ARIZONA STATE UNIVERSITY
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
(IACUC)

POLICIES AND PROCEDURES MANUAL

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Table of Contents

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MISSION

The Arizona State University (ASU) Institutional Animal Care and Use Committee (IACUC) is dedicated to the humane care and use of laboratory animals in activities related to research and teaching conducted by investigators and individuals associated with the University.

OVERVIEW

ASU provides an Animal Care and Use Program in support of its faculty's research and instructional activities. The focal point of the Program is the IACUC, an oversight committee. The IACUC is guided by regulations and guidelines provided by the federal government through two agencies, Health and Human Services (HHS) and the United States Department of Agriculture (USDA). The policies and procedures presented below describe many of the functional features of the IACUC and the ways in which faculty and investigators interact with the IACUC. The federal guidelines are extensive and, therefore, are often referenced and occasionally directly quoted.

This is a document which is reviewed periodically and revised as appropriate by the IACUC. Animal users and Program staff are encouraged to provide comments and feedback on these policies and procedures at any time.

REGULATORY AUTHORITIES GOVERNING ANIMAL USE

ASU's IACUC must comply with the USDA Animal Welfare Act (AWA) and National Institutes of Health Office of Laboratory Animal Welfare (OLAW) regulations governing the use of laboratory animals. ASU'S Animal Welfare Assurance, on file with the OLAW, provides written documentation of ASU's commitment to animal welfare and detailed information on the animal care and use program. The Assurance commits ASU to compliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals, the *Guide for the Care and Use of Laboratory Animals* (*Guide*), and the AWA.

The AWA applies to all mammals and birds used in research except for the following cases: (1) mice of the genus *Mus* and rats of the genus *Rattus* bred for use in research, (2) birds that were bred in captivity, and (3) mammals and birds used solely for field studies as defined in the Determination of USDA Field Studies Guidelines located on the ORIA IACUC webpage. Reptiles, amphibians, fish, and invertebrates are not covered by the AWA. The Public Health Service (PHS) Policy also requires IACUCs to follow AWA requirements. PHS Policy applies to all PHS-conducted (i.e., National Institutes of Health) or supported activities involving live vertebrate animals. Finally, ASU voluntarily maintains accreditation from AAALAC International, which applies AWA and OLAW standards to all vertebrate species and cephalopods.

U.S. Department of Agriculture (USDA)

The USDA, through its division of the Animal and Plant Health Inspection Service (APHIS) (http://www.aphis.usda.gov/animal_welfare/index.shtml) administers the AWA (https://www.aphis.usda.gov/animal_welfare/downloads/AC_BlueBook_AWA_508_comp_version.pdf of 1966 and its amendments, codified at 7 USC §2131 et. seq. and Code of Federal Regulations (CFR) Title 9. The AWA regulates the transportation, purchase, care and treatment of animals (as defined above) used for exhibition, basic and biomedical research, education, and product safety testing.

The AWA requires the establishment of an IACUC to review all activities using animals to ensure humane use of animals in research and to conduct semiannual assessments of the institution's animal care and use program, including inspections of all animal study areas and facilities. As a research facility ASU is subject to random inspections (conducted at least once every 12 months) by the USDA and must file an annual report regarding its animal care and use program. Failure to comply with USDA laws and regulations pertaining to the use of live animals can result in civil or criminal prosecution and suspension of all animal research activities at ASU.

Links to the AWA and related regulations are provided on the IACUC website at Animals | Research Compliance (asu.edu).

National Institutes of Health (NIH)
Office of Laboratory Animal Welfare (OLAW)

The PHS Policy on Humane Care and Use of Laboratory Animals was created to implement the provisions of the Health Research Extension Act of 1985. The National Institutes of Health's (NIH) OLAW (http://grants1.nih.gov/grants/olaw/olaw.htm) administers the Policy. The Policy applies to institutions conducting PHS-supported projects involving live vertebrate animals.

The Policy requires that the institution establish an IACUC. The IACUC, using the *Guide*, is responsible for reviewing the use of animals and conducting semiannual assessments of the institution's animal care and use program, including inspections of all animal study areas and facilities.

ASU files a new Animal Welfare Assurance every five years with the OLAW, providing written documentation of the University's commitment to animal welfare and detailed information on the animal care and use program. The Assurance commits the university and affiliated investigators to compliance not only with the Policy and *Guide*, but also with the AWA.

Failure to comply with the Policy, *Guide,* or AWA may lead to various actions including the termination of PHS funding for all projects at ASU involving the use of animals.

Every employee at ASU has access to a current copy of the Assurance, Policy, and *Guide*; these documents are posted on the Office of Research Integrity and Assurance (ORIA) website Animals | Research Compliance (asu.edu). ASU Policies & Procedures are posted at the same URL. This site is available to all investigators and staff who work with animals for teaching and research activities.

ADMINISTRATIVE ORGANIZATION

All research, teaching, and biological testing involving live vertebrate animals and octopus conducted at ASU, regardless of the source of funding, must be reviewed in advance by the IACUC. Additionally, all research, teaching, and biological testing projects conducted *at another institution or elsewhere* by faculty, students, staff or other representatives of ASU in connection with the investigator's institutional responsibilities, regardless of the source of funding, must be reviewed in advance by the ASU IACUC. Alternatively, work conducted by ASU personnel at another institution that has a PHS assurance can be approved by that institution's IACUC provided that a copy of such approval is provided to the ASU IACUC prior to commencement of the work. Other University-sponsored activities involving live vertebrate animals are reviewed on a case by case basis to determine if IACUC oversight is warranted.

Institutional Official (IO)

ASU's Vice President for Research is appointed by the President to serve as the IO. The IO is responsible for committing the University to comply with regulatory requirements of the AWA and for appointing members to the IACUC. The IO signs the Institutional Assurance.

University Attending Veterinarian (AV)

ASU's AV is a voting member of the IACUC and has been delegated authority and responsibility to implement the PHS Policy, recommendations of the *Guide*, and the AWA. The AV routinely inspects the animal facilities and all animals at ASU. The AV provides routine veterinary care and preventive medical care, as well as on-call emergency care and consultation for ASU's animals. The AV is available to make recommendations concerning preventive health care programs for animals, disease treatment, analgesia, post-operative recovery, euthanasia, general animal welfare, and technical training. The AV must review any animal research protocol before it can proceed and has the authority to suspend any protocols that do not follow the *Guide* or the AWA. Any such suspension will immediately be reported to the IACUC and will be discussed in a convened meeting of the IACUC.

When the AV delegates this authority or is unavailable, a clinical veterinarian on staff provides these services. With regard to "Emergency Care" as described in Chapter 4 of the Guide, the AV or delegated clinical veterinarian must be notified of and approve all emergency procedure(s).

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

Scope of IACUC Responsibilities

ASU has established an IACUC that fulfills the requirements outlined in the PHS Policy on Humane Care and Use of Laboratory Animals, Section IV.A.3., as well as 9 CFR 2.31, APHIS, USDA, and the *Guide*.

As an agent of this institution, the primary functions of the IACUC are to (per PHS Policy Section IV.B):

1. Review at least once every six months the institution's program for humane care and use of animals, using the *Guide* as a basis for evaluation.

2. Inspect at least once every six months all of the institution's animal facilities (including satellite facilities) using the *Guide* as a basis for evaluation.

3. Prepare reports of the IACUC evaluations conducted as required by the PHS Policy, and submit the reports to the IO.

4. Review concerns involving the care and use of animals at the institution.

5. Make recommendations to the IO regarding any aspect of the institution's animal program, facilities, or personnel training.

6. Review and approve, require modifications in (to secure approval), or withhold approval of those components of activities related to the care and use of animals in research and education as specified in IV.C. of the PHS Policy.

7. Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities.

8. Be authorized to suspend an activity involving animals in accordance with the specifications set forth in IV.C.6 of PHS Policy.

Additionally, the IACUC shall confirm that research projects will be conducted in accordance with the AWA insofar as it applies to the research projects and that all research projects are consistent with the *Guide* unless acceptable justification for a departure is presented. (The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of PHS Policy.)

Compliance with the *Guide*

The *Guide* is widely accepted as a primary reference on animal care and use, and its purpose is to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. The *Guide* is also intended to assist investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, humane, and ethical principles. Recommendations are based on published data, scientific principles, expert opinion, and experience with methods and practices that have proved to be consistent with high-quality, humane animal care and use.

The requirements and recommendations as outlined in the *Guide* are used as a basis for all policies and procedures established and followed by the ASU IACUC. Departures from established procedures stated in the *Guide* must be evaluated and approved by the IACUC.

Membership

The IO appoints the IACUC, qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities, and procedures.

Members are typically appointed for renewable three-year terms. The Committee consists of not less than five members of varying professional and personal backgrounds, including at least one veterinarian, one practicing scientist experienced in research involving animals, one member whose primary concerns are in nonscientific areas and one individual who is not affiliated with the institution in any way other than as a member of the IACUC and is not a member of the immediate family of a person who is affiliated with the Institution. An individual who meets the requirements of more than one of the categories listed above may fulfill more than one requirement. However, the committee may not consist of less than five members.

