UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

PRINCIPAL INVESTIGATOR MANUAL

Office of Animal Welfare Assurance

Principal Investigator Manual
Table of Contents

I. INTRODUCTION

The University of Maryland School of Medicine (UM SOM) is dedicated to the task of assuring the humane care and use of all animals involved in research, teaching or other activities carried out by the faculty, staff and students. Per federal requirements, an Institutional Animal Care and Use Committee (IACUC) has been established and is charged with oversight of all animal care and use to ensure compliance with all applicable laws, regulations and policies.

The UM SOM IACUC serves as the IACUC of record for the University of Maryland Baltimore (UMB) campus, the Baltimore Veterans Affairs Medical Center (BVAMC) and the Institute of Marine and Environmental Technology (IMET).

Faculty, staff and students must be aware that the use of animals in research, teaching or other activities is a privilege, not a right, governed by public scrutiny / concern; federal, state and local laws, regulations and policies; and the University of Maryland School of Medicine's policies. Failure to comply with the provisions set forth in the regulations and policies can lead to severe sanctions for the investigator and the university. Such sanctions include, but are not limited to:

- Loss of privilege to use animals in research
- Loss of funding for animal research
- Principal Investigator being held personally responsible for professional misconduct
- Criminal and civil penalties for the investigator and / or the University.

It takes only a single incident of serious non-compliance with these laws, regulations and policies to jeopardize an investigator's and the University's reputation and privilege to use animals. As such, it is EVERYONE's responsibility to assure the humane care and use of animals.

The UM SOM has an Animal Welfare Assurance on file with the Office of Laboratory Animal Welfare (OLAW) that assures compliance with all federal, state and local laws, regulations, and policies.

The UM SOM is committed to the advancement of science through the responsible conduct of animal research.

II. UM SOM ANIMAL CARE AND USE PROGRAM

The UM SOM Animal Care and Use Program include multiple components that work synergistically to support activities involving laboratory animals. According to the PHS Policy, all programs are expected to include:

- designation of an Institutional Official;
- appointment of an Institutional Animal Care and Use Committee (IACUC);
- administrative support for the IACUC;
- standard IACUC procedures;

- arrangements for a veterinarian with authority and responsibility for animals;
- adequate veterinary care;
- formal or on-the-job training for personnel that care for or use animals;
- an occupational health and safety program for those who have animal contact;
- maintenance of animal facilities; and
- provisions for animal care.

Several offices / departments play an essential role in the UM SOM animal care and use program; however, the three main offices that investigators interact with most frequently include:

Office of Animal Welfare Assurance
Veterinary Resources
Environmental Health and Safety

A description of each office's responsibilities and available resources are further discussed in Section VI (p. 11).

The UM SOM animal care and use program is fully accredited by Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC). This accreditation is voluntary and represents the SOM's commitment to the quality care and use of animals. The UM SOM animal care and use program has been accredited since 1983.

III. FEDERAL MANDATES / REGULATIONS

Three federal agencies are primarily charged with setting standards and providing oversight for animal care and use. Each agency is identified below along with the relevant regulations and/or policies that they enforce. Please note that a memorandum of understanding exists between these agencies to reduce duplication of efforts while ensuring the timely transfer of information allowing each agency to assure that their regulations, etc are being met at an institution.

A. The Animal and Plant Health Inspection Service (APHIS)
APHIS falls under the U.S. Department of Agriculture (USDA). USDA conducts annual, unannounced inspections of our facilities and the IACUC to assure that all laws, regulations and policies are being adhered to. Their two main documents include:

1. *Animal Welfare Act and Animal Welfare Regulations*
The act covers all warm blooded animals; however, those animals regulated are at the discretion of the US Secretary of Agriculture, who heads the regulatory agency. Currently, mice, rats, birds and domestic farm animals are not regulated. These regulations are enforced by the legal system.

2. *Animal Care Policies*
   This policy manual clarifies how certain sections of the Animal Welfare Act should be interpreted.

B. Office of Laboratory Animal Welfare (OLAW)
OLAW falls under the National Institutes of Health within the Department of Health and Human Services. If an institution receives funding from PHS or other cooperating federal agencies, such as the Department of Defense, it must adhere to the following:

1. *Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy)*
   Click on the hyperlink above or a copy can be found at
   http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf

2. *The Guide for the Care and Use of Laboratory Animals, 8th Edition (2011)*
   Click on the hyperlink above or a copy can be found at
   http://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf

PHS Policy requires that each institution submit an animal welfare assurance. This assurance document is a written contract with the government that details the institution's policies and procedures setting forth compliance with all applicable laws, regulations, and policies. The PHS Policy covers ALL vertebrate animals.

C. **US Department of Veterans Affairs** – Office of Research Development (ORD)
If research is conducted in the Baltimore VA or is funded by the Department of Veteran's Affairs, there is an additional layer of regulatory oversight.

ORD is responsible for establishing policy for laboratory animal use in the VA system. The Veterans Health Administration (VHA) Handbook "*Use of Animals In Research*" (#1200.07) sets forth the principles and procedures that govern research, testing, and teaching activities involving laboratory animals in the Department of Veterans Affairs (VA).

The Office of Research Oversight (ORO) serves as the primary VA office in advising the Under Secretary for Health on all matters of compliance and assurance regarding animal welfare, research safety, and research misconduct. This office conducts inspections of VA facilities similar to the USDA.

NOTE: The UM SOM IACUC serves as the IACUC of record for the Baltimore VA, as such the principles and procedures set forth in the VHA Handbook apply to any faculty conducting research in the VA or funded by the VA. Please note that once the UM SOM IACUC has approved a protocol it must then be approved by the Baltimore VA Research and Development Committee prior to initiation.

IV. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

A. Role and Major Functions

The IACUC is a federally mandated committee whose role is to evaluate the care, treatment, housing and use of animals, and to assure investigator and university compliance with all applicable regulations and policies.

The major functions of the committee include:

1. To review and approve, require modifications (to secure approval), or withhold approval of all proposed projects OR proposed changes to ongoing approved projects involving the use of animals for research, teaching or other activities.
2. To conduct a review at least every six months of the School of Medicine's program for humane care and use of animals. Program review includes, but is not limited to, review of IACUC membership and function; IACUC records and reporting requirements; Veterinary Care; Training Programs; Occupational Health and Safety Programs, etc.
3. To inspect at least every six months all animal facilities and animal study areas (including investigator laboratories).
4. To submit written reports to the Institutional Official of the IACUC's evaluation of the semi-annual review process.
5. To make recommendations to the Institutional Official regarding any aspect of the animal care and use program or facilities.
6. To hear and adjudicate grievances concerning the care and use of animals.
7. To communicate changes in federal, state, and local regulations and other pertinent information regarding animal experimentation to involved faculty.
8. To be authorized to suspend any activity involving animals as set forth in the PHS Policy and other applicable regulations. Incidents of non-compliance and/or suspensions must be reported to all applicable federal agencies, accrediting bodies, and funding agencies.

B. Committee Accountability

The IACUC reports directly to the Dean of the School of Medicine and is assisted by the Office of Animal Welfare Assurance.

The Dean of the School of Medicine serves as the Institutional Official. The Institutional Official is the individual that assures the federal agencies that the School of Medicine animal care and use program will comply with all applicable laws, regulations and policies.

IACUC → Institutional Official → Federal Agencies

C. Committee Membership

Per the PHS Policy, the IACUC is federally mandated to consist of not less than 5 members, and must include at least one veterinarian with program responsibility; one practicing scientist experienced in animal research; one non-scientific member (lay person); and one non-affiliated member.

The UM SOM IACUC is comprised of qualified and professionally competent individuals representing diverse disciplines and professions. The chair and members of the IACUC are appointed by the Institutional Official for terms consistent with prevailing school policies. The committee shall consist of not less than 10 voting members. Most committee members will be faculty of various academic ranks, largely selected from departments which use animals in research. Each UMB Professional School utilizing laboratory animals is represented on the UM SOM IACUC.

