Materials relevant to the Semi-annual Facility Inspection, including the most recent facility inspection report, are provided to inspection team(s) prior to the inspection.

9.3 Semiannual Facility Inspection Checklist
To facilitate the inspection, the IACUC uses a Semiannual Facility Checklist. (Appendix 3) Inspection teams will take notes during the inspection to assist in preparation of the final report. If possible, identified deficiencies will be addressed at the time of the inspection with those responsible for direct management or oversight to ensure the accuracy of the team's perception of the “deficiency” or “deviation”.

Including:
- Introduction and Instructions for Checklist
  URL http://grants.nih.gov/grants/olaw/sampledoc/cheklist.htm
- Facility Inspection: Animal Housing & Support Areas
- Facility Inspection: Cagewash
  URL http://grants.nih.gov/grants/olaw/sampledoc/chek2b.htm
- Facility Inspection: Aseptic Surgery
  URL http://grants.nih.gov/grants/olaw/sampledoc/chek2c.htm
- Facility Inspection: Procedure Areas, Non-Survival Surgeries, Laboratories, Rodent Surgeries
  URL http://grants.nih.gov/grants/olaw/sampledoc/chek2d.htm
- Facility Inspection Checklist: Additional Comments
  URL http://grants.nih.gov/grants/olaw/sampledoc/chek2e.htm

9.3.1 Inspection Findings
Results of the animal facility inspection are presented for review and discussion at a convened meeting of a quorum of the IACUC at which time the IACUC develops its recommendations to the IO.

9.3.2 Record Keeping
According to the University of North Carolina at Greensboro records retention schedule the ORI will send a copy of all IACUC minutes, reports, and Animal Welfare Assurance to the IO semiannually. All IACUC related documents noted above and including the actual IACUC
protocols will be destroyed by the ORI three years following the closure of the research as mandated by the Office of Laboratory Animal Welfare.

**10. IACUC Evaluation Reports to Institutional Official**

As an agent of the university, the IACUC is authorized to prepare reports of its evaluations at least every six months and submit them to the Institutional Official.

By law, the IACUC is responsible for meeting specific record keeping requirements which are handled by the ORI including

- Timely preparation and submission of reports to the Institutional Official and/or appropriate federal authorities
- Maintenance of records relating to the institutional animal care and use program for at least the duration of the activity plus an additional three years
- Release of records for purpose of inspection (and copying for removal from the university in the event of an alleged violation requiring further investigation) upon request of authorized representatives of OLAW or other PHS office, and/or USDA APHIS, at reasonable times and in a reasonable manner

**10.1 Semiannual Program Review Report**

The Semiannual Program Evaluation consists of a program review component and a facility inspection component. Together, these two activities comprise the Semiannual Program Evaluation.

The IACUC prepares and submits a report of the Institutional Animal Care and Use Program Review, reviewed, approved and signed by a quorum of the IACUC to the Institutional Official. Reports must be submitted at least every 6 months.

The program review report includes:

1. Date of the program review
2. Addressed to the Institutional Official
3. Names and IACUC title of members in attendance at the convened program review
4. Names and IACUC title of members not in attendance at the convened program review
5. Confirmation that a quorum of the committee was present during the program review
6. A list of the standards used for program review (check list)
7. A summary of the program review
8. A detailed account of any identified programmatic deficiencies and an explanation for each
9. A clear distinction between minor and significant* programmatic departures or deficiencies
10. A reasonable, specific action plan and time table for the correction of significant and minor programmatic departures or deficiencies
11. Recommendations for revision or modification of the current program, facilities, or personnel training
12. All minority views (if none, so state)
13. Signatures of a quorum of the voting IACUC members and corresponding dates signed
* A significant departure or deficiency is defined as any departure/deficiency, which is or may be a threat to the health, safety or welfare of an animal.

10.2 Failure to Correct Programmatic Deficiencies or Departures within the IACUC-Established Time Table

Any significant deficiency that is not corrected within the established timetable will be brought to the attention of the Institutional Official and documented in a written report.

The Institutional Official, in consultation with the IACUC, will promptly report the uncorrected deficiency, or any serious or continuing noncompliance with the PHS Policy, the Animal Welfare Act, USDA Animal Welfare Regulations or serious deviation from the provisions of the ILAR Guide including a full explanation of the circumstances and actions taken, to OLAW and USDA, if applicable, and any other regulatory agency including corresponding federal funding agencies as required.

During the notification period, the IACUC will prioritize efforts to investigate, develop and document a definitive corrective plan and a schedule for implementation and make every attempt to resolve the problem.