The voting IACUC membership comprises at least five (5) faculty who are or have been animal users, at least one each from Psychology, Biological and Health Systems Engineering, and Life Sciences; at least one non-animal user, an administrative or service professional staff person; at least one non-University affiliated, non-laboratory animal user; and the AV (ex officio). Not more than 3 voting members from the same administrative unit may serve on the IACUC.

Faculty members will be selected by soliciting nominations from the departments. These nominations will be reviewed and approved by the IO. Preferably, nominees will be tenured or have continuous status. The non-University member will be selected by the IO on recommendation of the IACUC.

Faculty members will serve for staggered three-year terms with the possibility of extended service. Staff and *ex officio* members serve at the discretion of the IO. The external member serves on a renewable annual basis.

IACUC Members agree to adhere to the policies and procedures of the IACUC laid out within this document, as part of the new member onboarding process.

Chair

The IACUC chair must be a faculty member who is, or has been, an animal user and who has served as a member of the IACUC for at least one year. The chair is selected to serve a multi-year term; however, service as chair will be renewed each year by the IO. If a person serving as chair wishes to relinquish the chair, he/she may continue as a member of the IACUC. The chair will be expected to attend appropriate national meetings dealing with animal care issues and the role of the IACUC. The cost of attendance at these meetings will be covered by ORIA.

Chair responsibilities include conducting IACUC meetings, assignment of protocol and RFC reviewers, response to reports of non-compliance, and communications with OLAW representatives when submitting reports.

TRAINING

IACUC Members

All IACUC members must complete an on-line training module on the humane care and use of laboratory animals, which provides them Level I certification as "animal users." This course familiarizes them with the relevant laws and regulations, as well as ASU related procedures and policies. All IACUC members are provided with a copy of the *Guide*. The chair of the IACUC meets with or calls each new member and explains the duties of members (familiarity with the *Guide*, protocol review process, program and facilities semi-annual inspections, etc.). At this time, the value of each member carefully, critically, and independently reviewing all protocols is stressed. Members can schedule a separate tour of facilities to familiarize themselves with the ASU animal care program. New members are encouraged to raise any concerns which they may have related to a protocol or to IACUC procedures and thus provide the benefit of new perspectives.

From time to time the University may provide opportunities for IACUC members to attend seminars and conferences (e.g., those by the Scientists Center for Animal Welfare, OLAW, or ORIA) on issues related to animal care at ASU.

Education items that are relevant to issues related to animal care at ASU are presented at each meeting and often discussed.

Authorized Animal User

In order to use live vertebrate animals at ASU, investigators (including faculty, students, and staff) must (1) achieve certification through the ASU IACUC animal care and use training program, and (2) receive clearance from the Occupational Health and Safety Program (OHSP).

Principal Investigator

Tenured faculty, tenure-track faculty and nontenure track faculty members are eligible to be a Principal Investigator on an IACUC protocol. For IACUC teaching protocols, other university employees and retired ASU faculty members may serve as PI with the approval (to be submitted with the IACUC protocol) of their authorizing department chair and college dean or equivalents (e.g., director or vice president) and the IACUC. Absent a specific agreement between ASU and a Non-ASU party regarding ASU being the "IACUC of Record" for a Non-ASU teaching or research protocol, non-ASU employees (e.g., students, post-docs, adjunct or visiting faculty) are not eligible to serve as a PI. In all instances, the PI identified on the protocol has primary responsibility for technical compliance with the protocol and animal welfare requirements.

Certification

All personnel listed on the protocol must have, at minimum, Level I certification. Furthermore, all personnel who will have direct contact with animals must also become Level II certified for the species with which they will work. Students who are involved in animal activities as part of a class are exempt from Level I and II training as they are being provided the instruction as part of their curriculum.

Finally, investigators must receive appropriate training before independently conducting technical procedures on animals (Level III certification).

Level I and Level II certification materials and exams are available through on-line training modules that are accessible from the ASU IACUC web site at Animals: Training Information | Research Compliance (asu.edu). The form for documenting Level III training may also be downloaded from the IACUC web site at Forms | Research Compliance (asu.edu). Training videos on various subjects can be viewed by contacting the Department of Animal Care and Technologies (DACT) at 480-965-4385. Additional information may be obtained by contacting ORIA at 480-965-6788.

Level I Certification: Rules and Regulations; Alternatives to Animal Use

Level I certification provides basic training to personnel who work either directly or indirectly with animals in research and teaching as required by the PHS Policy and the AWA. Level I certification training covers Federal regulations and laws, ethical considerations, principles of refinement, replacement and reduction, biological hazards, the IACUC, veterinary care, occupational health, and reporting deficiencies. This basic level training is required of every individual listed on an IACUC protocol as an animal user as well as all DACT staff. Training must be renewed every four years.

Level II Certification: Species-Specific Training

Level II certification is required of personnel (including DACT staff) identified on the basis of their interaction with particular species. This training covers housing, husbandry, basic health considerations, nutrition, handling and restraint, experimental techniques, and euthanasia. Level II training must be renewed every four years.

Level III Certification: Advanced Laboratory Animal Training

Level III certification covers training on specific procedures performed on animals and entails hands-on instructions by an authorized trainer, who may be DACT or research personnel (see below). It is required for all individuals who work with animals unsupervised.

A. Procedures requiring Level III certification:
   - Physical Identification: ear punch, ear tag, toe clip
   - Genotyping: ear punch, toe clip, tail clip
   - Injections: all forms including SC, ID, IM, IP, IV, RO
   - Administration: oral dosing, oral gavage, IN
   - Blood collection: all forms including submandibular, cardiac, lateral saphenous, tail vein, ear vein
   - Anesthesia: specify injectable or inhalation
   - Aseptic technique: prerequisite or concurrent with surgery
   - Surgery: procedure specific
   - Post-surgical monitoring
   - Perfusion
   - Euthanasia: procedure specific including the secondary method to be used

B. Offerings

   Level III training is provided as needed by (1) a highly skilled DACT staff member, (2) an investigator who is Level III certified and has been designated as an authorized trainer by DACT, or, for some situations only, (3) another highly skilled person.

   An authorized trainer is an individual that possesses the skills and knowledge to instruct others on a specific animal technique in a clear, concise, and understandable manner. They must demonstrate the following abilities: perform the procedure, accurately explain the steps of the procedure, recognize and critique when an individual is performing the procedure incorrectly, and troubleshoot unexpected situations. A person can be an authorized trainer in multiple techniques and on multiple species.

   ASU faculty members, investigators, and medical professionals who possess the required skills prior to coming to ASU may, instead of receiving training at ASU, demonstrate their experience by sending in a *vita* or list of published work that documents their experience with the procedures described in their protocol.

   Individuals who are not an ASU faculty member, investigator, or a medical professional must be trained at ASU for those procedures that they will perform. When the training

has been completed and the form is signed off by the person providing the training, the form must be sent to ORIA at IACUC@asu.edu. Submitted forms are reviewed and approved by one of the University's veterinarians. Once a veterinarian has approved the certification form, the trainee is considered authorized to perform the learned procedures without direct supervision.

All investigators are required to renew their on-line Level I and Level II training modules every four years. Refresher instruction for Level III training is offered on an as-needed basis.

Authorized Trainer

An authorized trainer is an individual that possesses the skills and knowledge to instruct others on specific animal technique in a clear, concise, and understandable manner. They must demonstrate the following abilities: perform the procedure, accurately explain the steps of the procedure, recognize and critique when an individual is performing the procedure incorrectly, and troubleshoot unexpected situations. A person can be an authorized trainer in multiple techniques and on multiple species.

DACT veterinary staff work with potential trainers to schedule the evaluation at a convenient time for the trainer, trainee, and veterinary staff member. An individual who is not an authorized trainer may train others on procedure for which they are level 3 certified, an authorized trainer is the only person who can complete the final training and sign the training document to enable the trainee to work independently.

PROGRAM REVIEW AND FACILITIES INSPECTIONS

All ASU animal facilities and programs are operated in accordance with the requirements and recommendations in the *Guide*, PHS Policy, the AWA, and other applicable federal, state, and local laws, regulations, and institutional policies.

The IACUC reviews the animal care and use program and inspects all animal facilities and activity areas. The Program review and inspection of locations where live animals are used is performed at least once every 6 months. The inspection includes all University buildings, rooms, areas, enclosures or vehicles used for animal confinement, transport, maintenance or breeding and all laboratories in which experiments on animals are performed including surgical manipulations.

