UNIVERSITY of MARYLAND
BALTIMORE

PRINCIPAL INVESTIGATOR MANUAL

Office of Animal Welfare Assurance

Principal Investigator Manual
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I. INTRODUCTION

The University of Maryland Baltimore (UMB) is dedicated to the task of assuring the humane care and use of all animals involved in research 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 UMB IACUC serves as the IACUC of record for all Professional Schools on 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 or other activities is a privilege, not a right, governed by public scrutiny / concern; federal, state and local laws, regulations and policies; and UMB'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.

UMB has an Animal Welfare Assurance on file with the National Institutes of Health (NIH) Office of Laboratory Animal Welfare (OLAW) that assures compliance with all federal, state, and local laws, regulations, and policies.

UMB is committed to the advancement of science through the responsible conduct of animal research.

II. UMB ANIMAL CARE AND USE PROGRAM

The UMB 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 UMB 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 UMB animal care and use program is fully accredited by AAALAC International (AAALACi). This accreditation is voluntary and represents the UMB's commitment to the quality care and use of animals. The UMB's animal care and use program has been accredited since 1973.

III. FEDERAL MANDATES / REGULATIONS

Four 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. Regulations established under the Animal Welfare Act set standards for the humane care and treatment of certain animals used in research. 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.

The USDA utilizes the Animal Welfare Inspection Guide as a tool to improve the quality and uniformity of inspections, documentation, and administration of the Animal Care Program.

B. Office of Laboratory Animal Welfare (OLAW)

OLAW falls under the National Institutes of Health (NIH) within the Department of Health and Human Services. If an institution receives funding from PHS or other cooperating federal agencies, such as DHHS, NSF and/or NASA, 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 https://olaw.nih.gov/sites/default/files/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 https://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 VAMC 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 "*VA Research with Animals*" (VHA Directive 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 UMB IACUC serves as the IACUC of record for the Baltimore VAMC, 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 UMB IACUC has approved a protocol it must then be approved by the Baltimore VA Research and Development Committee (RDC) prior to initiation.

D. Department of Defense (DoD)

If research is funded by the Department of Defense, there is an additional layer of regulatory oversight.

DoD Instruction 3216.01 - Use of Animals in DoD Conducted and Supported Research and Training applies to this work. Once a protocol has been approved by the UMB IACUC, it must be submitted to the applicable branch of the DoD.

U.S. Army: Animal Care and Use Review Office (ACURO)
U.S. Navy: Office of Naval Research (ONR)
U.S. Air Force: AF Research Oversight & Compliance

These entities will issue an approval letter following their review. These approval letters provide guidance on amendment submissions and reporting requirements that must be adhered to during the life of the award.

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 UMB'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 UMB Vice President and Chief Accountability Officer and is assisted by the Office of Animal Welfare Assurance.

The UMB Vice President and Chief Accountability Officer serves as the Institutional Official. The Institutional Official is the individual that assures the federal agencies

that UMB's 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 UMB 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 IACUC.

The membership of the IACUC is confidential. Confidentiality of the membership is also supported by the federal agencies.

D. Committee Meetings

The committee meets monthly. 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 UMB 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 UMB 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 UMB Vice President and Chief Accountability Officer, 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 always receive proper care. 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 UMB 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.
- PI's electronic signature on documents are accepted from the PI's or designated lab member's email account. In the latter case, the PI must be cc'd on the submission.
- Electronic documents without signature will be accepted from the PI's UMB email account only.
- CICERO submissions can only be executed by the PI.

This is the only way the IACUC can assure that the PI has reviewed and approved all correspondences.

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 (OAWA)

The Office of Animal Welfare Assurance (OAWA) is the regulatory oversight office for the UMB Animal Care and Use Program and provides support for the UMB Institutional Animal Care and Use Committee (IACUC). The OAWA reports to the UMB Vice President and Chief Accountability Officer. ***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 (VR)

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 -
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 Director, Veterinary Resources (or designee).

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 ensure 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 halt 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 discuss the findings, devise a plan to move forward, and vote to determine whether the suspension should remain in effect until the issue is resolved.

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 (EHS)

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: Research Safety (Biosafety, Radiation Safety, Chemical Safety, Lab Auditing), Occupational Safety and Health, Hazardous Material Management, Risk Management and Workers'

Compensation, and Training. For additional information on the services provided by these various divisions, please refer to the EHS website.