The membership of the IACUC is confidential per the Dean of the School of Medicine. Confidentiality of the membership is also supported by the federal agencies.

D. Committee Meetings

The committee meets on a monthly basis. The IACUC Chair may schedule additional meetings as warranted. A quorum, which is comprised of a majority (>50%) of the voting members, must be present for the Committee to conduct any business. The committee reviews are conducted with objectivity and in a manner which will ensure the exercise of independent judgment of the members. Members are excluded from reviews of projects and/or activities in which they have an active role or which could pose a conflict of interest.

All submitted materials are treated as confidential. In the case of trade secrets, proprietary information or patent applications, such information is protected by law.

E. Committee Oversight

The UM SOM IACUC policies and procedures apply to any activity involving live animals that is undertaken on the premises of the UMB campus, BVAMC or IMET regardless of funding source, or off the premises if funds for this activity are processed through the University's Office of Research and Development (ORD) for an UMB faculty member.

As a rule of thumb, any UMB faculty member using animals regardless of where work is being conducted must obtain UM SOM IACUC approval. The type of approval may vary depending on where the work is being conducted and the faculty member's level of involvement. OAWA Staff should be contacted for further guidance.

F. Institutional Support

The Dean of the School of Medicine, serving as the Institutional Official, is responsible for assuring that the proper resources are available to support the animal care and use program to ensure compliance with all applicable regulations and policies.

V. PRINCIPAL INVESTIGATOR (PI) RESPONSIBILITIES

A. Responsibility for Animal Care

The principal investigator assumes primary responsibility for the care and treatment of all animals used in, or purchased by funds from his / her laboratory. This includes, but is not limited to:

1. Assure compliance with all federal, state and local laws, regulations and policies.
2. Assure strict adherence to the IACUC approved protocol. If modifications are necessary, a formal amendment must be submitted to the IACUC for review and approval prior to implementation.
3. Assure that all research staff working on the protocol…
    a. have read, understand, and have access to a copy of the IACUC approved protocol,
    b. have been trained and determined competent to carry out the work described in the protocol,
    c. have taken or participated in any required training, i.e., CITI training, occupational health and safety training, etc.,
    d. are aware of the risks associated with working with animals, hazardous agents, etc.
    e. are knowledgeable of, have access to, and adhere to IACUC and Veterinary Resources policies and procedures.
4. Assure that animals receive proper care at all times. Veterinary Resources personnel act as support service for maintenance of animals and should never be relied upon for primary supervision, care and treatment of animals.
5. Provide a safe working environment.
6. Appropriate record keeping.

B. Activities Requiring IACUC Approval

IACUC approval must be obtained for:

1. any activity involving live animals that is undertaken on the premises of the UMB campus, BVAMC or IMET regardless of funding source,
2. any activity involving live animals that is undertaken off the premises of the UMB campus, BVAMC or IMET if funds for the activity are provided from the university, e.g. grant funding, internal / departmental funding, etc.,

3. any activity involving the use of animal parts or end products requiring the use of live animals or the specific euthanization of animals by an outside party, commercial or otherwise, that is initiated by the investigator's request (*that is, custom order for a part or product not previously listed for public availability*),
4. any activity involving live animals that is undertaken in foreign countries,

The IACUC should be informed of:

1. any activity in which a UMB, BVAMC or IMET faculty member travels to another site to conduct or assist with procedures involving live animals, e.g. collaborative project,
2. any activity in which a UMB, BVAMC or IMET faculty member receives animal tissues for analysis, e.g., collaborative project,
3. any activity in which a UMB, BVAMC or IMET faculty member receives otherwise discarded animal tissues for use in his/her own research.

As a faculty member of the UMB, you are considered a representative of this institution, hence your involvement in any activity will reflect upon the university. It is the responsibility of the IACUC to assure that your involvement in any animal related activity, regardless of where the work is being conducted, meets UM SOM IACUC standards.

C. Qualifications Required to Serve as a Principal Investigator

Only a full-time faculty member whose appointment fits one of the following categories qualifies to serve as principal investigator on an animal use protocol.

1. Professor
2. Associate Professor
3. Assistant Professor

D. Requirements for Signatures on a Protocol

The signature of the Principal Investigator on the animal use protocol form assures the IACUC that he/she will accept responsibility for the humane care and use of animals and will comply with federal, state and local laws, regulations, policies and guidelines.

- "Per" signatures are not permitted.
- Electronic signatures and / or electronic documents will be accepted from the PI's email account.

E. Faculty Status Change / Resignation / Termination

As noted above, only full time faculty members are permitted to serve as principal investigators. If an investigator's faculty status has changed such that it no longer meets the above criteria, he/she must appoint another faculty member (who meets the above criteria) to assume responsibility for the project or close the study.

If an investigator ceases employment, it is his/her responsibility: 1) to transfer the study to another faculty member or close the study by submitting a final report to the IACUC, and 2) to contact Veterinary Resources to determine the fate of any existing animals.

Please contact the OAWA for additional guidance as needed.

VI. RESOURCES AVAILABLE TO PRINCIPAL INVESTIGATORS & RESEARCH STAFF

The following resources are available to faculty, staff and students during the preparation, or during the conduct, of an animal use protocol:

A. Office of Animal Welfare Assurance (706-7859 / 8470)

The Office of Animal Welfare Assurance (OAWA) is the regulatory oversight office for the SOM Animal Care and Use Program, and provides support for the UM SOM Institutional Animal Care and Use Committee (IACUC). The OAWA reports to the Dean of the School of Medicine. ***All IACUC matters should be directed to this office.***

The OAWA's responsibilities include:

- IACUC Administration
- Animal Welfare Inspections and Compliance
- Regulatory reporting
- Training
- Outreach and Communications

OAWA Staff are available to assist faculty, staff or students with any questions they may have regarding the use of animals. OAWA staff are also available to pre-review any correspondence being submitted to the IACUC and to provide training relative to IACUC policies and procedures.

B. Veterinary Resources (706-3540)

The procurement, husbandry and veterinary care of all animals is the responsibility of Veterinary Resources. The staff consists of well trained and dedicated animal caretakers, veterinary technicians, veterinary assistants, and veterinarians.

Veterinary Resources offers the following resources:

1. Animal Care and Use Training
2. Veterinary consultation and guidance
3. Veterinary pre-review of animal use protocols
4. Adventitious & Animal Pathogen Testing Services (free of charge)

5. Contract services, i.e. blood collection, surgical assistance, etc. (there may be a fee for such service)
6. Other services, please contact Veterinary Resources for more information.

All animal orders (or animals brought to UMB) from any source must be coordinated through Veterinary Resources to assure that proper health records are obtained, reviewed and approved before animal shipment. Animals may be ordered once final IACUC approval has been granted.

In case of an emergency involving animal care at any time, veterinary assistance can be obtained by calling the Veterinary Resources telephone number posted in all animal facilities.

NOTE: Veterinary Resources' personnel provide routine care and husbandry on a daily basis and are available to Principal Investigators to assist with animal care, address issues, etc. However, the principal investigator must provide any and all special care to animals involved in research. This is especially critical for animals requiring frequent supervision during periods of experimental preparation, treatment and / or recovery. It is the responsibility of the principal investigator to provide adequate post-operative care. Veterinary Resources personnel act as support service for maintenance of animals and should never be relied upon for primary supervision of animals unless specific arrangements are made with the Chief, Veterinary Resources.