All IACUC members are invited to participate in the semi-annual inspection process, and customarily no fewer than two (2) committee members will review each animal facility and activity area at ASU. The following items are reviewed at these inspections to assure compliance with the *Guide*:

1. Animal health and well-being
2. The primary physical environment (e.g., cage content)

3. The secondary physical environment (e.g., animal room and other facility components)
4. Behavioral management (e.g., environmental enrichment)
5. Husbandry (e.g., proper provisioning of food, water, and bedding)
6. Population management
7. Personnel safety
8. Documentation (e.g., quality assurance logs, individual records, drug logs)

The semi-annual review of the animal care program evaluates the program in general, institutional policies and responsibilities, animal environment, housing and management, and IACUC functions. Veterinary care, occupational health and safety of personnel, and training procedures are also reviewed.

Results of the inspections are summarized and then presented to and commented on by the entire IACUC at a convened meeting. Any deficiencies noted during the review process are promptly handled in an appropriate manner.

A report to the IO is prepared at least once every six months upon completion of the required semi-annual inspections and evaluations and are maintained by the institution and made available to OLAW on request. The reports contain a description of the nature and extent of the institution's adherence to the *Guide* and PHS Policy, identify specifically any departures from the provisions of the *Guide* and PHS Policy, and state the reasons for each departure. The reports distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with PHS Policy, and, in the judgment of the IACUC and the IO, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports contain a reasonable and specific plan and schedule for correcting each deficiency. Any minority views are also documented in the report. Facilities accredited by AAALAC International or another accrediting body recognized by PHS, are identified in the report. ASU's entire Animal Care Program is accredited by AAALAC.

REVIEW AND APPROVAL OF PROTOCOLS

All faculty members, investigators, staff members, or students at ASU intending to use live animals in research or teaching, or for holding purposes, must submit an Animal Protocol to the IACUC. In addition, research professionals unaffiliated with ASU who wish to conduct research on campus or have animals housed in ASU facilities must submit a protocol for IACUC review. The only exception in which research or teaching using live vertebrates does not need IACUC approval is for free-ranging wild animals that are only observed and their behavior is not altered in any way. **In all other instances of animal use, a protocol must be submitted and approved by the IACUC before animals may be acquired, housed, or used.**

In addition to the standard ASU Animal Protocol form, there are two simplified protocol forms which may be appropriate in some cases: (1) the Non-ASU Research at ASU Request Form; and

(2) the Authorization for Non-Research or Teaching Use of Animals. All investigators and personnel involved in animal research, teaching, or holding must achieve training certification at the required level and receive OHSP clearance prior to working under the protocol. The training requirement is waived for Authorization for Non-Research or Teaching Use of Animals protocols that are contracting with external vendors to provide animals (e.g., petting zoos) if the vendor does not relinquish possession of the animals and is licensed by applicable regulatory agencies.

ORIA, 480-965-6788, handles all protocol submissions.

IACUC-approved procedural guidelines must be used except where sufficient scientific justification is provided within an approved protocol.

Submission of Protocols

All submitted protocols must be completed on a current version of the Protocol Form which is available at Forms | Research Compliance (asu.edu). The principal investigator (PI) is required to consult with the Attending or Clinical Veterinarian prior to submitting the protocol to the IACUC for committee review to ensure that proposed housing, source of animals, drugs and dosages, and animal use procedures meet standards of the *Guide* as well as comply with federal regulations and campus policies. The PI is required to submit the Protocol Form to ORIA electronically.

If the proposed research is outlined in a proposal submitted for funding (internal or external), the ASU proposal number or award number must be provided; if not, a copy of the proposal must be submitted along with the IACUC protocol. If collaborative work is being done outside of ASU under a protocol at another institution that has a PHS assurance, an ASU protocol is not required but the ASU investigator must submit a copy of the approved protocol from the other institution to ASU's ORIA

Since the information provided in the protocol will be reviewed by members of the IACUC, including non-scientist and concerned community members, it is essential to use terminology understandable to a lay person. The completed protocol (absent personal identifying features), when approved, is a public document available to anyone who requests it. The IACUC reviews protocols on a monthly basis. Protocol submissions must be received at least 15 business days prior to a meeting in order for the protocol to be reviewed at that meeting. Rare exceptions may be granted by the IACUC Chair, in conjunction with the AV, dependent on circumstances.

Protocol Review

All submitted protocols are reviewed by the entire IACUC. However, upon receipt of a submitted protocol, the IACUC Chair (or designee) will appoint a primary reviewer to conduct an initial review of the protocol (in addition to the pre-review performed by the Attending or Clinical Veterinarian). Comments of the primary reviewer are provided to the PI either directly or through ORIA, and the PI must revise the protocol upon receipt of these. Once the protocol has

completed the initial review to the satisfaction of the primary reviewer, the protocol is then made available to all IACUC members through a secure web-based portal. IACUC members can request alternate forms of the protocol (e.g., a hard copy). For projects that are funded by an agency that does not perform peer review, or is funded internally, or is unfunded, a peer reviewer will be identified as well to evaluate for scientific merit and may work with the PI directly or through the IACUC Chair.

The IACUC determines whether the protocol and the description of the proposed animal use are consistent with the institution's Assurance. The IACUC review includes the following topics:

1. Rationale and purpose for involving live animals.
2. Justification of the species and number of animals used. Whenever possible, the number of animals requested should be justified statistically.
3. Availability or appropriateness of the use of alternative, less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation (i.e., describe how alternatives to the use of live animals and alternatives to potentially painful or distressful procedures have been considered.)
4. Description of the proposed use of animals.
5. Description of procedures designed to assure that pain and/or distress to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and sedating/tranquilizing drugs where indicated and appropriate to minimize pain and/or distress to animals.
6. Unusual housing and husbandry requirements.
7. Unnecessary duplication of experiments.
8. Justification for conducting multiple operative procedures.
9. Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated.
10. Post-procedural care.
11. Method of euthanasia or disposition of animals.
12. Training and experience of personnel in the procedures used.
13. Safety of the working environment for personnel.
14. Identifies other significant factors not included in the above list.

The IACUC requires the PI and/or his/her designee to attend the meeting to answer any questions posed by the committee. Failure to attend the meeting will likely delay protocol approval. The IACUC may also invite consultants to assist in the review of complex issues.

At in-person meetings, the IACUC typically uses oral votes; when meeting virtually (e.g., during pandemic conditions), the committee uses a virtual platform (e.g., Zoom) that includes voting with on-screen buttons. However, any committee member can ask that a vote be made using a confidential vote. Requests for a confidential vote can be made by informing the Chair or ORIA Staff prior to or during the meeting. Committee members can choose to make their request for

a confidential ballot anonymous to the rest of the committee by using established procedures that hide the identity of the requestor.

The IACUC can (1) fully approve the protocol as presented, (2) require modifications to secure approval, (3) defer a vote until more information is provided, or (4) disapprove the protocol. Action of the committee must be approved by a majority of the members present and dissenting views as well as abstentions and recusals are recorded in the meeting minutes. In cases where modifications are required to secure approval, the Committee can, by unanimous vote of those present, elect to use the Designated Reviewer (DR) process to review the revised protocol. If designated review is used, the Committee shall specify the modifications that are required; the role of the DR is to confirm that the revised protocol adequately addresses these requirements. Minimally, the Chair serves as the DR. Additionally, any member of the IACUC may at any time request to review the revised protocol, request to have another specified member in addition to the Chair review the revised protocol, and/or request full committee review of the revised protocol. If there is more than one Designated Reviewer designated by the Chair, each reviewer will review identical copies of the protocol and their decision must be unanimous. If they cannot come to a unanimous decision, the protocol will be returned for full committee review.

Signed consent from members to allow the use of Designated Review of the revised protocol even if they are not present at a given meeting is obtained upon their joining the committee during their onboarding process. Designated review of the revised protocol may result in (1) approval, (2) a requirement for modifications (to secure approval), or (3) referral to the full committee for review. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest except to provide information requested by the IACUC. If referred to the full committee by the designated reviewer, the member may be in attendance at the meeting to give an overview of the protocol and provide information requested by the IACUC.

If the committee determines that it does not possess the expertise necessary to evaluate some details of the proposed protocol (or request for changes), it may choose to have a subcommittee review those details and provide a report to the committee-assigned DR. Makeup of the subcommittee is determined on a case-by-case basis by either the committee as a whole or the assigned DR to assure sufficient expertise is present. Subcommittee members may include members of the ASU IACUC, ASU faculty or staff that are not IACUC members, or non-ASU individuals. PIs are informed of the use of a subcommittee and are asked to work directly with the subcommittee.

The IACUC notifies PIs in writing of its decision. If the IACUC decides to withhold approval of an activity, it includes in its written notification a statement of the reasons for its decision and gives the PI an opportunity to respond in person or in writing. The PI may resubmit a modified protocol incorporating changes/modifications suggested by the committee to conform to the existing policies and guidelines. Revision of a disapproved protocol is reviewed in the same manner as a new protocol (i.e., requiring pre-review by a veterinarian, assignment of a primary reviewer, and full committee review at a convened meeting).

Animal procurement or use is not permitted until the protocol approval is processed. Additional approvals beyond that of the IACUC may be required before the work can be conducted (e.g., radiation safety, biosafety, or administrative) and space in animal holding areas may prohibit or delay the approved work.

