Protocol Approval Process

377.1 Purpose: One of the primary functions of the IACUC is to review and approve animal use protocols, and any subsequent significant changes to those approved activities. This document outlines those processes and the mechanisms employed to determine which steps are required to secure approval.

377.2 Definitions and Methods employed:

377.2.1 Protocol Pre-Review: These processes are carried out by multiple groups as described below. The purposes of these review processes and the group responsible for their completion are as follows:

377.2.1.1 Veterinary planning and consultation: This process is required for all new or three-year renewal protocol submissions which would be expected to cause more than momentary pain or distress to animals, but is carried out at Emory University for all new and 3-year protocol submissions. This process is conducted prior to protocol submission and is focused on refinement of the procedures proposed to minimize animal pain and discomfort, while meeting the experimental needs of the research. Note: completion of this step **is required** for subsequent submission of new protocols or 3-year renewals. Specific issues of emphasis include the following:

- The appropriateness of the animal model for the proposed experimental purpose
- Animal numbers and justifications, as well review of the potential pain/stress to the animals
- Review of the procedures and techniques employed, and the use of analgesia and anesthesia as needed to alleviate/reduce pain and discomfort
- Review of humane endpoints and euthanasia methods
- Discussion and review of any other issues pertinent to animal health and welfare during the conduct of the procedures proposed

377.2.1.2 IACUC Office Review: This process is initiated prior to submission, but may continue during the course of the subsequent review process. The following issues are generally addressed:

- Verification of training completion for all staff
- Verification of other required approvals such as chemical, biological, or radiation
- Completion of protocol to grant congruence analysis as required by funding agency and type
- Verification that all assurances, conflict of interest disclosures, and proper electronic signatures are obtained

- Review of protocol for completeness prior to submission

377.2.1.3 Behavioral Management Consultation: This process is required for all non-human primate (NHP) protocols and is initiated prior to submission, but may continue during the subsequent review process. It focuses on review of social housing, enrichment and preparation of animals for study-related procedures using training. Opportunities for refinement of procedures to maximize behavioral well-being and reduce associated stress are emphasized. The following issues are generally addressed:

- Review of the type of social housing selected for NHPs during the study
- Review of any requested accommodation to the enrichment program
- Review of animal training techniques and shaping plans used to prepare animals for research procedures, including restraint

377.2.1.4 Bio-safety Consultation:. This review focuses on the use of biological, chemical and radioactive agents in the research and ensures their safety and efficacy for use in animals. This review does not provide approval for the use of these agents themselves. It only serves to provide guidance for their use in animals, and to identify which agents would require separate approval by the appropriate unit of the Environmental Health and Safety Office (EHSO) as detailed below.

- Research Safety/BioSafety: http://www.ehso.emory.edu/programs/research-biosafety/index.html. This program manages the use biological toxins, recombinant DNA, infectious agents and selected cell- lines and tissues.
- Environmental Compliance: http://www.ehso.emory.edu/programs/environmental/index.html. This program manages the use of hazardous chemicals
- Radiation safety: http://www.ehso.emory.edu/programs/radiation/index.html. This program manages the use of radioactivity as well as providing training for the use of radiation-producing equipment.

377.2.1.5 COI Review: This review focuses on any potential conflict of interest. If potential conflict of interest is disclosed by the PI of the protocol, then it will be reviewed by the COI office, and if appropriate a management plan will be established.

377.2.2 Protocol Review: Full Committee Review (FCR): This review takes place at a convened meeting of the committee where at least a quorum of the members is present. No member may participate in the review of a protocol in which the member has a conflict of interest, and must recuse him/herself from the process except to provide specific information as requested by the IACUC. The member may not vote on the proposal, nor can the individual contribute to quorum. Determination of the outcome is by simple majority of the members present. A list of the types of protocols that ordinarily are subjected to FCR is provided in Appendix A.

377.2.3 Designated Member Review (DMR): This process can occur continually and does not require a convened meeting of the IACUC. For this process to occur all members must first have

access to the submitted protocol and have the opportunity to call for FCR. This is done through dissemination of the submitted protocol to the whole committee via the electronic protocol submission and review software. All members have three business days to respond to the request. Any member who does not respond within the three day window is deemed to have agreed to DMR. If any member calls for the submitted protocol to go to FCR, then that protocol is moved to the FCR process and is scheduled for discussion at the next available meeting of the committee. Once three business days have passed the protocol is assigned to at least one qualified member for review. Note that any IACUC member may elect to review the protocol and submit questions or comments to the PI without calling for FCR. If a protocol is assigned to more than one designated reviewer, the reviewers must be unanimous in any decision. They review identical versions of the protocol and, if modifications are requested by any one of the reviewers, the other reviewers must be aware of and agree to the modifications.

377.2.4 Veterinarian Verification and Consultation (VVC): This process can be used for specific, well- defined changes to approved protocols ONLY (Amendments) and its use is covered by NOT-OD-14-126 and is described in detail below.