1. **Role of the Veterinarian(s)**
   The role of the veterinarian in the animal care and use program includes, but is not limited to:
   a. providing for the health and welfare of animals,
   b. assuring adequate veterinary care
      i. preventive medicine, i.e. quarantine, monitoring of vendors, etc.
      ii. surveillance, diagnosis, treatment and control of disease, including zoonotic diseases
      iii. management of protocol-associated disease, disability or other sequelae
      iv. selection and utilization of appropriate anesthetics and analgesics
      v. proper performance of surgical procedures including pre-surgical, surgical, and post-surgical care
      vi. assessment of animal well being
      vii. selection and utilization of appropriate methods of euthanasia
   c. promoting regulatory compliance
   d. facilitating research

   For additional guidance regarding the role of the Veterinarian, please refer to the Animal Welfare Act, the Guide and the PHS Policy.

2. **Authority of the Veterinarian(s)**

The veterinarian has the following authority:

a. To modify a treatment regimen or procedure per his/her best clinical judgment. The IACUC must be notified of any change by the PI to insure that the protocol accurately reflects current procedures.
b. To euthanize any animal suffering pain / distress not described in the IACUC approved protocol.
c. To report incidents / concerns involving non-approved use or care directly to the IACUC.
d. To temporarily suspend an activity not compliant with the IACUC approved protocol or an activity which jeopardizes the safety of the animals or personnel involved in these activities. The IACUC will convene to review the reasons for suspension and determine whether the suspension should remain in effect.

The IACUC considers the veterinarians to be the resident experts relative to an animal's clinical condition, and it is their responsibility to place the best interest of the animal before the research needs of an investigator. The veterinarian will work with the investigator to determine whether an option exists such that the animal's treatment is humane while still meeting the research objectives of the study. If this option does not exist, the investigator must adhere to the veterinarians' decision. Please note that if the veterinarian's authority is not recognized by any investigator, their protocol will not be approved or an approved protocol will be suspended.

C. UMB Environmental Health and Safety (706-7055)

The University strives to provide people with a safe working environment and to operate in an environmentally friendly manner. In addition, there are Federal and State regulations that cover the work we do in our laboratories. The mission of the Environmental Health and Safety (EHS) is to provide you with the information and tools necessary to conduct your research safely, protect the environment, and meet regulatory requirements. EHS is comprised of several divisions: Biosafety, Radiation Safety, Occupational Safety, Environmental Management, Fire Safety, UM Immediate Care Center and Insurance Programs (workers compensation). For additional information on the services provided by these various divisions, please refer to the EHS website or EHS services or EHS programs.

D. Center for Innovative Biomedical Resources (CIBR)

CIBR serves as a center of excellence for state-of-the-art technologies, high-tech instrumentation and expertise to support biomedical research and health care needs. CIBR provides an organizational framework for the School of Medicine core facilities. These core resources provide investigators with access to expensive instrumentation or specialized services needed to support cutting edge funded

research. Technologies include genomics, imaging, structural biology, cytometric and assay development, animal models and biostatistics and bioinformatics.

VII. ANIMAL USE PROTOCOL APPROVAL PROCESS

A. Preparing and Submitting an Animal Use Protocol

The Animal Use Protocol Form and Instructions can be downloaded from the OAWA Website at http://medschool.umaryland.edu/IACUC/forms.asp

One original and one electronic copy of the completed protocol must be submitted to the OAWA by the first Friday of each month. The IACUC meets on the third Friday of each month. All animal use protocols submitted on the deadline are pre-reviewed by the OAWA staff, and logged into the IACUC database prior to assignment and distribution to IACUC Members. IACUC Members are provided with all meeting materials one week in advance of the meeting to assure adequate time to review and assess the proposed animal care and use.

A completed protocol will consist of:

- Animal Use Protocol (AUP) form
- A diagrammatic flow chart for each proposed experiment that includes the experimental course for each animal from initiation of the experiment through euthanasia.
- Environment Enrichment / Socialization Plan AUP Addendum (other species or nonhuman primate)
- Electronic copy of funded grants supporting the work proposed in the protocol. At minimum, the face page, research methods and the vertebrate animal section should be provided.
- AUP Addendums (as applicable): Rodent Breeding Addendum, Hazardous Agent Addendum, Institutional Biosafety Committee Approval, Radiation Safety Committee Approval, UMMC Hospital Administration Approval, etc.

RECOMMENDATIONS:

1. Prior to *any* submission, please review the OAWA Website to ensure the most current forms are being used and that the submission adheres to current policies and procedures.
2. Take advantage of the opportunity to consult with the veterinarian and OAWA Staff in the preparation of the animal use protocol. Although full approval cannot be guaranteed as result of the pre-review, it can be assured that the forms are complete, the most recent guidance, policies and procedures are incorporated, and that the veterinary care aspects are addressed appropriately. Please allow adequate time for pre-review to incorporate any changes in advance of the monthly deadline.
3. If any hazardous agents are being used, Institutional Biosafety Committee and/or Radiation Safety Committee review and approval are required prior to

final IACUC approval. These registrations should be submitted simultaneously to avoid delays in the approval process.

NOTES:

- *ALL animal use protocols submitted to the IACUC are reviewed in the same manner regardless of funding, species, their potential to cause pain or distress, utilization of alternative methodologies, etc. (the same criteria must be met).*
- *A consultation with a veterinarian is required pre-IACUC submission for those proposals involving survival surgery (all species) or non-survival surgery (USDA covered species only). Veterinary input is solicited for all protocols during the meeting, specifically for appropriateness of animal procedures, general monitoring and alternative endpoints.*
- *The IACUC weighs the potential adverse effects of the study against the potential benefits that may result from the proposed research by considering its relevance to human or animal health and carefully evaluating the impact on the proposed procedures on the animal's wellbeing taking into account possible refinements, proper pain management, appropriate monitoring and clearly defined humane endpoints.*

B. Committee Review, Determinations, & PI Notification

Routinely all animal use protocols undergo full committee review. Normally, the outcome of the committee's review is sent to the investigator within 3-4 working days following the meeting.

As a result of the committee's review, the protocol will be placed in one of the following categories:

1. Full Approval: The Committee has approved the protocol without question. A full approval letter is sent to the Principal Investigator (PI). Animals may be purchased through Veterinary Resources and used in the approved protocol only. Approval is given for a maximum of three years, with a continuing report of progress/status required annually.
2. Requires modification(s) to secure approval: The Committee has determined that final approval of the protocol is contingent upon receipt of additional clarifications / information before the project can be initiated. A query letter is sent to the Principal Investigator (PI) indicating the modifications that are required to secure final approval. The PI is advised to submit the requested information at his/her earliest convenience and is reminded that no animals may be ordered and no research may begin until final approval is granted by the IACUC. Upon receipt of the PI's response to queries, a designated member review (by the chair and/or other members as warranted) will take place to determine if the response is adequate. If the information is satisfactory, a final approval letter will be sent to the PI. Approval is given for a maximum of three years, with a continuing report of progress/status required annually.

3. Deferred: The Committee has neither approved nor withheld approval of the protocol. Substantive clarification, revisions and/or additions are needed to properly assess the proposed research. A query letter is sent to the Principal Investigator (PI) indicating that the committee has deferred further review of the protocol pending response to the IACUC's queries. The PI is advised to submit the requested information to the IACUC as soon as possible and is reminded that no animals may be ordered and no research may begin until final approval is granted by the IACUC. Upon receipt of the PI's response to queries, the protocol will be assigned to the original reviewers and placed on the agenda for re-review at the next scheduled IACUC meeting.
4. Withhold Approval: The Committee did not approve the protocol due to significant deficiencies and concurred that the Principal Investigator (PI) should resubmit a substantially revised protocol. A letter is sent to the PI indicating that the committee has voted to withhold approval of the study, the reasons for this determination, any comments the committee had that must be addressed in the next version, and recommend consultation with the IACUC Chair, OAWA Director and/or a Veterinary Resources veterinarian for guidance and assistance prior to submission of a new (revised) protocol. The letter also indicates that no animals may be ordered and no research may begin until final approval is granted by the IACUC.