Protocols are approved for a maximum of three years. The IACUC conducts continuing review of each approved, ongoing activity covered by PHS Policy at appropriate intervals as determined by the IACUC. PIs must complete and submit an Annual Review Form each year the protocol is active. All IACUC members have access to all Annual Review Forms via the secure online portal and these Annual Reviews are presented for discussion in a block at the monthly IACUC meeting. Any Committee member can ask for separate discussion of any Annual Review. After the meeting, Annual Review Forms are reviewed and signed by three committee members.

If research is to continue past the three-year approval period, a renewal protocol must be submitted and approved prior to the expiration of the originally approved protocol. The procedures for review and approval of a renewal protocol are the same as for a new protocol.

Electronic distribution of information (e.g., by fax, e-mail, or secure web site) is generally considered appropriate for promptly providing IACUC members with material and for providing all members the opportunity to call for a full review of a protocol request for changes prior to initiating the DR method of protocol request for changes review (see below). However, protocol approval and other voting is only conducted at an official IACUC meeting that requires a "convened quorum" of more than 50% of the members of the IACUC. Meetings are held in a hybrid environment.

Temporary Approval for Housing Animals Prior to Protocol Approval

It is standard practice of the ASU IACUC to not allow animals for research or teaching on campus until a protocol has been approved. However, there can be very rare situations where it is imperative for animals to be received prior to approval of the protocol by the IACUC. Examples of such circumstances include the arrival of a new PI who is transferring animals from his or her previous institution or unique opportunities for PIs to obtain otherwise unobtainable animals.

Approval of temporary housing is granted by the IACUC Chair and the AV and all committee members are notified of the intent to allow the housing at least 24 hours prior to granting the approval so that they can voice any concerns with the planned temporary housing approval. The temporary approval for housing animals is absolutely restricted to providing appropriate housing for the animals, and the animals, once received, cannot be used in any teaching or research activities until a protocol is approved by the full committee. Temporary approval to house animals is contingent on the submission of a new protocol (or request for changes) for review by the IACUC at a convened meeting.

Scientific Merit

The IACUC shall ensure that all use of animals has scientific merit. In those instances when a majority of the IACUC feels that outside consultation is required to evaluate the scientific merit of a protocol, the committee may solicit other scientists knowledgeable in the field of research indicated by the protocol to assist in the internal review. This is especially pertinent to those protocols that are not supported by external funding.

Collaborative Research

If an ASU faculty or staff member is an Investigator for a research project in which all animal related research activities will be performed at another PHS-assured institution, the ASU IACUC will defer protocol review to that PHS-assured performance site, with the following conditions:

(1) The Investigator will submit documentation of the review and approval of the research activity by the performance site's IACUC to the ASU IACUC. ORIA will assign an ASU IACUC number to the project and will establish and maintain a protocol file for tracking purposes.

(2) The Investigator will provide copies of the performance site IACUC approvals including requests for changes, annual reviews, and reports of inspection. All protocol related information will be reported to the IACUC and records will be maintained in the official protocol record.

Third Party Entity Usage

Requests by third party entities to use ASU vivarium space and/or IACUC services will be considered on a case-by-case basis. Should the request be granted, an ASU Representative will need to be identified that will be linked to the specific Facilities Use Agreement, and any other agreements that are made related to the specific request.

SIMPLIFIED PROTCOLS

The Non-ASU Research at ASU and the Authorization for Non-Research or Teaching Use of Animals simplified protocols may be reviewed through the Designated Review process which is outlined in the Changes to Approved Protocols section below. Any member who wishes to call for full committee review may do so at any time and approvals are documented in the minutes of the next convened IACUC meeting.

ASU events utilizing petting zoos or therapy animals that belong to and are under the continuous oversight of organizations or companies that are licensed and insured through the applicable regulatory agencies are not required to complete and submit protocol forms. Email notification to the IACUC of the animal activity is sufficient.

CHANGES TO APPROVED PROTOCOLS

During the course of the three-year term of protocol approval, circumstances may dictate changes in personnel or procedures. These changes may be necessary (1) when the PI learns of new data or procedures and wishes to alter or update current procedures, (2) when outdated, inconsistent, or missing information is noted during annual protocol review, or (3) when the IACUC revises policies and procedures as new information or regulations on animal use become available. Under these circumstances it is the PI's responsibility to submit a protocol request for changes (electronically) prior to any changes. To encourage and simplify the submission of requests for changes, a Request for Changes form is included with the Annual Review form when it is provided to the PI.

The AWA and the PHS Policy require that the IACUC review and approve proposed significant changes in ongoing activities involving animals. To ensure compliance with this Policy, the IACUC requires investigators to request approval for **any** proposed changes to an approved animal use protocol by submitting a written Request for Changes. IACUC approval of proposed changes to previously approved animal activities may be granted by the following review methods outlined in the criteria below: administrative with or without veterinary consultation and verification (VCV), designated review (DR), or full committee review (FCR).

Criteria for Evaluating Significance of Proposed Request for Changes

The IACUC Chair and the AV will evaluate the significance of any proposed addendum by comparing it to the investigator's currently approved protocol. Based on a USDA directive, requests for changes have been placed into three categories: minor, significant, and major.

Minor Request for Changes

A request for a change that does not in any way affect the animals or the use of animals can be termed a minor request for changes and can be administratively approved. The IACUC Chair grants administrative approval of requests for changes in this category or can designate approval privileges to another committee member or to a member of the IACUC administrative staff. Changes that may be handled administratively without IACUC consultation or notification include correction of typographical errors, correction of grammar, and contact information updates. Other administrative approvals are documented in the minutes of the next meeting of the IACUC, and any member can call for a discussion of any minor request for changes approval.

Veterinary Consultation and Verification (VCV)

The VCV process utilizes an IACUC-authorized veterinarian as a subject-matter expert to verify that a proposed change is consistent with established IACUC policies and is appropriate for the animals in the circumstances proposed. Upon VCV, the IACUC can handle the following changes administratively:

1. changes in the drugs, dosages, or durations used for anesthesia, analgesia, or sedation
2. changes in the dose, concentration, route, volume, timing or duration of an experimental substance

3. changes in euthanasia to any method approved in the AVMA Guidelines for Euthanasia of Animals

The VCV confirms that the proposed changes:

1. will not increase pain or distress in the study animals
2. will not negatively impact personnel safety

The veterinary verification must be adequately documented using any of the following resources:

1. ASU IACUC Standard Institutional Guidelines (SIGs)
2. published veterinary handbooks and formularies
3. online resources from other research institutions
4. peer-reviewed publications
5. expert consultation
6. professional judgement

Veterinarian consultation and documentation is included in the protocol file and in the minutes of the next IACUC meeting. The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the above stipulations.

Significant Requests for Changes

Any other changes that affect animals or the use of animals (i.e., any change in procedure, any increase in the number of animals originally approved, changes in the species used or addition of a species, any change in agents or equipment used) is to be considered a significant request for changes and cannot be administratively approved. However, the Chair may choose to send significant requests for changes through the Designated Review (DR) process, rather than full committee review, unless they meet certain criteria. The request for changes is compared to the currently approved protocol, Standard Institutional Guideline, or other IACUC-approved document, and the criteria listed below are used in determining whether a significant request for changes can go through the DR process.

Designated Review Process

If a significant request for changes meets the criteria for the DR process, the IACUC Chair appoints a committee member as the DR who, along with the AV, will review the request for changes. All IACUC members are electronically (or otherwise if pre-arranged) provided the request for changes as well as informed of the member selected as the DR. Committee members are given two business days to either accept the designation or call for full committee review. If a single committee member calls for a full committee review, then the request for changes is reviewed by the full IACUC membership at the next convened meeting. Alternatively, a committee member can submit comments to the DR to include in his or her correspondences with the PI. If the DR and the AV are accepting of the request for changes or revised version based on their comments, they both inform the Chair and ORIA staff of their decision and the approval is

processed. Alternatively, the DR (or AV) upon acquisition of additional information, may themselves call for a full committee review.

The IACUC Chair or the AV can serve as the DR, but, as with any DR, their assignment must be approved by the committee via an electronic notification. There cannot be blanket consent by IACUC members for DR approval; such consent must be given for each request for changes individually. DR approvals are documented in the minutes of the next meeting of the IACUC.

The following criteria are used to exclude the option of the DR process:

- Any new Category E procedures/procedures that result in unalleviated pain and/or distress
- If the proposed procedure cannot be performed by or under the direct supervision of an individual skilled in that procedure
- Chair discretion using other criteria which may include but is not limited to numbers of animals, species considerations, and researcher expertise

Major Requests for Changes

Major requests for changes are significant request for changes that do not meet the criteria for Designated Review. All requests for major changes to a protocol must be presented for discussion and approval by the IACUC at a convened meeting. Major changes from the original protocol may require a new or revised protocol.

