UNIVERSITY of HOUSTON | RESEARCH

THE UNIVERSITY OF HOUSTON
IACUC POLICY

Title: IACUC Protocol Review

Background:

The Animal Welfare Act and Animal Welfare Regulations (**AWAR**); Guide for the Care and Use of Laboratory Animals ("**the *Guide*"**); the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (**the "PHS Policy**"); and NIH Guidance document **NOT-OD-14-126** all provide guidance clarifying the roles and responsibilities of the IACUC regarding their review of animal use protocols and of changes to such protocols:

AWAR 9CFR, 2, C, §2.31 (d) (1) (i)-(xi) *Guide* (pg. 25)	PHS Policy IV.C.1-2	NOT-OD-14-126 Guidance on Significant Changes to Animal Activities
• AWAR: In order to approve proposed activities or proposed significant changes in ongoing activities, the IACUC shall conduct a review of those components of the activities related to the care and use of animals and determine that the proposed activities are in accordance with this subchapter unless acceptable justification for a departure is presented in writing. • *Guide*: The [institutional animal care and use] committee [IACUC] is responsible for oversight and evaluation of the entire Program and its components as described in other sections of the *Guide*. Its oversight functions include review and approval of proposed animal use (protocol review) and of proposed significant changes to animal use.	• In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy. In making this determination, the IACUC shall confirm that the research project will be conducted in accordance with the Animal Welfare Act insofar as it applies to the research project, and that the research project is consistent with the *Guide* unless acceptable justification for a departure is presented. Further, the IACUC shall determine that the research project conforms with the institution's Assurance.	The PHS Policy and AWAR define the responsibilities of the IACUC regarding review and approval of proposed significant changes to animal activities. Such changes must be conducted in accordance with the institution's Assurance, the USDA's AWAR, and the *Guide* unless an acceptable justification for a departure is presented. Additionally, IACUCs are responsible for assuring that the changes to approved animal activities meet the requirements described in the PHS Policy. IACUC approval of proposed animal activities or significant changes to previously approved animal activities is granted after full committee review (FCR) or designated member review (DMR). Additionally, institutions may establish and IACUCs may approve policies for the conduct of animal activities. These policies must be reviewed by the IACUC at appropriate intervals of no less than once every three years to ensure they are appropriate and accurate.

Scope:
The intent of this policy is to outline the IACUC Protocol Submission and review process.

Policy:
The IACUC shall review and approve, require modifications in (to secure approval), or withhold approval of activities related to the care and use of animals. The IACUC procedures for protocol review are detailed in the proceeding policy.

Investigators are not permitted to begin any *in vivo* animal related research, order animals for research, or make changes to any research already approved unless they have received an approval letter from the IACUC office. The IACUC meeting schedule and submission deadlines can be found on the IACUC website: http://www.uh.edu/research/compliance/iacuc/

I. Protocol Submission

IACUC protocols are to be completed and submitted electronically to the IACUC. Protocols submitted prior to the submission deadline (see the "meetings and deadlines" section of the IACUC website) are eligible to be placed on the agenda for the next IACUC meeting. In rare circumstances, protocols received after the submission deadline may be included on the meeting agenda if authorized by the IACUC chairperson.

II. Protocol Pre-Review

All protocols undergo both an administrative and veterinary pre-review of essential components. The pre-review includes, but is not limited to, a review of the following components within the protocol:

- Contact information
- Verification of personnel training and qualifications
  - Animal use location
  - Rationale for the following:
    - Animal use
    - Species and strain
    - Numbers of animals used
    - Search for alternative methods
    - Assurance of non-duplication of research
- Description of animal use
- Description of surgeries, including (if needed):
  - Pre-operative planning
  - Minimization of contamination
  - Intra-operative monitoring
  - Post-operative procedures
  - Scientific justification for multiple survival surgeries

on a single animal

- Type of exogenous substance administered, including:
  - Dosage
  - Route
  - Frequency
  - Scientific justification for the use of non-pharmaceutical grade substances, including consideration of grade, purity, sterility, acid-base balance, pyrogenicity, osmolality, stability, compatibility of components, expected adverse reactions, storage, and pharmacokinetics
- Hazardous substance approvals
- Euthanasia according to the current OLAW-adopted AVMA Guidelines
- Details regarding:
  - Unrelieved pain and distress
  - Tumors
  - Physical Restraint
  - Surgery
  - Breeding
  - Substance administration
  - Exemption from standards (departures from the *Guide* or AWA)
  - Field studies