All IACUC correspondences are sent via email to the Principal Investigator. At time of final approval, the PI will be sent a copy of the approval letter, a copy of the approved animal use protocol and a pre-populated Assurance of Compliance form that must be reviewed and signed by the PI and all lab personnel listed on the approved protocol. The completed Assurance of Compliance form must be returned to the OAWA within 30 days to be filed with the approved protocol.

C. Protocol Reporting Requirements

Once a protocol is fully approved by the IACUC, the Principal Investigator is responsible for the following reporting requirements:

1. **Amendments**

   Changes to the approved IACUC animal use protocol must be reviewed and approved by the IACUC prior to implementation. The Protocol Amendment Form and the Personnel Amendment Form can be downloaded from the OAWA Website. Amendments are accepted on a rolling basis; there is no deadline for amendment submissions.

   All "significant" modifications to an approved protocol are reviewed by full committee or by designated review. Examples of significant modifications include, but are not limited to, changes in the objectives of the study, change in species, addition of new strains, addition of new experiments, increase in animals greater than 10% of the approved total, change in principal

investigator, and change in the duration, frequency, or number of procedures performed on an animal, etc.

Minor modifications to an approved protocol are reviewed by the IACUC Chair, an IACUC member, or an IACUC designee. Minor amendments include, but are not limited to, addition or removal of lab personnel, change in location of animal use, change of title, change in administrative contact information, increase in animal numbers less than 10% of a previously approved species / strain, change in anesthetic, analgesic or method of euthanasia (as long as it meets one of the IACUC recommended agents / methods), change in procedure per veterinary consult, etc.

NOTE: *Conducting research without prior IACUC approval constitutes non-compliance with: 1) the approved protocol, and 2) all applicable laws, regulations and policies. The IACUC is obligated to investigate, remediate and fulfill regulatory reporting requirements, as applicable.*

2. **Annual Progress Reports**

The IACUC is required to conduct an annual review of each protocol every 365 days. An annual progress report is available on the OAWA Website and should be completed and submitted prior to the anniversary month [*month study was originally reviewed (expiration month)*].

The OAWA routinely sends annual report reminders a month prior to the report being due. Please note that an annual report must be submitted regardless of whether any animal work was conducted in the past year.

3. **Final Report / Third Year "de novo" Review**

PHS Policy requires that the IACUC perform a '*de novo*' review every three years. As such, a new protocol must be submitted detailing the results of the last three years and the proposed work to be conducted in the future.

A final report / 3rd year "de novo" review reminder is sent at three months, at two months and at one month in advance of a protocol's expiration. The OAWA recommends allowing a two-month time frame to obtain full approval of the renewal protocol. If the renewal protocol is not submitted in a timely fashion, there could be a lapse in approval in which all animal work on the given protocol must be halted. Any animals associated with an expired protocol must be reassigned to the SOM Animal Care and Use Program Holding protocol. This protocol provides for the basic care of the animals, but does not permit any experimental use. Animals will be re-assigned to an experimental protocol upon final IACUC approval.

The IACUC cannot administratively extend the expiring protocol.

4. **Inactivation of a Protocol**

   At any time prior to the expiration date, the approved animal use protocol may be closed by submitting a final report form.

NOTE: All correspondences to the IACUC must come from the Principal Investigator. No "per" signatures are permitted. This is the only way the IACUC can assure that the PI has reviewed and approved all correspondences.

D. Post-Approval Monitoring (PAM) Activities

All institutions using animals under the purview of the Animal Welfare Act Regulations, the PHS Policy, or the Guide are required to assure that animals are being used in a manner that is approved by the IACUC. The following mechanisms or procedures are used to facilitate ongoing protocol assessment and regulatory compliance:

- IACUC annual review of approved AUPs: *annual progress report or final report / 3rd year 'de novo' review*
- IACUC semi-annual inspection of all animal use areas, including PI laboratories
- IACUC review of proposed modifications
- IACUC review of animal welfare concerns
- IACUC post-approval monitoring surveys
- Veterinary Resources monitoring of procedures and animals
- Veterinary Resources monitoring procurement of animals
- Veterinary Resources review of post-operative surgical records

IACUC post-approval monitoring (PAM) surveys: A formal PAM program has been implemented in which comparative reviews, procedural observations and/or animal use area assessments are conducted on a proactive basis by OAWA staff on behalf of the IACUC. Results of the PAM survey are reported to the IACUC at its convened meetings. No observations and minor observations are reported for informational purposes only. Significant observations are referred to the IACUC for further action, i.e., discussion, corrective action, and/or suspension and reporting requirements. These surveys will be scheduled in advance at a time convenient for the PI, lab and OAWA. The goal is to survey most protocols at least once in their 3 year approval period. Once an animal use protocol is approved, a PAM survey introduction letter is sent along with a copy of the survey tool. The survey tool is provided again at the time a PAM survey is scheduled. Review the survey tool to prepare and ensure there are no surprises.

Veterinary Resources monitoring of procedures and animals by veterinarians, animal care technicians, and husbandry staff. Examples of such activities include daily monitoring of animals; their 'presence' in facility; protocol assistance; veterinary care of animals; routine clinical care of animals, etc. All of these activities provide an opportunity to assess the health and welfare of the animals

and/or evaluate investigator compliance with the approved protocol. Veterinary Resources will report any animal health/welfare findings, as warranted, to the IACUC through the OAWA. In addition, anytime there are questions regarding procedures, the vet staff will call the OAWA to ensure the proposed procedures are approved in the protocol.

Veterinary Resources monitoring procurement of animals: The OAWA sends weekly updates to Veterinary Resources. This report lists only the approved IACUC protocols including each species and the number of animals approved, expiration date, personnel, etc. This mechanism is in place to help insure that investigators do not unintentionally deviate from their approved protocol by ordering an unapproved species / strain, by ordering more animals than he/she is approved for, and to ensure that animals cannot be procured following a protocol's expiration.

Veterinary Resources review of post-operative surgical records: A program is in place for Veterinary Resources to receive all post-op and anesthesia records for large species (e.g. rabbits, swine, primates, etc.). We also review post-op records for small animal surgery/procedures (e.g. rodents) by inspection of special cage cards for this purpose.

VIII. GRANT PROCEDURES AND ROUTING INFORMATION

Please refer to the University of Maryland, Baltimore grant routing procedures as outlined on the Office of Research and Development (ORD), Sponsored Programs Administration website at
http://www.ord.umaryland.edu/ord_research/research_admin.html

A. 'Just in Time' IACUC approval

What are the IACUC's expectations?

The UM SOM IACUC expects that an animal use protocol will be submitted as soon as the investigator receives word of a favorable funding status, i.e., just in time requests. ***Investigators should allow 2 months to obtain full IACUC approval.*** Of course, an investigator may choose to submit his/her animal use protocol earlier if it is more convenient. What is not acceptable is submitting a new protocol submission within weeks of the funding date and expecting the IACUC to "rush" the proposal. There are rules and regulations that must be followed to avoid suspensions / fines. A thorough IACUC review not only assures animal welfare, but also protects and allows investigators and the institution to continue using animals in research. Research funds / support will be withheld if a protocol is submitted last minute, as NIH will not release funds without verification of IACUC approval.
Have other funding agencies accepted the "just in time" policy?

Many other funding agencies have accepted this policy, but not all. Therefore, the OAWA recommends that the investigator confirm adherence to this policy with the funding agency prior to submitting the grant application.

B. Grant / Protocol Congruency

Per PHS Policy, the institution is required to provide assurances that the protocol approved by the IACUC is consistent with the information contained in the grant. This process occurs by one of two mechanisms:

1. If an IACUC protocol is already in existence at the time of routing, the personnel in the SOM Office for Research will review the grant and assure that the basic procedures are contained within the animal use protocol on file in the OAWA. A more in-depth review is conducted by the OAWA staff upon notification of award. In these cases, the PI must submit a copy of the funded grant to the OAWA, and OAWA staff will perform a side-by-side comparison to insure congruency.
2. If "just in time" procedures are being implemented, the IACUC verification section of Kuali Coeus should be marked as 'to be submitted'. A final copy of the funded grant must be submitted to the OAWA at the time of initial review, in response to the committee's queries, or as soon as the final version of the grant is available.