MOVEMENT OF ANIMALS FROM ONE PROTOCOL TO ANOTHER

Any movement of animals from one approved protocol to another approved protocol must have prior approval by the IACUC. Typically, animal movement between protocols is a result of excess unmanipulated animals being available after a study or teaching exercise is completed. No movement of animals from one protocol to another will be allowed if standard operating procedures for animal care and use are compromised. Specific criteria allowing the movement of animals from one protocol to another protocol should be determined on a case by case basis. In general, when animals are moved from one protocol to another, this will be conducted in a manner which at least maintains accurate documentation of animal care and use activity. For example, when both protocols are approved and both protocols use the same species, transfer of animals should involve an appropriate adjustment in records that keep track of animal use within each protocol. Requests for transfer of animals from one protocol to another typically include the following:

(1) Donating PI name and protocol number
(2) Species and number of animals to be transferred
(3) Status of animals to be transferred – i.e., naive
(4) Recipient PI's name and protocol number

(5) Location of animals under the donating PI and location the animals will be under the recipient PI
(6) Rationale as why using animals that have previously undergone procedures will not affect interpretation of data

For standard transfers (e.g., those involving previously unmanipulated animals), the transfer can be approved administratively. For non-standard transfers of animals between protocols, the AV and IACUC Chair determine how extensive a review should ensue (e.g., administrative, DR, or full committee). This includes, for example, any transfer of previously manipulated animals from one protocol to another protocol which may raise issues that have not been reviewed or approved by the IACUC.

ANNUAL REVIEWS

An annual review must be completed every year in the anniversary month of the original approval date until the protocol is terminated. Prior to each anniversary of the approval date, an IACUC Annual Review Form is sent to the PI. The Annual Review Form requests information concerning the status of the work, a summary of the progress to date, a review of the appropriateness of animal numbers and use, a description of any problems encountered, and a list of currently participating personnel. The PI completes and signs the form to certify the accuracy and completeness of the report. Additionally, the Annual Review Form contains a reminder to submit a Request for Changes form to add any additional animals or describe proposed modifications to the approved protocol.

Annual Reviews are presented to the entire IACUC as a block at an IACUC meeting. Any IACUC member can request that any Annual Review be discussed at the convened meeting. Upon approval by the full committee and being signed by three committee members after the meeting, the Annual Review form is made part of the protocol file.

OVERSIGHT

If it becomes apparent to the IACUC, Chair, or AV that work with animals is being conducted contrary to what is approved in the protocol, or if the AV, Chair, and/or the IACUC identify critical changes that should be made to approved protocols, the following procedures will be implemented:

(1) All unapproved work will be immediately stopped (provided that doing so does not negatively impact the well-being of the animal).

(2) The PI (and possibly other personnel included in the protocol) will be required to attend a convened meeting of the IACUC to explain what work has been done and

why it was being done without approval by the IACUC. If the PI does not attend the IACUC meeting, access to animals by the PI and his/her research staff may be halted.

(3) A memorandum will be sent to the PI describing the changes and/or clarifications that must be made on approved protocols. The PI must promptly amend the protocol accordingly or provide justification as to why the requested changes are not appropriate. Additionally, the PI must explain changes in the lab which will prevent recurrence of non-compliance.

(4) If a response is not received by ORIA within one (1) week, a second memorandum will be sent to the PI requesting that the PI attend the next scheduled IACUC meeting to address the issue in front of the IACUC.

As one means of ensuring that animal use protocols are followed as approved, an anonymous whistle-blower policy is followed consistent with ASU and Arizona Board Of Regents (ABOR) policies (policy document is available at https://www.azregents.edu/policy-manual?page=1499367). In each animal facility, signs are posted providing information to both staff and investigators on how to report concerns with animal care or use. Individuals are also strongly encouraged to interact directly with investigators if they feel comfortable doing so. In addition to the planned semi-annual inspections by IACUC representatives, the IACUC members, IACUC Chair, AV, and DACT administrators make unannounced visits to animal housing and procedural spaces. Furthermore, KE designees, may, with or without the assistance of an IACUC member or the AV, periodically conduct thorough unannounced assessments of randomly selected locations.

The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with the description of that activity provided by the PI and approved by the Committee. Typically, the IACUC suspends an activity only after review of the matter at a convened meeting of a quorum of the IACUC and the suspension vote of a majority of the quorum present. If the IACUC suspends an activity involving animals, the IO, in consultation with the IACUC, shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OLAW and any Federal agency funding that activity.

If the safety or welfare of an animal appears to be at risk, or if the work being performed on a project is not in accordance with the approved protocol, the IACUC Chair or the AV is authorized to temporarily restrict such activities until review by the IACUC at a regularly scheduled meeting or specially convened meeting. Any suspension, even if not sustained by the IACUC, must be reported to the federal government when required.

POST-APPROVAL MONITORING

The IACUC has a statutory responsibility for review and oversight of research, teaching, or testing activities that have been approved. Approval is contingent upon performance of the activity as it was approved. Any changes or modifications must be submitted, reviewed, and approved by the committee before the requested research plan can be altered.

The IACUC is responsible for ensuring that ongoing research activities are accurately reflected in the approved protocol records. The IACUC uses several mechanisms to accomplish post-approval monitoring including: semi-annual inspections, annual reviews, veterinary/staff reviews, and in-laboratory spot monitoring performed randomly, based on suspected deficiencies, or in response to a complaint.

In-laboratory visits may include discussion with the research staff or review of the laboratory records, study procedures, methods of anesthesia, surgery, post-surgical care, euthanasia, animal housing, supply/drug storage, and safety issues that pose a threat to animal welfare or human safety.

The over-arching intent of post-approval monitoring is to protect the interest of the animals, the institution, and its researchers. Monitoring is done to help researchers achieve compliance, rather than to find instances of non-compliance.

Surgical procedures actively performed by a lab are observed on an annual basis by the DACT veterinary team. Every lab member that performs the surgery will be observed. If surgeries are not performed annually, then an observation is required when the surgery is next performed. All non-surgical procedures that involve a greater skill, such as tail vein injection or retro-orbital injection, are also observed on a yearly basis or when it is next performed. The post-approval monitoring team will reach out to the lab when an observation is required. While observations will typically be annual, the IACUC or veterinary team may, at their discretion, decide to have animal procedures monitored by the veterinary team at any time.

REPORTING CONCERNS

Anyone with a concern about any aspect of animal care and use at ASU or who wants to express a complaint about how animals are being treated is encouraged to contact the IACUC Chair, the AV, or ORIA. Contact information can be found at Animals | Research Compliance (asu.edu).

Any person with a complaint or concern should contact ORIA by mail, phone, or send an email to IACUC@asu.edu. The identity of the person making the complaint will be held in as strict a confidence as is possible, given the need to investigate the complaint. Particular efforts will be made to protect the identity of the complainant as well as the respondent. An inquiry at a level deemed appropriate by the IACUC Chair and AV will be implemented. For additional information on filing an anonymous complaint, please refer to the ASU Campus Safety and Compliance Hotline at https://secure.ethicspoint.com/domain/media/en/gui/56745/index.html or call 877-SUN-DEVL (786-3385).

Concerns received by ORIA will be confidentially forwarded in writing to the Chair of the IACUC who will provide written notice of the concern to the other members of the IACUC and the IO.

The Chair of the IACUC will appoint an Investigation Team. During the investigation, the Chair and/or the AV may suspend any activity, or take any actions necessary, in order to assure animal welfare is not compromised. An investigation will include interviews of all principals and witnesses as well as an inspection of the scene of the alleged event. The Investigation Team will prepare a factual written report. Copies of the report are sent to the IO and the originator (unless reported anonymously), and are incorporated into the minutes of the next IACUC Meeting. Regulatory agencies are notified by the Chair and IO together, as required by regulation.

NON-COMPLIANCE

The ASU Animal Care and Use Program requires that all animal usage be conducted in a humane and appropriate manner, in accordance with guidance from the AWA, PHS Policy, the *Guide*, and ASU's Assurance and policies. Any failure to comply with these policies and regulations jeopardizes all use of animals in research at ASU.

Some examples of situations that may constitute non-compliance include, but are not limited to, the following:

1. Use of animals without first obtaining IACUC approval
2. Procurement of animals without an approved protocol in place
3. Failure to use appropriate procedures during survival surgery
4. Neglecting or providing inadequate care for animals
5. Using procedures not approved by the IACUC
6. Using more animals than approved by the IACUC
7. Failure to provide an Annual Review of a protocol and continuing to perform research
8. Failure to correct a previous non-compliant situation
9. Housing animals for more than 12 hours outside of an approved animal holding facility without IACUC approval
10. Allowing untrained personnel to perform procedures or surgeries without direct supervision
11. Failure to inform the IACUC of an unexpected outcome that affects the welfare of animals
12. Failure to alleviate pain or distress of an animal when the exception has not been approved by the IACUC
13. Failure to confirm death of euthanized animals

Procedures in Cases of Alleged or Apparent Non-Compliance

The IACUC may suspend any protocol at any time if it determines that the activity is not being conducted in accordance with the protocol approved by the IACUC or not in accordance with guidance from the AWA, PHS Policy, the *Guide*, or ASU's Assurance or policies. Suspension of a protocol requires review and approval by the convened IACUC by majority vote. The AV has the authority to suspend any protocols that do not follow the AWA, PHS Policy, the *Guide*, or ASU's Assurance or policies and is authorized, in extreme situations, to confiscate animals, remove them from the control of the PI, treat the animals, and/or euthanize them pending an inquiry or investigation. Suspensions made by the AV are reported to, reviewed by, and voted on by the convened IACUC.