During the pre-review process, communication from the IACUC coordinator and/or veterinarian is initiated with the investigator for any of the above areas that, due to lack of information/clarity or procedures that may be replaced by less painful alternatives, would likely justify a decision of "withhold approval" by the convened committee. A protocol considered incomplete will not be placed on an IACUC meeting agenda until the identified areas have been addressed. For this reason, it is advised that investigators request veterinary consultation during the protocol writing phase.

In response to the pre-review, an investigator should revise the protocol as requested and either submit the updated version by the meeting deadline or submit it to a later meeting.

III. Reviewer Assignment

For items reviewed by the full IACUC (see **Section V** below), primary and secondary reviewers are assigned for each protocol by the Chair, in consultation with the Vice Chair, the IACUC Veterinarian, and the IACUC Coordinator. A protocol review checklist based on the current version of the *Guide* is provided to reviewers as a reference. Reviewer comments are then provided to the IACUC Coordinator in advance of the meeting.

All IACUC members are provided secure online access to the protocols submitted for the

upcoming meeting, along with all meeting materials that will be reviewed/discussed, at least one week prior to the meeting. IACUC members are encouraged to personally attend each meeting. If a member cannot attend, that member is encouraged to review the protocol and add comments as appropriate so that any concerns may be discussed by the committee members at the convened meeting. If it appears that quorum cannot be met with the regular appointed members, appropriate alternate members, also appointed by the Institutional Official (IO), are asked to attend the meeting. All alternates are appointed to serve in a specific capacity to assure the membership is still properly constituted according to PHS IV.A.3 and the *Guide*.

IV. IACUC Review

The IACUC conducts a review of proposed animal use (i.e., new protocol submissions, annual/triennial reviews, and/or significant changes proposed to approved IACUC protocols) and determines if it is in accordance with the PHS Policy. In making this determination, the IACUC confirms that the protocol will be conducted in accordance with the AWAR and that the animal care and use is consistent with the *Guide*. Should there be a deviation from the accepted care and use procedures, an appropriate and well justified explanation must be provided. Also, the IACUC ensures that the protocol conforms to the institution's PHS Assurance and meets the following requirements:

- The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et seq.) and other applicable Federal laws, guidelines, and policies.

- Procedures with animals avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.

- Procedures that may cause more than momentary or slight pain or distress to the animals are performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.

- Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved are painlessly euthanized at the end of the procedure or, if appropriate, during the procedure.

- Methods of euthanasia used are consistent with the current recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia, unless a

deviation is justified for scientific reasons in writing by the investigator.

- The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals is directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.

- Medical care for animals is available and provided as necessary by a qualified veterinarian.

- Personnel conducting procedures on the species being maintained or studied are appropriately qualified and trained in those procedures.

- Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.

- Potential adverse effects of the study have been weighed against the potential benefits that may result from the research.

- Animals and experimental group sizes have been justified.

- Where exceptions are required in relation to the provisions stated, the decisions do not rest with the investigators directly concerned but are made by the Institutional Animal Care and Use Committee.

V. Review Types

The following review methods are utilized by the IACUC:

Full Committee Review (FCR):

FCR is the default review for new protocols, annual reviews of protocols, *de novo* triennial reviews, and certain significant changes to protocols (see section VI). A quorum of IACUC members is required for a fully convened meeting. Each protocol is discussed and deliberated upon, with the discussion reflected in the IACUC meeting minutes.