C. Other Grant Related Information

NIH Funding Requirements

NIH grants (*competing or non-competing*) require that the Vertebrate Animal Section (VAS) be completed. The Office of Laboratory Animal Welfare has issued guidance on completing this section. Please refer to the below resources.

Grant Application VAS Worksheet: This worksheet is provided to assist applicants in preparing the VAS for submission to the NIH

VAS Factsheet

Grant Routing Information:

UM SOM Animal Care & Use Program

- OLAW Animal Welfare Assurance No.: A3200-01
- USDA Registered Research Facility
- AAALAC Accredited Program

Blanket statement for grants regarding the facility:

"*All animals are maintained in the animal facilities of the University of Maryland in Baltimore. Animals are housed, cared for and used strictly in accordance with the Guide for the Care and Use of Laboratory Animals (2011). The University of Maryland School of Medicine Animal Care and Use Program is fully accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care*

International (AAALAC). The program of animal care is directed by a full-time, specialty-trained (American College of Laboratory Animal Medicine, ACLAM), laboratory animal veterinarian. The institution has an Animal Welfare Assurance on file with the NIH Office of Laboratory Animal Welfare (OLAW), Assurance Number A3200-01 and is an USDA Registered Research Facility."

In COEUS, under Special Review Tab…

- Select "Animal Usage"
- Under approval, select appropriate category (*approved, exempt, not yet applied, or pending*)
- "IACUC #" – Protocol approved by IACUC. *NOTE: The work described in the grant must be approved under this protocol #.*
- "Latest approval date" – Original date of approval if within last year or annual report approval date

For program projects or training grants, the OAWA can provide IACUC grant lists for participating faculty. Please provide the office with a list of names and a grant list can be generated usually within 24-48 hours of a written request.

If a special letter is required relative to a *pending* IACUC review or title discrepancy between grant and IACUC protocol, please contact the office to generate the grant specific letter.

If the sponsor utilizes a separate "certification of approval" document, please contact the office to obtain the authorized signature (e.g., OAWA Director or IACUC chair signature), e.g., March of Dimes.

NOTES:

- *Please note that an IACUC protocol may include additional procedures which are not included in the grant, but must include at a minimum the animal work proposed in the grant.*
- *One IACUC protocol may be used for multiple grants, as long as the scientific aims are related and all the animal work proposed in the grants is approved under the specified IACUC protocol. Please contact the OAWA for additional guidance.*
- *For non-competing continuations, if the animal care and use procedures are modified for the upcoming year, an amendment must be submitted to the IACUC to include the proposed work.*

IX. PROCEDURES FOR COMMITTEE INSPECTION OF ANIMAL USE AREAS

The IACUC is mandated to conduct semi-annual inspections of all animal areas including animal facilities, approved satellite facilities, and investigator labs (if animals are used in the lab). These inspections are required to assure compliance with the approved IACUC protocol and all applicable federal, state and local laws, regulations, and policies. However, in addition to assuring compliance, these inspections permit the inspection team to learn more about an investigator's research as well as allow the investigator and/or research staff the opportunity to ask questions, discuss possible modifications, seek guidance, etc.

An inspection is conducted at least once every six months. Inspection teams consist of two IACUC members accompanied by the OAWA Director or designee. When an apparent deficiency is noted, it will be discussed with the principal investigator and/or research staff. The Principal Investigator may choose to send a formal letter to the IACUC noting what corrective actions have been taken or he/she may wait to respond to the IACUC letter documenting the deficiency found in his/her lab along with the corrective action that must be initiated within 15 working days. Either way, a written correspondence must be received in the OAWA notifying the IACUC of what corrective actions have resulted to rectify the identified deficiency.

If a situation is identified as requiring immediate veterinary care, the OAWA Director (or designee) will contact Veterinary Resources to follow up and provide a written report to the IACUC of their findings and any action taken.

A report of all inspection findings will be presented to the IACUC at the next convened meeting for recommendation of final approval or subsequent action. This report is also reviewed by the Institutional Official, Dean for the School of Medicine.

X. PROCEDURES FOR COMMITTEE REVIEW OF ANIMAL WELFARE CONCERNS

The IACUC is mandated to review any concerns regarding the care and use of animals within the UMB, BVAMC or IMET premises or by any UMB faculty, staff or student regardless of animal use location.

It is the policy of the UM SOM IACUC that ALL animals used for research, teaching or other activities receive the best possible care.

A. Procedures for Reporting Concerns

Individuals can report any animal care and use concerns to the IACUC via the following method: telephone contact followed by written documentation. It is preferred that the initial contact be made via telephone so that the appropriate action can be taken immediately to ensure the well-being of the animal(s) in question.

Subsequently, a written description of the concern should be submitted for further action. Anonymity of the individual initiating the concern will be respected, if requested and if possible.

All animal concerns should be reported to one of the following:

- Office of Animal Welfare Assurance: 410-706-4365
- Veterinary Resources: 410-706-3540
  After hours, on weekends or holidays: 410-706-3540. Please follow instructions in voice mail message regarding how to contact a veterinarian during these hours.

The above information is present on the OAWA Website and is posted throughout the SOM animal facilities.

B. Committee Action

The committee will act to obtain information from the individual initiating the concern and from all individuals involved in providing care or responsible for the animal(s) in question. The committee will conduct a thorough review and determine the appropriate course of action. All parties will be kept appraised of the progress and informed of the final outcome. The committee will notify and make appropriate recommendations to the Institutional Official regarding suspensions, reporting to applicable federal agencies, etc. as warranted.

In an attempt to protect the concerned party from possible reprisal, the IACUC will maintain anonymity of the individual initiating the concern, if at all possible. The individual will be kept informed of the final findings of the investigation relative to his/her concern, if requested. Additionally, it is University policy [UM Policy VIII-7.11 (A), (B) & (C)] to prohibit any discriminatory or retaliatory action against any UMB personnel reporting known or reasonably suspected wrongdoing. UMB personnel include administrative and academic officers, faculty, employees, fellows, students, volunteers or any person in the public who interacts with UMB.

XI. PROCEDURES FOR ADJUDICATION OF GRIEVANCE AGAINST COMMITTEE ACTION

The IACUC Chair and members of the IACUC will make all reasonable efforts to work with any individual involved with the care and use of animals to resolve any problem or difference. If, after exhausting this venue of appeal, an individual continues to feel that he/she has received improper treatment or process of judgment, then a grievance may be initiated.

A written complaint should be submitted to the IACUC Chair. Upon receipt of a written complaint, the IACUC Chair will gather all relevant documents and information, and forward these and the IACUC's recommendations to the Institutional Official for final

resolution. Please note that the IACUC's authority to review and approve animal use protocols is independent of the Institutional Official who may not overrule an IACUC decision to withhold approval (AWR 9 CFR 2.31).

XII. OTHER IACUC POLICIES

A. Procurement of animals

All animals approved for usage must be ordered through Veterinary Resources to assure the use of approved vendors and to avoid the introduction of adventitious pathogens into the animal facilities.

All animals brought to UMB from any source must be coordinated through Veterinary Resources to assure that proper health records are obtained, reviewed and approved before animal shipment.

Please contact Veterinary Resources for additional information regarding the procurement of animals for research, teaching or other activities.