Following completion of the *initial* inquiry, ORIA will advise regulatory agencies, as required, in accordance with the reporting policies of those agencies. Once the IACUC has completed the investigation and made a determination, the PI will be advised in writing, with copies sent to the IO and the PI's unit head. The correspondence will summarize the findings of the committee and provide IACUC implemented sanctions. The PI is given the opportunity to respond in writing to the IACUC decision.

Notification of Governing Authorities

Following completion of the investigation, ORIA will advise the necessary governing authorities, per the OLAW Assurance (OLAW, USDA-APHIS, the funding agency, etc.), if any, in cases where:

1. The protocol is suspended,
2. A determination is made that there has been serious or continuing non-compliance, or
3. It is determined that there has been serious deviation from the provisions of the *Guide*.

See the Adverse Event Assessment Reporting Plan for additional guidance.

Possible Consequences of a Finding of Serious Non-Compliance

Depending on the seriousness of the non-compliance, the IACUC may take the following actions:

1. Impose a period of suspension for some or all of an individual's ability to use animals until it is clear that the personnel and procedures have been brought into compliance with federal laws and policies.
2. Notify the NIH and APHIS (when required) and any funding agencies involved. This notification is mandatory for any suspended protocol(s).
3. A charge of scholarly or scientific misconduct may be lodged against the PI and others involved.
4. Should non-compliance activities continue by a PI, he/she may permanently lose the privilege of utilizing animals in teaching or research at ASU. This includes not being allowed in the vivarium, unless coordinated specifically with DACT.

Steps for Reinstatement of the Protocol

ORIA will schedule a follow-up inspection, which will be conducted by at least two members of the IACUC. This subcommittee will determine whether sufficient action has been taken by the PI to correct the cited deficiencies. The results of this inspection will be submitted in writing to the PI, IO, and the PI's unit head.

If the follow-up inspection is unsatisfactory, the IACUC will require appropriate action ranging from extension of the schedule for correcting the deficiencies to permanent suspension of the activity. This determination will be made by a quorum of the IACUC and will include consideration of the effect the deficiencies have on the welfare of the animals.

APPEAL OF IACUC OR VETERINARY DECISIONS

PHS policy requires that the IACUC take final responsibility for the use of animals in research. This prevents disapproval of a proposal by the IACUC from being appealed to other University authorities. Decisions of the AV, the DACT, or the IACUC can be appealed only to the IACUC itself. Such appeals are most likely to be effective if accompanied by additional evidence or comments of experts able to assist the committee in evaluating its concerns.

Despite the severity of the non-compliance policy, the IACUC recognizes that the PI is entitled to fair and just treatment and to a presumption that a reasonable explanation might be made for the appearance of non-compliance. Every effort will be made to maintain confidentiality and to protect the reputation and research of the PI throughout the inquiry and investigation process.

The PI, IO, and PI's unit head are notified in writing of the IACUC's determination regarding non-compliance. A deadline is given by which appeals may be made before the action is instituted. The PI may request an appeal hearing prior to the deadline by contacting the IACUC Chair or ORIA. Such a hearing will require a quorum of the IACUC, with a majority vote of that quorum required to overturn the previous action. The PI, IO, and PI's unit head will be notified in writing of the IACUC's decision.

ALTERNATIVES TO ANIMAL USE IN TEACHING

All teaching use of animals must occur under an approved protocol in which the benefits of animal use are weighed relative to the impact on the animals. The IACUC strongly recommends that instructors inform students at the beginning of the course that animal work will be involved and, where possible, arrange for alternatives to be made available to students who object. It is also recommended that students be informed of the role of the IACUC in educational animal care and use. However, the provision of such alternatives in a particular course is at the discretion of the individual instructor and unit that teaches the course.

IACUC POLICIES

Drugs and Supplies

No expired medical materials (i.e., drugs or supplies) can be used for procedures in which the animal survives. Expired supplies may only be used for acute non-survival procedures and only when their use does not adversely affect the animal's well-being or compromise the scientific validity of the study. Expired supplies must be appropriately labeled (i.e., Expired, For Terminal Use Only) and stored separately from other supplies.

If an investigator uses controlled substances, the PI is responsible for acquiring a Drug Enforcement Agency (DEA) license and for abiding with all DEA requirements.

The use of pharmaceutical grade substances in laboratory animals ensures that the substance administered meets established documentable standards of purity and composition. Non-pharmaceutical-grade substances may be used based on scientific necessity, non-availability of an acceptable veterinary or human pharmaceutical-grade compound, and specific review and approval by the IACUC. In addition to the justification, information about the substance needs to be documented on the protocol including the source and vendor item number (if applicable), as well as a description of the processes used to ensure the purity, sterility, and pH of each product are compatible with use in live animals. This information provided in the protocol will be reviewed by the veterinary team during the veterinary pre-review of the submitted protocol. If the veterinarians have any uncertainty about the proposed product or its properties, they can require that the veterinary team be contacted at the time of first use of the product in animals so that reactions, if any, can be evaluated. Additionally, all prepared substance containers should be evaluated for particulate matter, precipitation of solids, turbid/discolored appearance, and damage to the rubber stopper before each use.

Multiple Major Surgical Procedures

Multiple major survival surgical procedures on a single animal are discouraged, but may be permitted if scientifically justified by the PI and approved by the IACUC. Cost savings is not an adequate reason for performing multiple major survival surgical procedures.
Justifications for multiple major survival surgical procedures on a single animal include:

- The multiple surgical procedures are related components of a research project.
- The multiple surgical procedures will conserve scarce animal resources.
- The multiple surgical procedures are needed for clinical reasons.

Before a protocol which includes multiple major survival surgical procedures is approved, the IACUC will consider the animal species, the number of surgical procedures to be performed, the interval between the surgical procedures, and the rationale for performing the multiple procedures. After a protocol which includes multiple major survival surgical procedures has been

approved, the IACUC and the AV will monitor the well-being of the animals through evaluation of the surgical outcomes.

Distinguishing Major and Minor Surgeries

A major survival surgical procedure is considered to be any procedure that penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions (*Guide* page 61). Minor survival surgical procedures are primarily those in which only skin or mucous membranes are incised. Also included as minor are procedures involving minor manipulation of muscle (e.g., biopsy, placement of instrumentation) and entry into a body cavity through a needle or trocar.

The IACUC has the ability to alter this general distinction on a case-by-case basis, depending on the complexity of the surgery and its expected effect on the animal (e.g., fixation of stereotaxic devices permanently to the skull is considered a major surgical procedure).

Use of Paralytic Agents

No procedure will be approved involving the use of paralytic agents without anesthesia and without pilot procedures that demonstrate the anesthetic regimen is sufficient to prevent pain and distress (e.g., the procedure is done without the use of the paralytic agent).

Antibody Production

The IACUC recommends that animal care personnel or highly skilled unit personnel hired specifically for animal procedures perform all antibody production procedures. All personnel will follow IACUC-approved procedures for antibody production unless exceptions are documented in an IACUC protocol.

Euthanasia

The IACUC's policy on methods of euthanasia considers the recommendations of the American Veterinary Medical Association Guidelines for the Euthanasia of Animals: 2020 Edition (https://www.avma.org/KB/Policies/Documents/euthanasia.pdf), as well as methods provided in guidelines developed by other professional societies (see Procedural and other guidelines | Research Compliance (asu.edu) for key guidelines). Alternative means of euthanasia for nontraditional laboratory animals may also be permitted if sufficiently justified and approved in an IACUC protocol.

In general, physical methods are permitted only by experienced individuals after chemical means have been excluded, in sedated or unconscious animals when practical, and when scientifically or clinically justified. Chemical euthanasia must be followed by a physical method to assure death. Refer to the IACUC Standard Institutional Guideline (SIG) on euthanasia, which is located on the ORIA website Procedural and other guidelines | Research Compliance (asu.edu).

Training and Experience of Euthanasia Personnel

The PI is ultimately responsible to ensure that euthanasia procedures are performed properly. The names and experience of the individuals performing euthanasia should be included in the IACUC protocol, and the IACUC and the AV, during the animal protocol review process, ensure that the personnel have adequate knowledge and the necessary skills to perform euthanasia procedures properly. Investigators are strongly encouraged to solicit the advice of the AV and animal care personnel when questions arise concerning euthanasia. The DACT Veterinary Team is available to provide hands-on training to any personnel requiring such experience.