377.3 Initial Protocol Submission and Review Process: This process covers all new protocol submissions as well as three year renewals. Investigators complete and submit their submissions electronically via a web-based protocol management system to the IACUC office. Submitted protocols are first subjected to pre-review as described above and sent back to the PI for revisions prior to formal submission for IACUC review. Once returned by the PI the protocols are designated for either FCR or DMR initially using criteria established by the IACUC (appendix A) and sent out for review. Note however, that a protocol originally submitted for DMR will be transferred to FCR upon request of any IACUC member as defined above.

377.4 Annual Review (AR): This process is required annually of all approved protocols using AWAR covered species only. A list of all protocols coming up for AR is distributed to the IACUC committee monthly with an opportunity to call for FCR. If the protocol in question is not called the protocol is reviewed by the DMR process.

377.5 Review Outcome:

377.5.1: FCR: The following actions may be taken during FCR review:

1. Approve protocol as is.
2. Require Modifications to secure approval.
3. Withhold approval.

Note that if an application requires modification to secure approval or if approval is withheld, the Principle Investigator (PI) is provided with reasons for the decision in writing, and the opportunity to respond to the feedback. Protocols requiring modifications to secure approval after FCR are automatically routed to DMR unless a call for FCR review of the responses is made during the meeting. The IACUC adopted an updated "SOP for Reviewing Modifications to Protocol Applications or Amendments Requested for Currently Approved Protocols after Full Committee Review" on June 24, 2014, which was then signed by all IACUC members, pursuant to NOT-OD-09-035. All new IACUC members are made aware of this stipulation during

orientation training and are asked to sign the agreement as per the NOT.

377.5.2: DMR: The following actions may be taken during DMR review

1. Approve protocol as is.
2. Require Modifications to secure approval.
3. Call to FCR

377.6 Review of Significant Changes to previously approved protocols (Amendment Requests) : In addition to initial reviews for all protocols, and annual reviews for AWAR covered species, the IACUC must review and approve all significant changes to all approved protocols. Amendment requests are submitted to the IACUC office through the electronic protocol submission system. Requests for modification may be handled via DMR or FCR by the procedures indicated above. Criteria used to determine which method is used are outlined in appendix A Note that two additional processes are possible for amendment requests, Veterinarian Verification and Consultation (VVC) and administrative review. The VVC process is described in detail below. The criteria used to determine when IACUC office administrative review is appropriate is listed in Appendix A.

377.7 Veterinarian Verification and Consultation:
377.7.1 Purpose: The Office of Laboratory Animal Welfare (OLAW) published NOT-OD-14-126 "Guidance on Significant Changes to Animal Activities" on August 26, 2014. This document allows for flexibility in the evaluation of certain proposed changes to animal protocols. In order to take advantage of this flexibility in whole or in part, the IACUC has established criteria that address significant changes eligible for VVC (below and Appendix A).

377.7.2 Background: Changes to approved research projects must be conducted in accordance with the institution's Assurance, the United States Department of Agriculture (USDA) Animal Welfare Act and Animal Welfare Regulations and must be consistent with the Guide unless an acceptable justification for a departure is presented. 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). The VVC process is used to apply established policies and straightforward conditions (e.g., guidance documents, standard operating procedures, drug formularies) for the conduct of animal activities.

3.77.7.3 NOT-OD-14-126. This document outlines the specific significant changes which may be handled administratively according to IACUC-reviewed and -approved policies in consultation with a veterinarian authorized by the IACUC. The veterinarian is not conducting DMR, but is serving as a subject matter expert to verify that compliance with the IACUC-reviewed and -approved policy is appropriate for the animal activity in this circumstance. This includes changes in:

a. anesthesia, analgesia, sedation, or experimental substances;
b. euthanasia to any method considered acceptable or acceptable with conditions in the AVMA Guidelines for the Euthanasia of Animals
c. duration, frequency, type, or number of procedures performed on an animal.

377.7.4 VVC Process and Associated Policies.

377.7.4.1 Euthanasia: The assigned veterinarian may use his/her discretion to authorize the use of any currently acceptable AVMA method including those acceptable with conditions (providing the conditions are met). Note that protocol associates must be adequately trained in the use of the new procedure under the stipulations of Emory IACUC policy ***0354: Education and Training***.

377.7.4.2 Anesthesia, Analgesics and Sedatives: The assigned veterinarian may use his/her discretion to authorize changes to the dose, route, concentration, volume, and/or duration of any anesthetic, analgesic or sedative agents already approved on the protocol. Changes to other agents not previously approved on the existing protocol may also be authorized under this mechanism providing the agent under request is listed in an IACUC-approved formulary and the requested usage is within the approved dose range. Note that all authorized changes must be in accordance with Emory IACUC Policy ***0364: Anesthesia and Analgesia***, and policy ***0366 Injectable Agents*** as applicable. In addition, protocol associates must be adequately trained in the use of the new drug under the stipulations of Emory IACUC policy ***0354: Education and Training***. Changes that might require additional training would include changing from an injectable to an inhalant anesthesia.