Designated Member Review (DMR):

The IACUC may choose to review protocols (after initial review at a convened meeting) or amendments to currently approved protocols using the Designated Member Review (DMR) method. Prior to the review, each IACUC member is provided access to the submitted protocol or amendment (completed by the investigator), which includes a full description of the animal manipulations and/or proposed change(s) to be reviewed. Each member is then given two business days to request a full committee review (FCR). If there is no request for FCR within the given time frame, it is assumed that the members have no objections to the utilization of the DMR process for the submission received. To begin DMR, at least one member of the IACUC, designated by the chairperson, is assigned to review the submission and has the authority to approve, require modifications in (to secure approval), or request FCR of the amendment. If multiple designated reviewers are used, their decisions must be unanimous; if even one reviewer calls for FCR, the protocol will be referred to the full IACUC for review. Approval of these protocols may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. Records of protocols reviewed and approved via the designated member review method are maintained in the IACUC meeting minutes.

In rare cases, an amendment may need to be approved in a time period of less than two full business days. In this case, the protocol amendment may be provided to committee members, who will then be contacted individually to assure that the amendment has been received and reviewed and that there is no call for FCR. As long as every member is contacted and understands the changes under consideration and no member calls for FCR of the amendment, the DMR can proceed and be completed as soon as the assigned designated member(s) review and approve the amendment.

DMR subsequent to FCR, following "Modifications Needed to Secure Approval" determination by the convened IACUC:

When the fully convened IACUC requires that modifications be made to a submitted protocol in order to secure approval (modifications needed to secure approval, or MNSA), such modifications can either be reviewed via FCR or DMR.

Protocol responses to a MNSA determination may be reviewed via DMR if the required modifications are voted upon unanimously by all members at the meeting AND if the entire current committee has previously approved the use of this method (i.e., in advance and in writing, that the quorum of members present at a convened meeting may decide by unanimous vote to use DMR subsequent to FCR when modifications are needed to secure approval). However, any member of the IACUC may, at any time, request to see the revised protocol and/or request FCR of the protocol.

Minor modifications, of an administrative nature (e.g., typographical and/or grammatical errors, required signatures, CITI training, etc.), may be verified by the IACUC office.

VI. Modifications to an Approved Protocol

The IACUC must review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities, in accordance with the PHS Policy IV.C. The submitted amendment should include a complete and accurate account of the proposed changes, a description of how the changes relate to the approved protocol, and a justification for the changes.

Non-significant Changes:

Non-significant changes to the protocol (i.e., those that do not have the potential to substantially and directly impact the health and well-being of the animals) may be approved administratively through the IACUC office. Examples of such changes include, but are not limited to:

- Addition/deletion of appropriately trained personnel
- Change in protocol title (does not involve any changes in procedure)
- Change in room number if the room is already on the IACUC inspection schedule
- Decrease in animal numbers

Mechanisms are in place to ensure that any personnel added to a protocol are appropriately identified, adequately trained and qualified, and enrolled in applicable occupational health and safety programs prior to their addition to the protocol. In

instances when the title change to a protocol is due to the addition of a funded research proposal, mechanisms are in place to ensure that the information the IACUC reviews and approves is congruent with what is in the funded research proposal. Other changes deemed non-significant by the IACUC Chair may also be reviewed by this mechanism.

Significant Changes:

A significant change is based upon guidance provided by OLAW. Examples of changes considered to be significant include, but are not limited to, changes:

- In the objectives of the study
- From non-survival to survival surgery
- Resulting in greater discomfort or in a greater degree of invasiveness
- In the species or in approximate number of animals used
- In Principal Investigator
- In anesthetic agent(s) or the use or withholding of analgesics
- In housing and/or use of animals in a location that is not part of the current animal program overseen by the IACUC
- In the method of euthanasia
- In the duration, frequency, or number of procedures performed on an animal

The review of significant changes to an IACUC protocol may be conducted under one of the following processes:

- **FCR**
- **DMR** (as described in **Section V)**
- **Veterinary Verification and Consultation (VVC)**

The determination of the review type depends on the specific changes made to the protocol. The IACUC Chair is consulted on this determination if the classification is not clear-cut, based upon the impact to the animal subjects.