10.3 Semiannual Facility Inspection Report

The Semiannual Program Evaluation consists of a program review component and a facility inspection component. Together, these two activities comprise the Semiannual Program Evaluation.

The IACUC prepares and submits an inspection report, reviewed, approved and signed by a quorum of the IACUC, to the Institutional Official. Reports must be submitted at least every 6 months.

The facility inspection report includes:

1. date(s) of the inspection
2. addressed to the Institutional Official
3. names of IACUC inspection team members
4. names and titles of consultants to the inspection team
5. names of IACUC members in attendance at the convened inspection review
6. names of IACUC members not in attendance at the convened inspection review
7. confirmation that a quorum of the committee was present during the convened inspection review
8. a list of the standards used for inspection (check list)
9. a list of the areas inspected including study rooms and areas outside the central animal facility
10. a summary of the inspection results including a description of the nature and extent of the university's adherence to the standards
11. a detailed account of any identified facility departures or deficiencies and an explanation for each
12. a clear distinction between minor and significant facility departures or deficiencies
13. a reasonable, specific action plan and timetable for the correction of significant and minor facility departures or deficiencies
14. recommendations for changes or improvements to the facility or facility operations
15. all minority views (if none, so state)
16. signatures of a quorum of the voting IACUC members and corresponding dates signed

8 Items #5, 6, and 7 may be documented in the inspection report itself, the corresponding meeting minutes and/or in an attached cover memo

9 A significant departure or deficiency is defined as any departure/deficiency which is or may be a threat to the health, safety or welfare of an animal.

10.4 Report of Failure to Correct Facility Deficiencies or Departures within the IACUC-Established Time Table

Any significant deficiency that is not corrected within the established timetable will be brought to the attention of the Institutional Official and documented in a written report.

The Institutional Official, in consultation with the IACUC, will promptly report the uncorrected deficiency, or any serious or continuing noncompliance with the PHS Policy, the Animal Welfare Act, USDA Animal Welfare Regulations or serious deviation from the provisions of the ILAR Guide including a full explanation of the circumstances and actions taken, to OLAW and USDA, if applicable, and any other regulatory agency as required.

During the notification period, the IACUC will prioritize efforts to investigate, develop and document a definitive corrective plan and a schedule for implementation and make every attempt to resolve the problem.

11. Animal Facility Visitor Policy

All University animal facilities are open upon request to the IACUC, Office of Research Integrity, inspection agents from the United State Department of Agriculture, the Office of Laboratory Animal Welfare, and other federal agencies as required by law.

Access to animal facilities by other visitors is restricted and monitored to protect the health and safety of both the visitors and research animals and to avoid disruption of research activities. To achieve this goal all visitors will be apprised of the occupational health risks and program. Clearance to enter the facilities must be obtained through both the ORI and the Animal Facility Manager (see Appendix 1)

The PI will complete all required forms and send them to the ORI. Once ORI has verified all trainings are completed and either an Occupational Health Clearance or a waiver form is presented to the ORI, ORI will forward the form on to the Animal Facility Manager. Additional requirements and documentation, including picture identification, may be required by the Animal Facility Manager prior to entrance in any animal facility.
1. It is preferred that visitors complete all necessary paperwork prior to their arrival. However, it is understood that this is not always possible and will work with individuals in time frames shorter than two weeks.

2. All non-institutional or federal visitors will need to complete both the “Agreement for non-employees” and “Animal Exposure Questionnaire.”

3. Visitors that will have direct contact with animals will need to enroll in the Occupational Health Program or sign the appropriate waiver.

4. During visit(s), every effort must be made to avoid disturbing laboratory animals and settings. To avoid personal injury, visitors must follow all posted facility rules and refrain from unauthorized contact with animals.

5. Use of cameras or sound recording devices is not permitted in any animal facility unless approval is obtained from Animal Facility Manager and the PI of the animal room prior to the visit.

6. Persons receiving permission to visit animal facilities agree to observe all rules and conditions established for the visit. Permission to visit campus animal facilities may be revoked at any time by the Animal Facility Manager, PI whose animal room is being visited, or a representative of the campus administration.
APPENDIX 1

Some visitors at UNCG observe or participate in research activities involving animals. Exposure to research animals can include risk to visitors and to research animals. For example, persons with suppressed immune systems are vulnerable to illness from some animals. On the other hand, some diseases like M. tuberculosis can be managed medically in humans, but is deadly for some animals.

*Please note* This signed and approved form will serve as the record of your visit to the Animal Facility on the dates listed below. This form will be kept on file in both the Office of Research Integrity (ORI) and the Animal Facility. Additional requirements and documentation, including picture identification, may be required by the Animal Facility Manager prior to entrance in any animal facility.