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, clinical practice, and health care. CIBR provides an organizational framework for all School of Medicine biomedical core resources. These core resources provide investigators with easy access to fair-priced, state-of-the-art technologies, services, and expertise necessary to catalyze high-impact science and support the clinical mission. 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

All animal use protocol (AUP) applications must be submitted through CICERO, the IACUC online protocol management system. The CICERO platform manages all activities associated with a protocol including protocol creation / submission, any required surgery or VA consults, protocol revisions, protocol approval, amendment submissions, adverse event notifications, progress reports and final reports. The following resources are available to help you navigate the system and begin drafting a new animal use protocol:

CICERO Instructional Videos are available at: https://www.umaryland.edu/oawa/Education-and-Training/cicero-instructional-videos/

CICERO Frequently Asked Questions (FAQs) are available at: https://www.umaryland.edu/oawa/frequently-asked-questions/

OAWA Staff are available to answer questions. Please email iacuc@umaryland.edu or contact an IACUC Analyst for assistance.

IACUC Seminar on *How to get your protocol approved by the IACUC* is available at: https://www.umaryland.edu/oawa/education-and-training/

The IACUC operates on a new protocol submission deadline. The Deadline Dates and instructions for New Protocol submissions can be found on the OAWA website at: https://www.umaryland.edu/oawa/forms/ under **Animal Use Protocols (as of December 2022).** Please note…

- Protocols submitted on the deadline date without the required consults, will NOT be accepted that month. *If you need a VA or Surgery consult, please*

allow an extra two weeks in advance of the IACUC submission deadline for this to occur. This means the protocol needs to be completed and submitted by the VA/Surgery Consult deadline so the system can route it through that review, if required. When the protocol enters the "Administrative Review" state it has been received by the OAWA for the next new protocol submission deadline.

- If you submit a protocol mid-month, it will be accepted for the next new protocol submission deadline.
- If you need an extra day or two to finalize your submission (in response to a VA or Surgery consult or a protocol that does not require a consult), you must contact the office by email (iacuc@umaryland.edu) in advance of the deadline to discuss any possible extension with an OAWA Staff member.
- Please plan ahead, submit early, and allow adequate time for processing.

RECOMMENDATIONS:

1. Prior to *any* submission, please review the OAWA Website to ensure the submission adheres to current guidelines, policies, and procedures.
2. Take advantage of the opportunity to consult with a VR 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 application is ready for IACUC review, i.e., the correct sections have been completed, the information provided utilizes the most recent guidance, policies, and procedures, 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 under review, 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

The UMB IACUC adopted the use of the Designated Member Review (DMR) process as the primary review method for all new animal use protocols. If a protocol warrants Full Committee Review (FCR), any IACUC member can request FCR, and the protocol will be placed on the agenda for the next scheduled meeting for IACUC review and determination.

Normally, the outcome of the committee's review is sent to the investigator within 5-10 business days following receipt of all reviews.

DMR Review Outcomes: The protocol will be placed in one of the following categories:

1. Full Approval: The DMRs have 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 progress report due at eighteen (18) months.
2. Requires modification(s) to secure approval: The DMRs have 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 IACUC 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 progress report due at eighteen (18) months.
3. Require Full Committee Review (FCR): If the DMRs or any member of the committee requests full committee review, a letter will be sent to the PI notifying him/her of the decision and the rationale for that decision.

If a protocol is triaged to Full Committee Review (FCR), the protocol will be placed on the agenda for the next scheduled IACUC meeting. Following 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 progress report due at eighteen (18) months.
2. Requires modification(s) to secure approval: One of the following review mechanisms will be implemented based on committee discussion and vote:

- *DMR subsequent to FCR*: 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 IACUC 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 progress report due at eighteen (18) months.
- *FCR:* The Committee has decided the revised protocol needs to return to full committee review at an upcoming meeting.

3. 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 maintained within the CICERO platform. Once an IACUC determination is available, CICERO will send an email alert to the Principal Investigator and his/her designated lab members. At time of final approval, the PI will be sent 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. Amendments are accepted on a rolling basis; there is no deadline for amendment submissions.

For those protocols in CICERO, amendments are incorporated into the approved protocol. Log into CICERO, click on the approved protocol you wish to amend, then on the left-hand tool bar, click "Create Amendment". For guidance on submitting amendments in CICERO, FAQs and Instructional Videos can be found on the OAWA website. If you have questions, please contact an IACUC Analyst for assistance and guidance.

For those protocols expiring in paper, the Protocol Amendment Form and the Personnel Amendment Form can be downloaded from the Forms page of the OAWA Website, under the subheading, *Expiring Approved or Pending Protocols (submitted between 2019 – November 2022)*. Completed forms should be emailed to the office (iacuc@umaryland.edu).

All "significant" modifications to an approved protocol are reviewed by one of the following mechanisms in accordance with NIH Notice NOT-OD-14-126: full committee review (FCR), designated member review (DMR), administratively according to IACUC-reviewed and -approved policies in consultation with a Veterinary Resources Veterinarian (VVC), or administratively according to IACUC-reviewed and -approved policies without additional veterinary consultation.