B. Animal Housing and Satellite Facilities

All animals must be housed in the designated, centralized animal facility. The IACUC prefers that all animal work be conducted in the animal facility, unless the animal(s) will not be returned, e.g. procedures performed and animal euthanized in the lab. The IACUC understands that there may be extenuating circumstances which necessitate the need to remove animals from the facility and return them to the facility. If this is necessary, precautions should be taken to reduce the risk of introducing adventitious pathogens. Transport procedures must be coordinated and approved by Veterinary Resources. Animals are not permitted outside the facility for time periods exceeding 24 hours.

If animals must be maintained outside the designated animal facility for periods exceeding 24 hours, a formal request must be submitted to the IACUC requesting approval of a Satellite Housing Facility. Guidelines for requesting permission to establish a satellite housing facility are available on the OAWA Website.

C. Protection of the Animal Facility from Outbreaks of Adventitious Pathogens

The inadvertent introduction of pathogens and parasites into an animal facility can cause a significant disruption of research in terms of wasted time / effort /funds, unwanted effects on experimental systems, potential pain / distress to animals, euthanasia of animals, etc. All animal procurement must be conducted by Veterinary Resources to assure that animals are obtained by approved vendors. It is equally important that all animal biologics be adventitious pathogen-free prior to their introduction into any of the animals housed in our facilities. Veterinary Resources

will test these biologics for adventitious pathogens at no cost to the investigator. [*Biologics should be tested every three years to assure that testing has been performed for all potential pathogens*.] Finally, an investigator should limit his/her animal work to a single animal facility in order to decrease the chances of fomite transfer of some infectious agents.

D. Transport of Animals within the University

Non-rodent species should be transported only on freight elevators.

Rodents transported in public elevators must be covered in a manner to conceal and prevent exposure of others to rodent allergens.

Transport of any species between buildings must also be done in a manner to secure the animal(s) and to conceal (cover) and prevent exposure to environmental extremes.

The transport of animals from the BVAMC animal facility to other areas must be approved by the Veterinary Medical Officer in the VA Research Office.

No live animals should be transferred between the BVAMC animal facility and SOM animal facilities. In addition, animals housed within SOM must not be transferred to animal facilities in other buildings without prior notification and approval by Veterinary Resources.

E. Use of hazardous agents

Projects involving hazards such as recombinant DNA; pathogenic microorganisms; select agents; ionizing radiation; or lasers must obtain the appropriate Environmental Health and Safety (EHS) approvals prior to final IACUC approval.

If ionizing radiation or lasers are used in animals, EHS Radiation Safety Committee approval is needed. A copy of their approval must be provided to the IACUC.

If pathogenic microorganisms; select agents; hazardous / toxic chemicals; or recombinant DNA are used in animals, EHS Institutional Biosafety Committee approval is needed. A copy of their approval must be provided to the IACUC.

If one of these agents is being used and the animals are housed in the Baltimore VAMC or the project is funded by the VA, approval must be obtained from the VA R&D sub-committee on research safety (SRS).

Contact Info:
UMB Environmental Health and Safety (EHS): 410-706-7055
http://www.ehs.umaryland.edu
Baltimore VA Research Office: 410-605-7130

In addition to providing the above approvals, the IACUC requires that specific information be contained in the animal use protocol. A Hazardous Agent Addendum is required for each agent used.

F. Pain Categories

The UM SOM IACUC has adopted the use of the USDA classification system for pain and distress. The pain categories are as follows:

CATEGORY B – Animals bred, conditioned or held for use in teaching, testing, research, but not yet used for such purposes. (*NOTE: If tail snips are necessary for genotyping, this category is not appropriate*.)

CATEGORY C – Procedures that involve no or only very brief pain or distress, with no need for or use of pain relieving drugs.

CATEGORY D – Procedures involving potential pain or distress for which appropriate anesthetics, analgesics, or tranquilizers are given. *(NOTE: Contact Veterinary Resources for "appropriate" agents as needed*)

CATEGORY E – Painful or distressful procedures for which drugs to relieve the pain or distress would adversely affect the research study. STRONG SCIENTIFIC JUSTIFICATION MUST BE GIVEN FOR ANY RESEARCH FALLING UNDER THIS CATEGORY.

G. Survival Surgery

All animal surgeries must be performed in accordance with federal regulatory and accreditation standards.

All protocols must detail surgical preparation of the animal and surgical team, detailed surgical procedures, and post-operative care. Surgery must be performed or directly supervised by trained, experienced personnel.

Non-rodent aseptic surgery must be conducted only in facilities intended for that purpose. These facilities must be maintained and operated to ensure cleanliness, and directed and staffed by trained personnel. Please contact Veterinary Resources for location and scheduling of these approved facilities. Aseptic preparation of the surgical field; use of sterile instruments; and the appropriate surgical attire (sterile surgical gloves, gowns, shoe covers, caps, and face masks / shields) must be utilized during these procedures.

Survival surgery on rodents does not require a special facility but should be performed using aseptic techniques, sterile instruments, and surgical gloves to prevent clinical infections. A rodent surgical area can be a room or portion of a room that is easily sanitized and not used for any other purposes during the time of surgery.

Please refer to the Rodent Surgery Guidelines available on the OAWA Website. These guidelines must be adhered to unless otherwise justified.

Appropriate facilities and equipment must be available for all post-surgical care regardless of species. The Principal Investigator is responsible for post-surgical care. Post-surgical care should include monitoring of animals to ensure uneventful recovery from anesthesia and surgery; administering supportive fluids, analgesics, and other drugs as required; maintenance of body temperature; providing adequate care for the surgical incision; and maintaining appropriate medical records. Please contact Veterinary Resources for more information regarding appropriate post-operative care, as necessary.

H. Multiple Survival Surgery / Multiple Major Survival Surgery

The IACUC's policy is that multiple survival surgeries (major or minor) on a single animal is acceptable if they are essential to the outcome of a single animal use protocol and scientifically justified by the investigator.

The conduct of multiple major survival surgeries on a single animal used in two separate protocols is strongly discouraged. Any such request would be critically scrutinized by the IACUC and Attending Veterinarian. If such a request involved an USDA covered species, Animal Care Policy # 14 would be adhered to relative to the Institutional Official seeking permission from USDA APHIS to proceed.

The IACUC evaluates the following information to determine the potential impact on animals' well-being:

- the investigator's justification for performing multiple survival surgeries (major or minor) on a single animal,
- the nature of the procedures,
- the potential for pain and distress,
- the length of time between procedures, and
- post-operative care procedures, general monitoring plan and alternative endpoints

I. Non-survival Surgery

While aseptic surgical procedures are not required for non-survival surgery, the surgical set up, prep of animals, assessment of depth of anesthesia, use of clean surgical instruments, etc. should be briefly described in the animal use protocol.

J. Dietary Manipulations

Any time dietary manipulations are proposed, the plan must be discussed with the Vet Resources Facility Manager (706-1601). Additionally, the logistical details relative to the delivery of these diets must be described in the animal use protocol. Specifically, the following items should be addressed:

Specialized Diet – Food

1. Species
2. Identify the specialized diet being administered to animals.
3. Indicate the source from where the specialized diet will be obtained.
    a. If the specialized diet is generated by the lab, identify the compound(s) that are added to the diet and briefly describe how it will be made.
    b. Is the compound being added to the diet pharmaceutical grade? If "no", provide scientific justification for the use of a non-pharmaceutical grade compound.
4. Specify which group will be responsible for purchasing the specialized diet.
5. Indicate how and where the specialized diet will be stored.
6. Identify the individual(s) responsible for administering the specialized diet.
7. Indicate the frequency of changing / replenishing the specialized diet.
8. Indicate how the cages on specialized diet are identified.
9. Specify the duration of time animals will be administered the specialized diet.
10. Discuss any anticipated side effects of the specialized diet on the animal.
11. Discuss any specialized husbandry requirements as result of administering the specialized diet, i.e., singly housed vs. group housed. If "Not Applicable", indicate NA.
12. Discuss how diet intake will be measured, if applicable. If "Not Applicable", indicate NA.
13. Discuss how the correct dose per animal will be confirmed, if applicable. If "Not Applicable", indicate NA.
14. Indicate date of consultation with VR Facility Manager and/or Supervisor regarding the specialized diet details. Identify the VR staff member consulted.

