IACUC Protocol Review Procedures - SOP

New protocol applications and related submissions (e.g., triennial reports, amendments) for activities involving animals are forwarded to the Office of Regulatory Services. Regulatory Services will perform an initial review of the protocol to ensure that it is complete and ready for review by the IACUC. If there is any additional information or clarification required, Regulatory Services will coordinate with the Principal Investigator (hereinafter referred to as the PI) to properly complete the protocol application.

The PI of a protocol application must be a UTA full time faculty or staff member. External collaborators, undergraduate students, graduate students, or post-doctoral students must arrange a UTA faculty member to serve as the "faculty sponsor" of the protocol. The faculty sponsor will be responsible for the conduct of the research and the terms of protocol approval.

It is the PI's responsibility to respond to requests for additional information/modifications during the IACUC review and approval process in a timely manner. If there is no response by the PI for a request made by the IACUC or Office of Regulatory Services after 60 days, the protocol may be withdrawn from the review process.

When research covered by this SOP is conducted at or in cooperation with another entity, all provisions of this SOP remain in effect for that research. The UTA IACUC may accept the review of another entity's IACUC established under a policy of compliance with the Public Health Service (PHS), Office of Laboratory Animal Welfare (OLAW). Procedurally, the contact information page only of the UTA IACUC Protocol Application Form may be submitted with the full application form of the cooperating entity. UTA's IACUC approval will be contingent upon the cooperating entity's IACUC approval. A copy of the approved protocol and approval letter from the cooperating entity must be submitted to the UTA IACUC for recordkeeping purposes. UTA's post-approval processes still apply, i.e., continuing reviews and notification of changes to the protocol or animal procedures.

New protocols are either reviewed at fully convened IACUC meetings via Full Committee Review (FCR) or by email via Designated Member Review (DMR).

1) IACUC Criteria for Approval:

a) During review of protocols and related submissions, the IACUC will consider if the protocol meets the requirements of the Animal Welfare Act (AWA), the recommendations in the Guide for the Care and Use of Laboratory Animals, 8th Edition (the Guide), and the following items as required by PHS Policy IV.C.:
b) Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
c) Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.
d) Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized at the end of the procedure or, if appropriate,

during the procedure

e) The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and non-medical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. Location(s) for animal housing and procedures must be approved by the IACUC. Transport of animals between multiple locations requires prior approval by the IACUC and documentation through the "Request for Transportation of Animals" form.
f) Medical care for animals will be available and provided as necessary by a qualified veterinarian.
g) Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.
h) Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia unless a deviation is justified for scientific reasons in writing by the investigator.
i) Demonstrated consideration of the "three Rs." The three Rs are Reduction in number of animals used, Refinement of methods to minimize pain and distress, and Replacement of the animal model with a non-animal model or a species phylogenetically lower. With respect to procedures proposed that have the potential to result in pain and/or distress, the PI must explain how they determined that there are no alternative procedures that could be used instead. When the protocol involves USDA-covered species, a thorough literature search should accompany the protocol application in order to document possible alternatives, similar activity in the proposed research field, related publications and references, and that a search has been performed for the current and best methods for conducting the procedures in the protocol.
j) Drugs and compounds used in animal research and teaching, including acute procedures will be pharmaceutical grade. If non-pharmaceutical-grade chemical compounds are to be used, the investigator will provide in writing justification for their use.
k) Conflict of Interest (COI)disclosures are required for all Covered Individuals included as personnel in accordance with UTA's RCOI Policy, in order to identify and manage any potential COIs related to the proposed research. A COI is defined as "Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of Research." RCOI training is required for personnel on protocols that have pending or awarded PHS funding.

2) Procedures for Research Review at Fully Convened IACUC Meetings:

a) Protocol submissions are distributed to the IACUC via e-mail or Teams in advance of the scheduled meeting (typically one week) to allow reasonable time for preview. During the preview period before the scheduled meeting, IACUC members are free to pose questions or request additional information/clarification to be provided for formal discussion of the protocol during the scheduled meeting. All questions and requests will be communicated to the PI by the Office of Regulatory Services. It is strongly

recommended for the PI to attend the scheduled IACUC meeting to discuss the protocol, provide clarification, and/or answer questions posed by the IACUC.

b) Once all of the above outlined requirements of PHS Policy IV.C. have been reviewed and verified, the IACUC will conduct a vote. A vote to 1) approve the protocol as submitted, 2) require modifications for approval, or 3) to withhold approval, requires a majority of the Committee members from the quorum of members present, although votes against and abstentions will be recorded in the meeting minutes. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest (e.g., is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum. The IACUC will vote to:

   i) Approve the protocol as submitted –no modifications are needed to secure approval. The PI is notified in writing of the protocol approval and the official IACUC approval date.
   ii) Require modifications to secure approval – the IACUC requests modifications to comply with the regulatory requirements or improve procedures relating to the care and use of animals in the project. The IACUC will request that the modified version of the protocol be reviewed via DMR process in order to obtain final approval. If the IACUC determines that the modifications requested are significant, they may request that the modified protocol be presented for review and discussion at the next fully convened meeting. The PI will be notified in writing that modifications are required to secure approval, and the PI will be provided with a summary of these modifications. Occasionally the IACUC will also identify procedures or processes that could improve the techniques or efficiency of the protocol. These IACUC suggestions will also be presented to the PI for consideration of modification to the protocol. The PI will have the opportunity to submit a modified protocol based on the IACUC's requests, and also respond to any IACUC suggestions for improvements. The PI will submit the modified protocol to Regulatory Services to be sent to DMR (unless the IACUC had determined earlier that it will require FCR at a convened meeting). If the reviewer determines that the protocol meets all of the requirements and no further modifications are needed to secure approval, the PI is notified in writing of the protocol approval and the official IACUC approval date.
   iii) Withhold approval – the IACUC finds that the protocol, as submitted, does not meet the requirements of PHS Policy IV.C., the AWA, or recommendations in the *Guide*, and/or finds that significant changes are necessary before the IACUC can appropriately review and consider the protocol for approval. The PI will be notified in writing of the IACUC's decision to withhold approval, and for what reasons. The IACUC Chair may meet with the PI to discuss the IACUC's concerns and provide guidance on the PHS Policy IV.C. requirements.

3) Procedures for Review of Research Via the Designated Member Review (DMR) Process:

a) DMR is handled via email, including all the voting IACUC members and their alternates. All new protocols and related submissions are eligible for DMR. However, protocols involving Category E procedures and/or USDA-regulated species will be highlighted for the IACUC to determine if full committee review is more appropriate.

b) If the item is a triennial report or amendment, the email will include a full copy of the original-approved protocol (a link to IACUC OneDrive can be utilized for the full protocol instead of attaching to the email).

c) IACUC members are granted a "comment period" of 1-5 business days (standard is 5 business days and the specific date/time for the comment deadline is listed in the email) during which they have the opportunity to present any questions, concerns, or requests for clarification, or to request FCR of the project. The IACUC may consider a shorter comment period to accommodate special circumstances such as a Just in Time request from a funding agency.

d) If any member during the comment period feels that the protocol/submission should go before a full committee, then its review will be deferred to the next full IACUC meeting. Protocols containing unrelieved pain or distress, major survival surgery on USDA-covered species, multiple major survival surgeries, death as an endpoint, or breeding are example justifications for full-committee review (these should be pointed out in the email to the IACUC for the protocol's original comment period). If no member calls for FCR, then the process proceeds to DMR. New protocols received close to the deadline for submission (typically two weeks before the meeting date) may automatically be scheduled for FCR for expedience.

e) Once the comment period is over, the IACUC Chair will complete the designated review or designate at least one other member of the IACUC, qualified to conduct the review, to review the submission and have the authority to approve, require modifications in (to secure approval) or request FCR of the item. The DM Reviewers are typically granted a time period of 1 – 3 business days to complete their review, but the DM reviewer can return their notice of approval anytime within the review time period.

f) The Specialist and the IACUC Chair will track/coordinate the comment and review periods via a shared calendar. If modifications or clarifications are requested from the IACUC or DM Reviewer(s), the Specialist or designee will notify the PI and facilitate the revision process. The revised version will be sent back to the IACUC (if still in the comment phase) or DM Reviewer (if in the DMR phase) with the IACUC Chair copied. If a revised version is sent back to the IACUC or DM Reviewer, the Specialist will use discretion in determining the remaining time period for comments or designated

review.

g) Once the item is approved by the DM Reviewer, the PI is notified in writing of the approval and the official IACUC approval date.

4) Review of Protocol Changes and Closure Requests:

a) Administrative: Changes in personnel, project title, and/or funding agency will be approved administratively after appropriate verification. This does not include changes of the PI or project title that changes the objective of the protocol, which are handled via DMR or FCR. Closure requests: A protocol can be closed administratively by ORS upon request from the PI, if the project has been inactive since the protocol's previous triennial review. When a protocol has been active since the previous triennial review, the Closure Report Form shall be submitted by the PI and processed via the DMR or FCR process as described above.

b) VVC: In accordance with NOT-OD-14-126, changes in aseptic surgery technique, euthanasia, anesthesia, analgesia, and sedation will be forwarded to the IACUC Chair and Attending Veterinarian (AV) and reviewed according to the Veterinarian Verification and Consultation (VVC) procedure as follows: The AV serves as a subject matter expert to verify that compliance with the IACUC-reviewed and -approved policy is appropriate for the animals in this circumstance. IACUC-reviewed and –approved policies include evaluation criteria such as guidelines and the UTA formularies within the Analgesia SOP. Consultation will be documented by having the AV send an email (or appropriate documentation) approving the change to the IACUC Chair/Office of Regulatory Services in an expeditious manner, but typically within 3 business days. The Chair will then send an approval letter with a summary of the change to the PI. This email will be appended to the protocol for which the change is authorized. The protocol will be updated by the Office of Regulatory Services. The AV may refer any request to the IACUC for DMR or FCR for any reason and must refer any request that does not meet the parameters of the IACUC-reviewed and -approved policies and/or procedures.