Examples of revisions that are reviewed via FCR include, but are not limited to, the following:

- Significant changes in study objectives/goals (such a change may require a new protocol)
- Change in pain category

- Adjusting experimental endpoint for later termination of the study resulting in increased potential for the animals to experience pain and or distress
- Adding new test substances that will increase the potential for pain/distress or discomfort
- Change of non-survival surgery to survival surgery
- Changes from an immunocompetent to an immunocompromised animal strain
- Changing to a non-conventional anesthesia/analgesic/euthanasia method
- Change of PI

Examples of revisions that may be reviewed via the DMR process include, but are not limited to, the following:

- Significant change in age of animals (e.g., adults to neonates)
- Approval of animal housing/use area not currently part of the animal program overseen by the IACUC (i.e., not on the IACUC's facility inspection list); inspection required prior to approval of area
- Modification of the conventional environmental or husbandry practices
- Adding a subgroup for an additional time point, with no additional clinical consequences
- Addition of, or change in, experimental substances[1] to be administered, if no increased potential for pain, distress, or discomfort is anticipated
- Increase in number of animals
  NOTE: The original rationale for the numbers of animals should continue to support the increase in percent being requested. ***If not, a revised rationale is required that may require FCR review.***

Veterinary Verification and Consultation (VVC):

Significant changes to a protocol must be approved either by a majority vote of a convened quorum of the IACUC (see FCR above) or by DMR. However, in the following IACUC-approved circumstances, the veterinary verification and consultation (VVC) process, defined below, permits a veterinary member of the IACUC, as coordinated by the IACUC office, to verify that the proposed significant change(s) to previously approved animal activities are eligible for administrative veterinary review.

The VVC process cannot be used to add new procedures to a previously approved protocol; if new procedures are proposed, they must undergo FCR or DMR review as appropriate.

[1] Additional experimental substances may require biosafety review prior to use.

The veterinarian is not conducting a DMR but is serving as a subject matter expert in certain circumstances. This consultation will be documented. The veterinarian may refer any request to the IACUC for further DMR or FCR for any reason and must refer any request that does not meet the parameters of this policy.

Veterinarian Responsibilities of VVC:

1. **Verify:**
    a. Certify that the requested significant change is covered by this IACUC Policy
    b. Determine whether the change is appropriate for the specific circumstances
2. **Consult:** Request clarifications if appropriate and within the scope of this Policy.
3. **Defer:** Refer the significant change for FCR or DMR by the IACUC, if necessary/indicated.

Changes that may be reviewed using VVC (pre-approved by the IACUC):

1. A change in strain of non-USDA covered animals when the change does not deleteriously impact the health of the animals or the scientific aims of the approved protocol
   Examples include:
    a. Changing from one outbred strain to another
    b. Adding any strain if there are no deleterious clinical consequences
    c. Transferring from another protocol or ordering any strain for training purposes or practicing complex procedures that require proficiency verification, as approved in current protocol[2].
2. Change in, and/or addition of, anesthesia, analgesia, or sedation[3] (if the change does not increase the pain/distress that the animals will experience)
3. Change in and/or addition of euthanasia to any method approved in the most current *AVMA Guidelines for the Euthanasia of Animals*
4. Change in duration, frequency, type[4], or number of procedures performed on an animal (only if the change does not increase pain/distress)

[2] If animals are not approved in the protocol for training/practice purposes, the change will be reviewed by DMR.
[3] This typically applies to changes *within* the type of anesthesia, analgesia, or sedation, rather than alternating among these methods.
[4] As previously stated, the VVC process cannot be used to add new procedures to a previously approved protocol; however, if, for example, "blood draw" is already approved on the protocol, a change in the method of blood

VII. Continuing Review

The IACUC must conduct continuing review of each previously approved ongoing activity at appropriate intervals as determined by the IACUC; this includes a complete review of an approved protocol in accordance with the PHS Policy IV.C.1-4 at least once every three years (*de novo* triennial review), and at least annually (annual review) for USDA-covered species. Annual review documentation, submitted by the researcher, for all ongoing activities is reviewed by the IACUC as part of post-approval monitoring. The IACUC review of this documentation can be conducted via FCR or DMR (except for USDA-covered species, which are always reviewed by FCR) as designated by the Chair. All annual reviews are recorded in the IACUC meeting minutes, which are reviewed and approved by the committee.