Specifically, the following is considered a significant change requiring FCR or DMR:

- Changes from non-survival to survival surgery;
- Changes resulting in greater pain, distress, or degree of invasiveness;
- Changes in housing and/or use of animals in a location that is not part of the animal program overseen by the IACUC (*e.g., newly proposed investigator managed satellite housing facility*);
- Changes in species;
- Changes in study objectives;
- Changes in Principal Investigator (PI); and
- Changes that could impact personnel safety.
- Addition of a new procedure.
- Addition of exemptions, exceptions, or deviations from the PHS Policy, Animal Welfare Act/Regulations, The Guide for the Care and Use of Animals, or IACUC approved policies / guidelines.
- Any change not described as being handled by VVC or administrative review.

Some protocol modifications may be reviewed using Veterinary Verification Consult, according to IACUC-reviewed and -approved policies in consultation with a Veterinary Resources (VR) veterinarian. Examples of these modifications include, but are not limited to: changes in duration, frequency, type, or number of specific *previously approved* procedures, such as pre-mortem sample collection and delayed weaning, and changes in anesthesia,

analgesia, and / or euthanasia methods while still adhering to the UMB IACUC approved guidelines and policies.

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: an increase in animal numbers of a previously approved species / strain to repeat a previously approved experiment, add a rodent breeding colony, add a new strain of a previously approved species, etc.

Per the IACUC approved policy, OAWA staff may administratively handle some minor modifications to a protocol. Examples include, but are not limited to, personnel changes (excluding the PI), change in title, correction of grammar and typographical errors, contact information updates, etc.

NOTES:

- *The amendment approval date does not affect the expiration date of the protocol.*
- *Conducting research without prior IACUC approval constitutes non-compliance with the approved protocol, and all applicable laws, regulations, and policies. The IACUC is obligated to investigate, remediate, and fulfill regulatory reporting requirements, as applicable.*

2. Eighteen (18) Month Progress Report

All approved protocols are required to submit an 18-month progress report. Investigators receive a reminder by email at least one month in advance of the due date. Investigators are required to report on the progress made to date, the number of animals bred, generated, and used experimentally to date, discuss whether any unexpected mortality, morbidity, disability, infection, or other event was encountered that adversely affected animal welfare, and to address various questions regarding any proposed modifications for the upcoming year. [*Delinquency in submitting an 18-month progress report will result in an administrative hold being placed on animal procurement until the report is received, reviewed, and approved. Second and third reminders are sent to the investigators, as necessary to ensure compliance*.]

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

PHS Policy requires that the IACUC perform a '*de novo*' review every three years. All animal use protocols are approved for a maximum of three years. All approved protocols are closed on the day of expiration. No protocol is administratively extended beyond its three-year approval period.

At four months, three months, two months and one month in advance of a protocol's expiration date, the Investigator is sent a final report reminder by

email indicating that a final report is due and if he/she wishes to continue the research, a new animal use protocol must be submitted for review and receive approval prior to the current protocol's expiration date.

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 are reassigned to the UMB Animal Care and Use Program Holding Protocol. This protocol provides for the basic care of the animals but does not permit any experimental use or breeding. Animals will be re-assigned to an experimental protocol upon final IACUC approval.

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.

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 semi-annual inspection of all animal use areas, including PI laboratories.
- IACUC review of protocol specific progress reports.
- IACUC review of proposed modifications.
- IACUC review of animal welfare concerns.
- IACUC post-approval monitoring (PAM) 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 Survey program has been implemented in which comparative reviews, procedural observations and/or animal use area assessments are conducted by OAWA staff on a proactive basis. A Veterinary Resources Veterinarian is invited to participate in all PAM survey visits. Results of the PAM surveys are reported to the IACUC at its convened meetings. No observations and minor observations are reported for informational purposes only. Potentially reportable 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 the facility; protocol assistance; veterinary care of animals; routine clinical care of animals, etc. All these activities provide an opportunity to assess the health and welfare of the animals and/or evaluate investigator compliance with the IACUC-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 can access a copy of the IACUC-approved protocol or contact the OAWA to ensure the proposed procedures are approved in the protocol.

Veterinary Resources monitoring procurement of animals: Veterinary Resources has access to all IACUC-approved protocols. Protocol specific data is imported into the Veterinary Resources' electronic resource management system and is maintained to help ensure investigators do not unintentionally deviate from their approved protocol by ordering an unapproved species or ordering more animals than he/she is approved for, and that they are not able to order animals 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.). They 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 https://www.umaryland.edu/spa/

A. 'Just in Time' IACUC approval

What are the IACUC's expectations?