c) Protocol Amendment: An Amendment is to be used to gain acceptance for a variation in the conduct of a protocol. In general, an amendment is used to correct problems that arise during the conduct of a study or to continue a study where the goal has not changed but the methods and procedures have been modified to better achieve the goals. An amendment requires action by the UTA IACUC before the changes can be initiated. Justification must be given for the changes requested. These changes must be submitted via Amendment Form and will be processed according to the DMR procedures described above. The Amendment Form will clearly explain and document what changes are proposed in accordance with PHS Policy IV.C. Examples requiring this method include, but are not limited to, a change regarding:
   i) The number of animals per group.

ii) The number of groups in an experiment.
iii) The treatment schedule.
iv) The duration of an experiment.
v) An improvement in the procedures which does not affect the pain classification.
vi) The use of paralytics.
vii) The species used as the animal model.
viii) Methods of statistical analysis, i.e., change from descriptive to nonparametric statistics.
ix) Number and complexity of surgical procedures.
x) Confinement/restraint procedures.
xi) Treatment methods.
xii) Frequently during the course of a study, findings may lead an investigator to seek additional information, which can be easily accrued using the same methods as the existing protocol. Since the information to be sought is related to the previously approved study, an amendment may be submitted by the PI. If any change in instrumentation or surgical procedures must be made to accommodate the new treatment, it must be described. Examples of situations where more extensive addenda, but not entirely new protocols, are required are:
    (1) Testing of the efficacy of a different type of antimicrobial agent to prevent infection.
    (2) Testing the efficacy of different resuscitation fluids, which have entirely different modes of action to prevent ischemia/reperfusion injury.
xiii) Other investigators may be interested in using a particular protocol to study their subject of interest. If the original PI will be conducting the protocol using the other investigator's material but otherwise not changing the procedure, this procedure may be considered using an expanded amendment. The new investigator must be included as an associate investigator.

d) Amendments are not allowed under the following circumstances, i.e., full protocols must be submitted:
    i) If an investigator wants to independently perform a procedure that is similar to one in an existing protocol that belongs to someone else, an amendment for that protocol cannot be used; a new, separate protocol must be submitted.
    ii) If a PI leaves the Institute with unfinished active protocols and an existing associate investigator does not want to continue the study as a primary investigator, those protocols must be terminated. An exception may be made if a new person is interested in continuing the study. That individual must be present at the Institution, be familiarized with the existing protocol and the use of animals, and demonstrate his/her qualifications to use the species and perform the work.
    iii) A new protocol is required when the overall approach to a research issue must be changed. These changes are of such magnitude that the resulting protocol would bear little resemblance to the original protocol once the proposed changes are implemented. Initiating a new protocol ensures that the new approach or procedure

has scientific soundness and statistical validity and that impact on the experimental animal is given due consideration.

5) Continuing Review of Approved Research Protocols:

The IACUC performs two types of continuing review in accordance with the regulations: a) annual protocol follow-up via email and b) triennial review in accordance with the PHS Policy at IV.C. 1-4 and the Animal Welfare Act.

a) Annual Protocol Follow-Up – Once a year, the Office of Regulatory Services sends an email to the PI asking if the protocol has been active, the number of animals used in the last year, if there have been any unanticipated events not yet reported, if any personnel need to be added or removed, and if the study has ended.
   i) PIs have 30 days to respond to the initial request. Failure to respond will result in a second notice to the PI with a 15-day deadline. If the second 15-day deadline is not met, another notification will be sent and the PI's Chair/supervisor will be copied and informed that the PI's report is past due, and it will be considered non-compliance, reported to the IACUC, and the protocol may be suspended if they do not respond.
   ii) If there have been unanticipated events, the PI will complete an Unanticipated Event Report Form and submit it to the Office of Regulatory Services. It will be processed according to the Reporting Unanticipated Events SOP for follow-up as needed.
   iii) Annual Protocol Follow-Up correspondence is maintained by the Office of Regulatory Services.

b) Triennial Review
   i) On the third year of protocol approval, the IACUC requires full de novo review of the protocol in accordance with PHS and USDA/APHIS regulations. The PI is requested to submit a completed Triennial Report ensuring that all animal use procedures, personnel, and training are current and updated. To ensure that the triennial review is completed before the anniversary of the original approval date of the protocol, the PI is required to submit the Triennial Report with sufficient time allowable to complete this process. Reminders are sent by Regulatory Services, typically one month out from the date of expiration. Once received, the triennial review will enter the DMR process as described above. The IACUC will perform a full and complete review of the protocol in conjunction with the Triennial Report as outlined in the procedures above for review of new protocol applications (i.e,, all regulatory criteria for approval must be met). The PI will be notified in writing of IACUC approval.
   ii) The approved number of animals for a protocol starts over at the time of the Triennial review. The PI is not to include any animals left over at the end of the last project period in the request for new animals. The PI should only specify and justify the number of animals requested for the next three-year project period.