Housing of Social Species

In accordance with the *Guide*, social animals should be housed in stable pairs or groups of compatible individuals. Single housing of social species should be the exception and justified in the IACUC protocol based on experimental requirements or veterinary-related concerns about animal well-being. In these cases, single housing should be limited to the minimum period necessary, and, where possible, visual, auditory, olfactory, and tactile contact with compatible conspecifics should be provided. In the absence of other animals, enrichment should be offered such as positive interaction with the animal care staff and additional enrichment items or addition of a companion animal in the room or housing area. The need for single housing is reviewed on a regular basis by the IACUC and veterinarians.

In some species, social incompatibility may be sex biased; for example, male mice are generally more prone to aggression than female mice. Risks of social incompatibility are greatly reduced if the animals to be grouped are raised together from a young age, if group composition remains stable, and if the design of the animals' enclosure and their environmental enrichment facilitate the avoidance of social conflicts. Social stability should be carefully monitored; in cases of severe or prolonged aggression, incompatible individuals need to be separated.

Transportation of Animals Off-Campus

Transportation of animals in private vehicles is discouraged because of potential animal biosecurity, safety, health, and liability risks for the animals, personnel, and institution. Therefore, transportation of animals should be performed in DACT vehicles that are inspected semi-annually by the IACUC. However, there are situations where transportation by other university or private vehicles may be warranted. Use of such vehicles must follow the IACUC SIG on *Off-Campus Transport of Animals by Laboratory Personnel* and be approved by the IACUC either in the protocol or on a one-time basis.

The IACUC does not require semi-annual inspections of private vehicles used to transport animals because the infrequent use for such purposes and the inability to inspect vehicles while they are being used for transport makes inspections less relevant. Instead, the IACUC requires PIs to sign

an assurance that they and members of their lab will abide by the requirements set forth in the SIG.

OCCUPATIONAL HEALTH AND SAFETY PROGRAM FOR ANIMAL USERS

The care and use of research animals may expose individuals to hazards that could adversely affect their health and safety. Therefore, the OHSP for animal users promotes and protects the health and safety of employees, visitors, and students who work with teaching and/or research animals. The risks inherent in the animal-based teaching and research activities at ASU have been identified, and practical, relevant methods for controlling the hazards contributing to those risks have been addressed. Participation is required for all campus faculty, students, and staff who have frequent or substantial contact with animals.

This program involves the collaborative participation of people representing all institutional activities related to the care and use of teaching and research animals at ASU including:
the IACUC, DACT, research units, Environmental Health and Safety, Employee Health, and ASU administration. ASU employs both an occupational health nurse and physician whose jobs include the oversight of the OHSP for animal users. It is the goal of the ASU IACUC to foster sustained collaboration and interaction of these University factions.

FEEDBACK FROM USERS

The IACUC values feedback on its policies and procedures from active animal users in the University community. In order to continue to improve its interactions with that community, the IACUC periodically holds an open forum meeting with animal users to invite feedback from them. This is not a regular business meeting of the IACUC and does not require a quorum of IACUC members, but all are encouraged to attend. Invitations are issued to heads of units which include animal users, and each unit head is encouraged to assure that at least one unit representative attends. Invitations are also sent to all PIs with active protocols. At the same time the invitations to this meeting are issued, unit heads are reminded that feedback on committee policies and procedures can be conveyed to the chair of the IACUC at any time.

RECORDKEEPING

ORIA shall maintain records relating to proposed activities and significant changes in on-going activities reviewed and approved by the IACUC for the duration of the activity and three years after the end of the activity. Such records include, but are not limited to, records of protocol and request for changes submissions, annual reviews, minutes of IACUC meetings, and records of investigations of non-compliance related to an approved protocol. All records shall be accessible for inspection and copying by authorized USDA, OLAW, or other PHS representatives at reasonable times and in a reasonable manner. Records include:

1. Minutes of meetings, including records of attendance,
2. Activities of the IACUC and deliberations, records of proposed activities and proposed significant changes, including whether IACUC approval was given or withheld,
3. Records of semiannual reports and recommendations, Assurance, USDA Registration, and annual reports.

These records shall be retained as follows:

a. Five Year Retention. The IACUC shall retain the Assurance for at least five years or until such time as a new Assurance is approved, whichever is later.

b. Three Year Retention. The IACUC shall retain the following records for at least three years: records of semi-annual IACUC reports and recommendations; records of animal protocols; records of any accrediting body determinations, if applicable; annual reports; and USDA registration.

Resource Materials

IACUC Forms and Guidance

A1. Protocol Forms and Instructions
(New Protocols, Request for Changes, Annual Reviews, Display)
Forms | Research Compliance (asu.edu)

A2. Information Regarding Classroom Animal Use
Animals | Research Compliance (asu.edu)

A3. Information on Working Safely with Animals
Occupational Health and Safety Program | Research Compliance (asu.edu)

A4. Standard Institutional Guidelines
Procedural and other guidelines | Research Compliance (asu.edu)

A5. Regulations Governing Animal Use
Regulations and Resources | Research Compliance (asu.edu)

A6. Adverse Event Assessment and Reporting Plan
Regulations and Resources | Research Compliance (asu.edu)

Resources for Identifying Alternatives in Animal Care and Use

ALTBIB - Bibliography on Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing, ALTBIB is a searchable bibliographic collection on alternatives to animal testing. It includes citations from published articles, books, book chapters, and technical reports from 1980 to present. The bibliography features citations concerning methods, tests, assays, and procedures that may prove useful in establishing alternatives to the use of intact vertebrates. ALTBIB can be accessed at https://ntp.niehs.nih.gov/whatwestudy/niceatm/altbib/index.html?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=altbib . Alternatively, ALTBIB contents can be accessed directly through PubMed® searches, which can be conducted at https://www.ncbi.nlm.nih.gov/pubmed/ .

Altweb, the Alternatives to Animal Testing Web Site, was created to serve as a gateway to alternatives news, information, and resources on the Internet and beyond. It is a world wide web site devoted to replacement, reduction and refinement alternatives for research and testing, maintained by the Johns Hopkins Center for Alternatives to Animal Testing (CAAT). The Altweb home page is: https://caat.jhsph.edu/. Specifically, Altweb has an excellent resource for finding appropriate databases to search for alternatives: https://caat.jhsph.edu/resources/index.html

Center for Animal Alternatives, The UCDavis Center for Animal Alternatives places special emphasis on disseminating up-to-date information concerning animal alternatives through every level of public and private education. It also seeks to provide investigators who use animals with information on the most current methods for improving all aspects of animal care during their work. The Center is available at: https://www.library.ucdavis.edu/guide/alternatives/ ***This link is being migrated by the owner. We will update the PPMs when we are notified that the new link is ready.

Information Resources for Adjuvants and Antibody Production: Comparisons and Alternative Technologies, 1990-1998, is published by the USDA's Animal Welfare Information Center (AWIC), NAL, USDA, 10301 Baltimore Boulevard, Beltsville, MD 20705. It is available on-line at: https://naldc.nal.usda.gov/download/7095637/pdf

Norwegian Reference Centre for Laboratory Animal Science and Alternatives, provided by the Norwegian School of Veterinary Science, provides information on laboratory animal science and alternatives to the use of animals in research, teaching and school dissection classes. The Reference Centre is available at: https://norecopa.no/alternatives

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), provided by the Department of Health and Human Services' National Toxicology Program, coordinates interagency technical reviews of new and revised toxicological test methods with regulatory applicability, including alternative test methods that reduce, refine, or

replace the use of animals. This resource is available at: http://ntp.niehs.nih.gov/pubhealth/evalatm/iccvam/index.html

USDA National Agricultural Library's Animal Welfare Information Center (AWIC) provides guidance on building and conducting a 3Rs alternative literature search. They also will provide assistance conducting an alternatives literature search for free via a request form; results are returned within 10 business days: https://www.nal.usda.gov/services/literature-searching-animal-use-alternatives

Acronyms

Acronym	Description
AAALAC	Association for the Assessment and Accreditation of Laboratory Animal Care International (Independent Accreditation Organization)
APHIS	Animal & Plant Inspection Service, USDA
ASU	Arizona State University
AV	Attending Veterinarian
AWA	Animal Welfare Act
CDC	Center for Disease Control
DACT	Department of Animal Care and Technologies (ASU)
GUIDE	*Guide for the Care and Use of Laboratory Animals*
IACUC	Institutional Animal Care and Use Committee
HHS	U.S. Department of Health and Human Services
IO	Institutional Official – at ASU, the Associate Vice President of Research
KE	Knowledge Enterprise
NIH	National Institutes of Health
OHSP	Occupational Health and Safety Program
OLAW	Office of Laboratory Animal Welfare (Office at the NIH)
ORIA	Office of Research Integrity & Assurance
PHS	Public Health Service
PI	Principal Investigator
PPE	Personal Protective Equipment
SIG	Standard institutional Guideline
USDA	United States Department of Agriculture

Definitions

AAALAC International – A private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs.