Specialized Diet – Water

1. Species
2. Identify the compound being added to the water.
3. Specify dose and concentration of compound being added to the water.
4. Is the compound being added to the water pharmaceutical grade? If "no", provide scientific justification for the use of a non-pharmaceutical grade compound.
5. Identify the individual(s) responsible for administering the specialized water.
6. Identify the fluid delivery system *(e.g., water bottle, water pouch, etc.)* and describe how the compound will be added to the water.
7. Indicate the frequency of changing / replenishing the specialized water.
8. Indicate how the cages on specialized water are identified.
9. Specify the duration of time animals will be administered the specialized water.
10. Discuss any anticipated side effects of the specialized water on the animal.
11. Discuss methods utilized to ensure adequate hydration of animals while specialized water is administered

12. Discuss any specialized husbandry requirements as result of administering the specialized water, i.e., singly housed vs. group housed. If "Not Applicable", indicate NA.
13. Discuss how the correct dose per animal will be confirmed, if applicable. If "Not Applicable", indicate NA.
14. Indicate date of consultation with VR Facility Manager and/or Supervisor regarding the specialized water details. Identify the VR staff member consulted.

K. Food and Fluid Regulation

Food and fluid restrictions for research purposes must be scientifically justified. The least restriction that will achieve the scientific objectives must be used in these instances. A plan must be developed for monitoring the animals during and after the restriction. Endpoint criteria must be identified, e.g., IACUC policy states animals must be euthanized if weight loss is >20% of the animals normal body weight.

In the case of conditioned-response research protocols, use of food or fluid as a positive reinforcement is much preferred and recommended in lieu of negative reinforcement.

The following information must be provided in the animal use protocol:

Food / Fluid Restriction

1. Species
2. Indicate type of food / fluid regulation: Food - Scheduled access, Food – Restriction, Fluid – Scheduled access, Fluid – Restriction.
3. Provide scientific justification for this type of food / fluid regulation.
4. Describe food / fluid regulation procedure(s).
5. Indicate the duration of food / fluid regulation (e.g., how many hours a day for ___ days / weeks).
6. Describe how food / fluid regulated animals will be monitored with sufficient frequency to ensure food / fluid intake meets nutritional needs.
    a. Confirm body weights will be recorded at least weekly.
7. Discuss any possible adverse consequences of regulation and the fate of animals exhibiting any behavioral and/or clinical changes.
8. Confirm written (*or electronic*) records will be maintained for each animal to document daily food / fluid regulation, daily health observation and at least weekly body weight measurements.
9. Confirm animals on food / fluid regulation will be identified at the cage level. Cage level documentation must also contain phone and email contact information for responsible lab personnel.

L. Prolonged Restraint

It is the policy of the IACUC that any prolonged restraint be scientifically justified by the investigator. The following justification and details must be presented in the AUP under the subheading "prolonged restraint":

- A discussion of why less restrictive means cannot be used, that devices are not used as normal housing or for convenience and that the duration of restraint is minimized
- A description of the restraint method or device
- Duration and frequency of restraint
- A description of how animals are acclimated to the restraint method / device
- A description of the procedures implemented to assure proper observation and monitoring of the animal while restrained
- Clarification of whether the proposed method of restraint require specialized housing / husbandry conditions? If yes, a description of the specialized housing / husbandry conditions must be provided, e.g., alternative methods of food / water provision, sanitation methods, etc.
- Confirmation that a veterinary consult will be obtained should lesions or illness with restraint methods be observed.
- Confirmation that animals that fail to adapt will be removed from the study.
- Confirmation that all individual(s) working with this restraint method or device have been properly trained in its humane use in this species.

Restraint procedures must be shown to be the only method of achieving the experimental goals. Other options such as training to cooperate with research procedures, sedation, use of systems that permit normal postural adjustments, etc. must be considered, if applicable.

M. Humane Endpoints

The IACUC has adopted the Guidelines of the NIH Animal Research Advisory Committee: Endpoints in Animal Study Proposals that provide criteria for neoplasia studies, death or moribundity as an endpoint, early clinical signs, and frequency of observation. Endpoint Guidelines can be located on the OAWA Webpage.

Studies should be terminated when animals begin to exhibit morbid signs or clinical signs of disease if these endpoints are compatible with meeting the research objectives. All animal use protocols should contain clearly defined endpoints including criteria for early termination of study if warranted.

Death as an endpoint is not acceptable unless scientifically justified. This discussion should include the reason(s) morbidity or other clinical signs cannot be used in lieu of death as an endpoint.

N. Euthanasia

The method(s) of euthanasia proposed in any animal use protocol must follow the recommendations of the 2013 AVMA Guidelines for the Euthanasia of Animals.

IACUC Recommended Methods of Euthanasia (*by species*) can be located on the OAWA Guidelines webpage. Alternatively, Veterinary Resources is available to provide guidance on the most appropriate method of euthanasia for a given species with consideration of the specific aims of the study.

O. Production of Monoclonal Antibodies

In the past, a popular method of producing monoclonal antibodies (mAb) implemented ascites production in mice. The ascites method of producing mAb involves animal procedures that would by classified as unrelieved pain and distress. In the last several years, improved techniques and culture media have demonstrated that in vitro methods of producing mAb are comparably or more successful than in vivo (ascites) methods. Therefore, per federal requirements, alternatives to animals use (in vitro methods) must be considered in place of the ascites method.

As the unrelieved pain and distress category requires strong scientific justification, the IACUC requires that a Principal Investigator provide a documented attempt to expand the hybridomas in vitro as justification prior to consideration of approval for ascites production.

This is best done on this campus by submitting the cells to μQuant Facility directed by Dr. Brian Taylor at IHV (410-706-4648; brtaylor@ihv.umaryland.edu) If Dr. Taylor concurs that the hybridomas will not grow well in vitro, then in vivo ascites production could be justified. Off-campus resources may also be used for these purposes.

P. Production of Transgenic Animals

If a transgenic animal will be produced for an investigator, the following policies must be adhered to:

1. The recombinant DNA used in the production of the transgenic animals must be registered with the Environmental Health and Safety Institutional Biosafety Committee. This registration is the responsibility of the Principal Investigator, not the person producing the transgenic animal.
2. A breeding protocol to establish and maintain the breeding colony must be attached as an addendum to the Principal Investigator's experimental protocol. The Rodent Breeding Addendum is available on the OAWA Website.

The IACUC recommends the use of the SOM Transgenic Core Facility (6-0453).

NOTES:

- If the transgenic animals will be produced by the investigator in the laboratory, all animal procedures must be detailed in the animal use protocol.
- If the transgenic animals will be produced by another SOM investigator (e.g., transgenic core facility) using a previously approved protocol, only the investigator's name and protocol number are required. If an investigator outside the SOM will be producing the transgenic animals, please contact the OAWA for instructions.

Q. Cold anesthesia in Xenopus

The use of Tricaine Methanesulfonate (MS-222), Isoflurane, halothane or Ketamine are the preferred anesthetics for Xenopus. Immobilization by hypothermia is not permitted unless the investigator can justify that the use of these agents interfere with experimental results. If the IACUC approves the use of immobilization by hypothermia, at NO TIME may the animal come in direct contact with the ice.

R. Use of Hospital Equipment or Facilities

The use of hospital equipment in laboratory animal research, teaching or other activities requires the prior approval of the IACUC and UMMC Hospital Administration. The two most frequent scenarios encountered include: 1) the use of animals in the hospital, and 2) the use of portable equipment (owned by the hospital) in UMB facilities. Guidelines have been developed to assist investigators in obtaining IACUC and UMMC Hospital Administration Approval. This guidance document can be located on the OAWA Website.