All visitors need to complete the Animal Exposure Questionnaire and the Visitor Agreement and submit to the ORI.

**Things to consider at least TWO WEEKS BEFORE your visit:**

1a. **Will the visitor be in the facility but not in any animal rooms?**
   - Yes
     - Proceed to question 2
   - No
     - No further action is needed

1b. **Will the visitor be in the animal facility working with animals or tissue?**
   - Yes
     - Proceed to question 2
   - No
     - No further action is needed

2. **Will the visitor be at UNCG for more than 3 days?**
   - Yes
     - Complete the Occupational Health Prescreening form and send directly to the Anna Grove Student Health Center
     - The sponsor will need to add the visitor to their IACUC protocol(s) by submitting an Amendment - Personnel Only Form to the ORI.
   - No
     - Although the visitor is here for only a short period, animal research-related medical and training requirements still apply (item 1.a or 1.b above). The visitor should be escorted at all times by the UNCG sponsor, or designee. It is recommended that the UNCG sponsor retain a copy of the Visitor Agreement in department files.
3. What are animal related training, safety and medical requirements?
The linked Animal Contact Table and Occupational Health Table list requirements and is provided for information purposes. For actual requirements, use the contacts above. Requirements depend on species, level of exposure to animals, and the type of activities that will performed.
APPENDIX 2

Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals

Notice Number: NOT-OD-05-034

Key Dates

Release Date: February, 24, 2005

Issued by

Office of Laboratory Animal Welfare (OLAW), Office of Extramural Research
(http://grants.nih.gov/grants/olaw/olaw.htm)

This Notice provides guidance to Public Health Service (PHS) awardee institutions and Institutional Animal Care and Use Committees (IACUCs) on the prompt reporting requirements of the PHS Policy on Humane Care and Use of Laboratory Animals (Policy) (http://grants.nih.gov/grants/olaw/references/phspol.htm). This guidance is intended to assist IACUCs and Institutional Officials in determining what, when, and how situations should be reported under IV.F.3 of the Policy, and to promote greater uniformity in reporting. This Notice supersedes the January 12, 1994 Dear Colleague letter from the former Division of Animal Welfare, Office for Protection from Research Risks (now the Office of Laboratory Animal Welfare, or OLAW).

Background

PHS Policy, IV.F.3, requires that:

“The IACUC, through the Institutional Official, shall promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to:

a) Any serious or continuing noncompliance with this Policy;

b) Any serious deviation from the provisions of the Guide [for the Care and Use of Laboratory Animals] ; or

c) Any suspension of an activity by the IACUC.

IACUC suspensions of activities are cited at IV.C.6 and 7 of the Policy, and require a convened meeting of a quorum of the IACUC and the vote of a majority of the quorum present. The Institutional Official must review the reasons for suspension in consultation with the IACUC, take appropriate corrective action and report that action with full explanation to OLAW.

All institutions with Animal Welfare Assurances are required to comply with the provisions of IV.F.3. The Institutional Official signing the Assurance, in concert with the IACUC, is responsible for this reporting.
Reporting promptly to OLAW under IV.F.3 serves dual purposes. Foremost, it ensures that institutions deliberately address and correct situations that affect animal welfare, PHS-supported research, and compliance with the Policy. In addition, it enables OLAW to monitor the institution's animal care and use program oversight under the Policy, evaluate allegations of noncompliance, and assess the effectiveness of PHS policies and procedures.

The underlying foundation of the PHS Policy is one of institutional self-evaluation, self-monitoring and self-reporting. Public Law 99-158 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm) requires that institutions be provided a reasonable opportunity to take corrective action before a grant or contract is suspended or terminated, and it is OLAW's role to assess whether the corrective actions reported by institutions under IV.F.3 are adequate. OLAW will assist the reporting institution in developing definitive corrective plans and schedules if necessary. Compliance actions affecting an award are rare because institutions are usually able to address incidents successfully and take appropriate actions to prevent recurrence.

**Guidance on Prompt Reporting**

A comprehensive list of definitive examples of reportable situations is impractical. Therefore, the examples below do not cover all instances but demonstrate the threshold at which OLAW expects to receive a report. Institutions should use rational judgment in determining what situations meet the provisions of IV.F.3 and fall within the scope of the examples below, and consult with OLAW if in doubt. OLAW welcomes inquiries and discussion and will provide guidance with regard to specific situations. Situations that meet the provisions of IV.F.3 and are identified by external entities such as the United States Department of Agriculture or the Association for Assessment and Accreditation of Laboratory Animal Care International, or by individuals outside the IACUC or outside the institution, are not exempt from reporting under IV.F.3.