Alternative – The possibility of choosing between two different things or courses of action.

Animal Plant Health Inspection Service (APHIS) – As a part of the USDA, APHIS is responsible for protecting and promoting U.S. agricultural health, administering the AWA, and carrying out wildlife damage management activities.

Analgesia – Absence of sensibility to pain, particularly the relief of pain without loss of consciousness.

Analgesic – An agent that relieves pain without causing loss of consciousness.

Anesthesia – A loss of feeling or sensation.

Anesthetic – An agent used to produce anesthesia.

Animal – PHS Policy defines an animal as "any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing, or for related purposes". The AWA defines an animal as "any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes captive bred birds, mice of the genus *Mus* and rats of the genus *Rattus* when bred for use in research, and other animals as listed under U.S. Code, 7 U.S.c. Sections 2132." The IACUC does not require a PI to report the use of dead animals via a protocol unless the animals are killed for the purpose of the research or teaching activity.

Animal Facility – An animal facility is any and all areas, buildings, enclosures, rooms or vehicles, including satellite facilities, used for: animal confinement, breeding, experiments including surgical manipulation, maintenance or transport. All spaces where live animals enter must be approved by the IACUC.

Animal Welfare Act (AWA) – Regulation signed into law in 1966. The original intent was to regulate the care and use of animals in the laboratory, but it has become the only Federal law in the United States that regulates the treatment of animals in research, exhibition, transport, and by dealers. Other laws, policies, and guidelines may include additional species coverage or specifications for animal care and use, but all refer to the AWA as the minimum acceptable standard. The Act was amended four times (1970, 1976, 1985, and 1990) and can be found in *United States Code*, Title 7, Sections 2131 to 2156.

Animal Welfare Assurance – Provides assurance of compliance with PHS Policy on Humane Care and Use of Laboratory Animals. The assurance includes a description of policies and procedures for Institutional Animal Care and Use Committee.

Anxiety – Emotional states involving increased arousal and alertness prompted by an unknown or known danger.

Appeal – To make a request for the rehearing or review of a decision.

Attending Veterinarian (AV) – Position appointed by the I.O. as the Attending Veterinarian with direct or delegated program authority and responsibility for activities involving animals at the institution as defined under the AWA and PHS policy. This person serves ex officio on the IACUC and shall have appropriate training or experience in laboratory animal medicine and science and have direct or delegated program responsibilities for activities involving animals at the institution.

Department of Animal Care and Technologies (DACT) – The organization responsible for managing and administering a centralized program of laboratory animal care and use that complies with all applicable standards and regulations for husbandry as set forth in the AWA, National Research Council's *Guide for the Care and Use of Laboratory Animals,* and the PHS policy on the Humane Care and Use of Laboratory Animals. These functions include daily animal husbandry, purchase of all live animals as well as some supplies and equipment related to animal care, procedures related to animal health under the direction and guidance of the AV and Clinical Veterinary staff, provision of research services including surgical assistance and monitoring, and training of research and technical personnel.

Distress (suffering) – The inability to adapt to an altered environment leading to an unpleasant emotional response. To cause strain, anxiety, or suffering.

Euthanasia – The act of putting to death painlessly.

The Guide – *Guide for the Care and Use of Laboratory Animals* published by the National Research Council (NRC) is widely accepted as a primary reference on animal care and use, and its purpose is to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. The online copy can be accessed at http://www.nap.edu/openbook.php?record_id=12910. Paper copies of the *Guide* are available in ORIA.

Health and Human Services (HHS) – The United States government's principal agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves. The list of HHS agencies is available at http://www.hhs.gov/about/index.html.

Institutional Animal Care and Use Committee (IACUC) – Committee mandated under the AWA and the Health Research Extension Act (HREA). The IACUC is charged under the AWA with representing "… society's concerns regarding the welfare of animal subjects …" The University President is charged with appointing an IACUC but may delegate this authority to a senior administrator. At ASU the Associate Vice President of Research is delegated the authority to appoint the IACUC and the IACUC reports to this individual as the IO. The ASU IACUC has adopted uniform policies that apply to all vertebrate animals used in research and teaching regardless of whether the species are covered by the AWA or PHS.

IACUC Chairperson – The chairperson needs to be knowledgeable and effective as a leader. This individual needs to have the full support of the IO and sufficient stature to perform the functions of the position without jeopardy to career or position. The Chairperson is appointed by the IO. The chairperson plays an active role in the oversight of all IACUC activities. The Chair serves five constituent groups: Senior Administration (Institutional Official, Vice President of Knowledge Enterprise Development, and the President); the scientific community; other members of the IACUC; the federal government; the public. At ASU, the AV cannot be the IACUC chairperson due to real or perceived conflicts of interest.

Institutional Official (IO) – The individual who has the authority to sign the Institution's Assurance, and make a commitment on behalf of the university that the requirements of the Public Health Service policy will be met. The Institutional Official at ASU is Tamara Deuser, Associate Vice President of the Office of Knowledge Enterprise Development.

National Institutes of Health (NIH) – A part of the U.S. Department of Health and Human Services, NIH is the primary Federal agency for conducting and supporting medical research. Helping to lead the way toward important medical discoveries that improve people's health and save lives, NIH scientists investigate ways to prevent disease as well as the causes, treatments, and even cures for common and rare diseases. Composed of 27 Institutes and Centers, the NIH provides leadership and financial support to researchers in every state and throughout the world

Non-Affiliated Member – An individual who is not affiliated with the University in any manner and is intended to represent the general community interests in the proper care and treatment of animals. This person cannot be an immediate family member of a person affiliated with the institution. Public members should not be a laboratory animal user.

Non-Scientist – A person whose primary concern is in a non-scientific area having no obvious connections to any area of science. Individuals may have some scientific training, but clearly do not qualify as a practicing scientist with experience in research involving animals.

Office of Laboratory Animal Welfare (OLAW) – Reporting through the NIH Office of Extramural Research this organization provides guidance and interpretation of the PHS Policy on Humane Care and Use of Laboratory Animals, supports educational programs, and monitors compliance with the Policy by Assured institutions and PHS funding components to ensure the humane care

and use of animals in PHS-supported research, testing, and training, thereby contributing to the quality of PHS-supported activities.

Pain – Unpleasant sensory and emotional experience associated with actual or potential tissue damage. Pain is a perception that depends on activation of a discrete set of receptors (nociceptors) by noxious stimuli, e.g. thermal, chemical or mechanical. Further processing in neural pathways, e.g. spinal cord, brain stem, thalamus and cerebral cortex, enables noxious stimuli to be perceived as pain. Pain perception varies according to site, duration, and intensity of the stimulus and can be modified by previous experience, emotional states and innate individual differences.

Paralytic Agent – An agent that causes paralysis.

Public Health Service (PHS) – The Public Health Service includes the Alcohol, Drug Abuse, and Mental Health Administration, the Centers for Disease Control (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration, the National Institutes of Health (NIH), and the Office of the Assistant Secretary for Health, Department of Health and Human Services.

Public Health Service Policy – Requires institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities conducted or supported by the PHS.

Sedation – The allaying of irritability and excitement. Drowsiness is usually a feature.

Stress – The effect of physical, physiologic, or emotional factors (stressors) that induce an alteration in the animal's homeostasis or adaptive state. This may include changes in the neuroendocrine function, autonomic nervous system, or mental state of an animal.

Scientist – A practicing scientist is someone who is knowledgeable about the types of laboratory or field research and teaching being reviewed and conducted at ASU. ASU policy is to represent all areas having involvement with animal research. No more than three scientists from one administrative unit should be appointed to the IACUC concurrently.

Species – The major subdivision of a genus or subgenus, regarded as the basic category of biological classification, composed of related individuals that resemble one another and are on a distinct evolutionary trajectory.

References

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2. Public Law
   89-544 - Animal Welfare Act of August 24, 1966
   91-579 - Animal Welfare Act Amendments of 1970
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   99-198 - Food Security Act of 1985, Subtitle F - Animal Welfare
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3. Final Rules: Animal Welfare; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 54, No. 168, August 31, 1989, P. 36112-36163
4. Final Rule: Animal Welfare; Standards; 9 CFR Part 3. *Federal Register*, Vol. 55, No. 32, February 15, 1991, P. 6426-6505
5. Final Rule: Random Source Dogs and Cats; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 58, No. 139, July 22, 1993, P. 39124. Final Rule: Correction, Random Source Dogs and Cats; 9 CFR Parts 1 and 2. *Federal Register*, Vol. 58, No. 164, August 26, 1993, P. 45040
6. Public Health Service Policy on Humane Care and Use of Laboratory Animals
7. Health Research Extension Act of 1985, Public Law 99-158
8. Endangered Species Act
9. Public Health Service Policy on Humane Care and Use (reprinted Oct. 2000) US Gov. Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training
10. USDA APHIS Animal Care Policies Guide for the Care and Use of Laboratory Animals