S. Press Releases and/or Filming Animal Usage

An investigator who desires media coverage of their research that involves animal usage must contact the School of Medicine Office of Public Affairs to coordinate coverage, or to issue a press release. A copy of the press release must be forwarded to the OAWA with a cover memo indicating the approved IACUC protocol under which the research was accomplished.

Investigators must immediately notify the Office of Public Affairs of any request by the news media to view, photograph, film or videotape animal usage. Concurrently, the investigator must immediately notify the Office of Animal Welfare Assurance (OAWA) to inform the IACUC of any such requests. Any request by the news media to view, photograph, film or videotape animal usage must be approved in advance by the IACUC and the Institutional Official. No filming by the news media may take place without prior approval.

Any filming, photographing or videotaping of animal usage must be coordinated with the Office of Public Affairs. The IACUC must also be informed of the filming schedule. A member of the IACUC and a representative from the Office of Public Affairs must be present during filming. In addition, a veterinarian must be present if the filming involves a surgical procedure, or if it is recommended by the IACUC.

Stock video footage of several species is/or will be available for media use. If you cannot use this stock footage, please provide justification for the necessity of additional filming. Please contact the OAWA for information regarding all stock video footage.

T. Training

The IACUC requires that all investigators and their research staff complete any required training. A description of the training resources available to investigators and their research staff are available on the OAWA Website. In addition, please review Section IV. A. Principal Investigator Responsibilities relative to research staff training.

U. Veterinary Resources Policies

The IACUC expects that all Veterinary Resources policies and procedures will be strictly adhered to unless an exception is granted by Veterinary Resources and/or the IACUC. For example, housing requirements, environmental enrichment, reporting requirements for injured or sick animals as result of study, housing, etc.

V. Consideration of Alternatives / Literature Database Search

The regulations require that investigators consider alternatives to minimize animal use and pain / distress. The concept known as the "3 R's" must be considered when composing an animal use protocol. The 3 R's include:

Replacement of animal use with non-animal techniques.
Reduction in the number of animals used.
Refinement in experiments or procedures to reduce pain and distress.

This requirement is fulfilled by providing detailed information and justification in the required sections of the animal use protocol narrative.

A literature database search must be performed for any protocol that involves a potentially painful / distressful procedure. Please refer to the IACUC animal use protocol form and the IACUC Policy on Alternative Searches for Potentially Painful / Distressful Procedures for more information.

W. Animal Re-Use

In general, the re-use of animals may be an appropriate way to reduce the number of animals used if it can be accomplished without a negative effect on the animals or the scientific integrity of multiple projects.

Animals may be re-used…

- Within a protocol as required to meet the objective of a single animal study activity. Re-use must be scientifically justified and animal procedures clearly defined to ensure animal welfare.
- Within two separate protocols provided the second use does not constitute a second major survival operative procedure and can be accomplished without a negative effect on the animal or the scientific integrity of either project.

The following information must be provided in the animal use protocol:

1. Will any of the proposed experiments utilize animals that have already undergone experimental procedures in this animal usage protocol or in a separate animal usage protocol?
    a. If "yes", justify the reuse of animals in this animal usage protocol.
    b. Identify which animals will be reused including the source of the animals and what experimental procedures they previously underwent.
    c. Identify what procedures will be performed on these animals in this animal usage protocol.
    d. Confirm that animal reuse can be accomplished without negative effects on the animals or the scientific integrity of multiple projects.

X. Use of Non-Pharmaceutical Grade Drugs and Other Substances

The IACUC has established a policy that requires the use of pharmaceutical grade drugs and other substances if they are available through human or veterinary suppliers.

The use of non-pharmaceutical grade drugs or other substances must be identified, described and justified in the AUP. The description must address how the drug / substance will be compounded to insure sterility of the final product as well as minimize the risks of inaccurate drug concentration, bacterial growth or endotoxin contamination. The IACUC policy includes compounding instructions / recommendations.

In accordance with OLAW and USDA guidance, the use of non-pharmaceutical grade drugs / substances must be scientifically necessary, appropriately justified, and approved by the IACUC.

XIII. IACUC GUIDELINES / GUIDANCE DOCUMENTS

The OAWA Website contains several IACUC guidance documents to assist investigators and their research staff in preparing an animal use protocol. Guidance documents are updated on a routine basis and placed on the web for easy access. Version dates are noted in the bottom right hand corner. New guidance documents are developed on an as needed basis. Please refer to these documents in the preparation of animal use protocols and amendments.

XIV. DEFINITIONS

Anesthetic Recovery - an animal will be considered recovered from anesthesia when it has regained consciousness and has the ability to swallow and hold its head upright while in a sternal recumbency.

Animal Welfare Assurance – this is a formal, written contract between an institution and NIH which details the institution's policies and procedures setting forth compliance with all applicable laws, regulations, and policies.

Aseptic Surgical Facilities - dedicated facilities used for major survival surgery in non-rodent species. The facilities must be inspected and approved for that purpose by the IACUC.

Aseptic Techniques - this technique includes wearing of sterile surgical gloves, gowns, shoe covers, caps, and face masks / shields; use of sterile instruments; and aseptic preparation of the surgical field using standard methods of clipping hair, multiple antiseptic scrubs followed by an antiseptic solution, and using sterile drapes. Please refer to Rodent Surgery Guidelines and Surgical Guidelines available on the OAWA Website.

Euthanize & Harvest Procedures - any procedure which involves euthanizing an animal (via IACUC approved methods) prior to removal of tissues, etc.

Institutional Official – is the individual who signs, and has the authority to sign the institution's assurance, making a commitment on behalf of the institution that the requirements of the PHS Policy and the AWA will be met.

Major (Invasive) Surgery - Per the Guide (p. 117), any surgical intervention which "*penetrates and exposes a body cavity, produces substantial impairment of physical or physiologic functions, or involves extensive tissue dissection or transection*". This is interpreted to include abdominal and thoracic surgery and certain open orthopedic procedures or other types of highly invasive surgery.

Minor Surgery - Per the Guide (p. 117), any surgical intervention which "*does not expose a body cavity and causes little to no physical impairment; this category includes wound*

suturing, peripheral vessel cannulation, percutaneous biopsy… and most procedures routinely done on an outpatient basis in veterinary clinical practice".

Multiple Survival Surgery - multiple major survival surgical procedures conducted on a single animal.

Non-rodent Species - for the purpose of this policy, the term non-rodent species includes hamsters, guinea pigs, gerbils, ferrets, rabbits and all other species on the phylogenetic scale up to and including non-human primates.

Non-Survival Surgery - any surgical procedure which involves anesthetizing an animal, performing some type of experimentation on the animal while under anesthesia, and then euthanizing the animal prior to its recovery from anesthesia.

Post-operative Care - this term includes the observation of the animal by trained investigative personnel to ensure uneventful recovery from anesthesia and surgery; administering supportive fluids, analgesics, and other drugs as required; maintenance of body temperature; providing care for surgical incisions; and maintaining appropriate medical records. It also includes being available for dealing with emergencies or unexpected complications which may occur as a result of surgery.

Survival Surgery - any surgical procedure which involves an animal recovering from anesthesia.

Training - The IACUC must determine that technical and professional personnel who perform animal anesthesia, surgery or other experimental manipulations are qualified through training or experience to accomplish these tasks in a humane and scientifically accepted.

XV. ADDITIONAL LITERATURE RESOURCES

In addition to the regulatory documents referenced in Section II. Federal Mandates, the following documents serve as useful references:

AVMA Guidelines for the Euthanasia of Animals: 2013

Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research

Methods and Welfare Considerations n Behavioral Research with Animals (NIMH)

Recognition and Alleviation of Distress in Laboratory Animals

Occupational Health and Safety in the Care and Use of Research Animals

Occupational Health and Safety in the Care and Use of Nonhuman Primates