Examples of reportable situations:

* Conditions that jeopardize the health or well-being of animals, including natural disasters, accidents, and mechanical failures, resulting in actual harm or death to animals;

* conduct of animal-related activities without appropriate IACUC review and approval;

* Failure to adhere to IACUC-approved protocols;

* Implementation of any significant change to IACUC-approved protocols without prior IACUC approval as required by IV.B.7.;

* Conduct of animal-related activities beyond the expiration date established by the IACUC (note that a complete review under IV.C is required at least once every three years);

* conduct of official IACUC business requiring a quorum (full Committee review of an activity in accord with IV.C.2 or suspension in accord with IV.C.6) in the absence of a quorum;

* conduct of official IACUC business during a period of time that the Committee is improperly constituted;
* Failure to correct deficiencies identified during the semiannual evaluation in a timely manner;

* Chronic failure to provide space for animals in accordance with recommendations of the Guide unless the IACUC has approved a protocol-specific deviation from the Guide based on written scientific justification;

* Participation in animal-related activities by individuals who have not been determined by the IACUC to be appropriately qualified and trained as required by IV.C.1.f;

* Failure to monitor animals post-procedurally as necessary to ensure well-being (e.g., during recovery from anesthesia or during recuperation from invasive or debilitating procedures);

* Failure to maintain appropriate animal-related records (e.g., identification, medical, husbandry);

* Failure to ensure death of animals after euthanasia procedures (e.g., failed euthanasia with CO₂);

* Failure of animal care and use personnel to carry out veterinary orders (e.g., treatments); or

* IACUC suspension or other institutional intervention that results in the temporary or permanent interruption of an activity due to noncompliance with the Policy, Animal Welfare Act, the Guide, or the institution's Animal Welfare Assurance.

OLAW recognizes that there may be levels of morbidity and mortality in virtually any animal-related activity, including those associated with the care and use of animals in research, testing, and teaching that are not the result of violations of either the Policy or the Guide. OLAW offers the following examples of situations which may not meet the threshold for reporting, based on consideration of the circumstances by the IACUC.

Examples of situations not normally required to be reported:

* Death of animals that have reached the end of their natural life spans;

* Death or failures of neonates to thrive when husbandry and veterinary medical oversight of dams and litters was appropriate;

* Animal death or illness from spontaneous disease when appropriate quarantine, preventive medical, surveillance, diagnostic, and therapeutic procedures were in place and followed;

* Animal death or injuries related to manipulations that fall within parameters described in the IACUC-approved protocol; or

* Infrequent incidents of drowning or near-drowning of rodents in cages when it is determined that the cause was water valves jammed with bedding (frequent problems of this nature, however, must be reported promptly along with corrective plans and schedules).

**Time Frame for Reporting**

Institutions should notify OLAW of matters falling under IV.F.3 promptly, i.e., without delay. Since IV.F.3 requires a full explanation of circumstances and actions taken and the time required
to fully investigate and devise corrective actions may be lengthy, OLAW recommends that an authorized institutional representative provide a preliminary report to OLAW as soon as possible and follow-up with a thorough report once action has been taken. Preliminary reports may be in the form of a fax, email, or phone call. Reports should be submitted as situations occur, and not collected and submitted in groups or with the annual report to OLAW.

**Information to Be Reported**

Include as many of the following items of information as possible in the initial contact with OLAW. A follow-up report may address anything not known at the time of the initial report and should summarize the institution's corrective action. If a long term plan is necessary, describe the plan and include a reasonable schedule. This information will allow OLAW to assess the circumstances and actions taken to correct and prevent recurrence of the situation.

Information to be included:


- Relevant grant or contract number(s) if the situation is related to an activity directly supported by PHS;

- A full description of any potential or actual affect on PHS-supported activities if the situation is not directly supported by the PHS but is in a functional, programmatic, or physical area that could affect PHS-supported activities (e.g., inadequate program of veterinary care, training of technical/husbandry staff, or occupational health; inadequate sanitation due to malfunctioning cage washer; room temperature extremes due to HVAC failures);

- Full explanation of the situation, including what happened, when and where, the species of animal(s) involved, and the category of individuals involved (e.g., principal or co-principal investigator, technician, animal caretaker, student, veterinarian, etc.);

- Description of actions taken by the institution to address the situation; and

- Description of short- or long-term corrective plans and implementation schedule(s).

**Preliminary and final reports should be made to:**

Axel V. Wolff, M.S., D.V.M., Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982
Phone: 301-594-2061
FAX: 301-402-2803
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**Inquiries**

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Should include the February 2013 updates:  