The UMB 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 in CICERO at the time of routing, personnel in the UMB Sponsored Programs Administration 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 ensure congruency.
2. If "just in time" procedures are being implemented, the IACUC verification section of Kuali Research 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:

UMB Animal Care & Use Program

- OLAW Animal Welfare Assurance No.: D16-00125 (A3200-01)

- USDA Registered Research Facility
- AAALAC International Accredited Program

Blanket statement for grants regarding the facility:
"*All animals are maintained in the animal facilities of the University of Maryland 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 Baltimore Animal Care and Use Program is fully accredited by AAALAC International (AAALACi). 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 D16-00125 (A3200-01) and is an USDA Registered Research Facility*."

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 one or two IACUC member(s) accompanied by a member of the OAWA Compliance Team. 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 Quality Improvement and Compliance Manager (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, UMB Vice President and Chief Accountability Officer.

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 UMB IACUC that ALL animals used for research 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. If an individual chooses to remain fully anonymous, they may submit their concern through UMB EthicsPoint. EthicsPoint is a neutral third-party and their system was designed to protect an individual's anonymity.

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

- Office of Animal Welfare Assurance: 410-706-4365 / 4374
- Veterinary Resources: 410-706-7615
  After hours, on weekends or holidays: 443-835-9841. Please follow instructions in voice mail message regarding how to contact a veterinarian during these hours.
- UMB Hotline: Online or 866-594-5220

The above information is present on the OAWA Website and is posted throughout the 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. If warranted, visitation to the location or immediate veterinary care will be initiated. The committee will conduct a thorough review and determine the appropriate course of action.

To protect the concerned party from possible reprisal, the IACUC will maintain anonymity of the individual initiating the concern to the extent possible if the concern is not submitted anonymously through UMB EthicsPoint. 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 Policies: USM VIII-7.11, UMB VIII-7.11(B) & UMB VIII-7.11(C)] to prohibit any discriminatory or retaliatory action against any UM personnel reporting known or reasonably suspected wrongdoing. UM personnel include administrative and academic officers, faculty, employees, fellows, students, volunteers, or any person in the public who interacts with UM.

In general, all issues affecting the care and use of animals are brought to the attention of the IACUC at its regular monthly meeting, or on an emergency basis when necessary. Issues are discussed, and resolutions are documented in the IACUC minutes. Likewise, the Institutional Official is informed, in a timely manner, of all issues affecting the care and use of animals by the OAWA Director and/or IACUC Chair. Routine updates are provided to the IO regarding the concern, any findings, and actions taken.

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, 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 adhere to VR policies and procedures.

Rodents – cannot be maintained outside the animal facility for periods of time exceeding 24 hours.

USDA Covered Species – cannot be maintained outside the animal facility for periods of time exceeding 12 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 PI-managed Satellite Housing Facility. Please contact an IACUC Analyst in the OAWA for assistance and guidance.

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. Please contact Veterinary Resources to test these biologics for adventitious pathogens. [*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 UMB animal facilities. In addition, animals housed within UMB must not be transferred to animal facilities in other buildings without prior notification and approval by Veterinary Resources.

Please review the following VR SOPs and Guidance on Transporting Animals:

AH119: Transport and Use of Rodents Outside the Animal Facility

AH132: Animal Transportation to and from Offsite Campus Locations

Information of Safely Transporting Cages

E. Use of hazardous agents

Projects involving hazards such as recombinant DNA, pathogenic microorganisms, select agents, ionizing radiation, radioactive materials, or lasers must obtain the

appropriate Environmental Health and Safety (EHS) approvals prior to final IACUC approval.

If radioactive materials, 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
https://www.umaryland.edu/ehs/
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 and Hazardous Agent Addenda must be completed based on the agent(s) used.

F. Pain Categories

The UMB 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 genotyping or animal identification procedures are performed, 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 a Veterinary Resources (VR) Veterinarian 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, the Animal Welfare Act requires the Institutional Official to obtain approval from USDA APHIS for such work 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

For non-survival surgeries where euthanasia is performed less than 6 hours after the start of surgery, instruments must be clean (use of soap/water rinse) but do not need to be sterile. A description of 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. 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 animal's 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

The IACUC definition of "prolonged" is greater than 15 minutes. 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 2020 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.

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 submitted for IACUC review and approval.

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 UMB investigator using a previously approved protocol, only the investigator's name and protocol number are required. If an investigator outside UMB will be producing the transgenic animals, please contact the OAWA for guidance.

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 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.

S. Press Releases and/or Filming Animal Usage

Please refer to the IACUC Photo and Video Policy available on the OAWA Website.

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.

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 ensure 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 left-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: 2020 Edition

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

Methods and Welfare Considerations in 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