No animal activities are allowed to continue beyond the protocol expiration date.

VIII. Memorandum of Understanding (MOU)

A Memorandum of Understanding (MOU) is utilized when some or all of the animal research described in a funded proposal will occur at an institution other than the primary institution. This inter-institutional agreement defines the collaborative activity involving the animals and addresses each institution's responsibility for animal use. The MOU also captures information regarding the collaborating institution's IACUC review (the IACUC approval letter is required in all cases; however, if the collaborating institution is not AAALAC-accredited and PHS assured, the full protocol is also required), ownership of the animals, and accreditation and assurance information. Signatures from both the collaborating investigator and the University of Houston investigator, as well as signatures from the signatory officials of both institutions are required, providing assurance that all institutional, state, and federal guidelines will be followed.

The IACUC office works with the PI and the collaborating institution to put this agreement in place and verifies congruency regarding the role of each institution with the funded proposal. The IACUC is informed of finalized MOUs by placement of this information on the agenda of the next fully convened IACUC meeting as an informational item. MOUs are acknowledged with a memo once all required

collection to another IACUC-approved method, or a change to blood sampling times or volumes, may be reviewed under the VVC process.

collaborating approval letters have been submitted. The review and acknowledgment are documented in the IACUC minutes.

IX. Voting

A quorum of IACUC members must be present during a fully convened committee meeting in order to vote to approve, require modifications in (to secure approval), or withhold approval. Protocols reviewed by the full committee must receive the approval vote of a majority (>50%) of the quorum present in order to receive approval. Tele-/electronic communications may be utilized to achieve quorum in accordance with NIH Notice NOT-OD-06- 052.

X. IACUC Review Outcomes

The IACUC must notify investigators and the institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval, as set forth in the PHS Policy IV.C.4.

Investigators and the institution are notified in writing of IACUC protocol review decisions, generally within 5-7 business days following the IACUC meeting, as follows:

- **Approvals**

  Approval letters are sent to the Principal Investigators electronically (via ICON).

- **Modifications Needed to Secure Approval (MNSA)**

  When modifications are required to secure an IACUC approval, the investigator is sent a memo electronically, indicating the review outcome and detailing the modifications needed in order to secure an IACUC approval.

  Depending on the modifications or clarifications needed, the IACUC can either request for the response to be reviewed administratively (for administrative details), or by designated member review. DMR reviewers are assigned by the IACUC Chair at the meeting, and the information (administrative and DMR) is noted in the meeting minutes.

- **Withhold Approval**

The IACUC may determine that the information provided in the protocol submitted does not adequately address all of the requirements detailed in the PHS Policy, the *Guide for the Care and Use of Laboratory Animals*, and/or the Animal Welfare Act (AWA). In instances such as this, the IACUC must withhold the approval of the submission. When this occurs, the investigator is sent a memo electronically, including a detailed list of the findings that substantiated the determination.

When further clarification has been provided by the investigator, the protocol may come back to the fully convened committee for review.

Designated reviewers cannot withhold approvals; only a fully convened IACUC meeting may withhold the approval of a protocol. Higher institutional authority may not overrule an IACUC decision to withhold approval of a proposal.

The Institutional Official (IO) has access to all IACUC meeting minutes and meets regularly with the Executive Director of Research Compliance to discuss Committee decisions. The IACUC Chair has open access to the IO to discuss outcomes as necessary.

XI. Conflicts of Interest

Except to provide information to the IACUC, IACUC members with conflicting interests are not eligible to participate in the IACUC review and/or approval of a protocol. In addition, IACUC members with conflicting interests are not to contribute to the constitution of a quorum.

XII. Consultants

The IACUC may invite consultants to assist in reviewing complex issues, but the consultants may not participate in the vote to approve or withhold approval of an activity unless they are members of the IACUC.

Document Log

Version Number	Approval Date	Description of Changes
1		Initial Policy created and approved
2	4/17/2017	Updated policy to add VVC and make consistent with online (not paper) submission system
3	10/19/2020	Updated language and added clarification of ICON processes