377.7.4.3 Experimental Substances: The addition or deletion an experimental substance, adjustment in dose, alternate formulation, or less invasive route of administration may also be authorized under this mechanism, assuming all conditions of IACUC Policy ***0365: Non-pharmaceutical grade Drugs***, and policy ***0366 Injectable Agents*** are met. This includes special diets and medicated water. Note that the addition of a non-pharmaceutical grade drug, or a change from a pharmaceutical grade to a non-pharmaceutical grade drug requires additional justification and will not be authorized under this mechanism.

377.7.4.4 Duration, frequency, type, or number of procedures performed on an animal: The assigned veterinarian may use his/her discretion to authorize minor procedural changes providing in the judgment of the VVC veterinarian the change will not unduly impact animal welfare (i.e., lessens or involves equivalent pain, acute or chronic stress, distress or effects upon animal welfare) and is consistent with current standards of veterinary practice or specifically addressed in IACUC policy. Common examples include:

- Changes related to blood collection (e.g., frequency, volume, vessel of access) providing they fit within the guidance of IACUC policy: ***0355 Blood Collection*****.**
- Revision of sample collection intervals or total samples collected.
- Addition of a non-invasive sampling method.
- Additional perimortem tissue collection or tissue collection from a new organ system or anatomical site when the animal is under terminal anesthesia.
- Substitution of one accepted biopsy method for another for tissue or DNA analysis.
- Altering the duration or interval between procedures (e.g., lengthening an imaging episode or the time between episodes).
- Changing an identification means.
- Adding or altering behavioral testing methods providing they do **not** involve unrelieved pain or distress.

- Increases or enhancements in enrichment or uses of non-standard enrichment, not including exceptions to IACUC policy
- Programs of post-anesthetic care that are enhanced above IACUC minimums.

377.7.5 Role of the VVC Veterinarian: Any veterinarian approved by the IACUC may conduct VVC. This includes all staff or faculty Veterinarians at either EU-DAR or Yerkes DAR, as well as third-year veterinary residents. The responsibilities of the vet are as follows:

- Ensure that the requested change is eligible for VVC
- Verify that the requested change is addressed by existing IACUC policy
- Determine if the change is appropriate under the specific circumstances. If so the change may be authorized. If not the following actions are appropriate under VVC
  - Recommend revision to the existing request if it is within the scope of the policy and is appropriate for the conditions of the experiment
  - Defer the request to DMR or FCR

377.7.6 Documentation The following process must be followed in regard to conduct and subsequent documentation of the VVC process:

a. All amendment requests are submitted by the PI or their designee through the standard electronic submission process. Note that in emergency situations where animal health or welfare would be negatively affected by delay, this submission requirement can be waived. In these cases, requests can be made to the IACUC office directly. The office will act to expedite the request and then work with the PI to ensure its proper entry into the protocol after authorization has been granted
b. The IACUC-office protocol analyst assigned to the protocol will evaluate the request and determine if it is eligible for VVC.
c. A VVC-Vet will then be assigned to the protocol amendment. If the request is deemed to be urgent, the protocol analyst will contact the VVC-Vet via email or phone call to alert them of the situation, so as to expedite the request.
d. If the VVC vet verifies that the request can be authorized via VVC, the protocol analyst will process the request, and alert the PI.
e. If the vet feels that the request does not fit within the established policies and procedures for VVC, then the amendment will be processed by the IACUC office and reassigned for DMR or FCR as appropriate.

Note: Requests can be authorized at this point, and changes instituted immediately. There is no delay between approval and ability to institute the alteration.

377.8 DocumentProperties

Authored by: IACUC
Administering Division/Department: IACUC Office
Original Approval Date: 07/15/15
Review/Revised: 5/18/16
Version: 20160518

New or Three Year Protocol Applications	FCR	DMR	VVC	Admin
All nonhuman primates studies	X			
All studies involving multiple survival surgeries (other than those using frogs)	X			
All studies involving the use of paralytic or neuromuscular blocking agents	X			
All studies involving euthanasia methods other than those approved and/or listed as acceptable or acceptable with conditions by the AVMA Panel on Euthanasia.	X			
All studies involving procedures classified in USDA Pain Category E	X			
All studies involving unrelieved pain and/or stress in protocols NOT involving USDA Regulated species	X			
All studies with death as an endpoint, or endpoints that are more severe than the default recommendations of the IACUC	X			
All studies involving infectious agents (e.g. SIV, LCMV, etc.)	X			
All Studies involving Exceptions to "The Guide"	X			
All studies involving exemptions or exceptions from established IACUC policy.	X			
All studies involving multiple survival surgeries using frogs		X		
All studies involving acceptable euthanasia methods as delineated by the AVMA Panel on Euthanasia.		X		
All studies involving procedures classified in USDA Pain Category B, C, and D		X		
All studies involving the administration of toxic or hazardous chemicals or radioisotopes (e.g., MPTP, F-18, carcinogens)		X		
All other studies not specifically described above ….		X		

Annual Reviews	FCR	DMR	VVC	Admin
All studies involving USDA covered species		1 member		

Modification Requests	FCR	DMR	VVC	Admin
All Studies involving Exceptions to "The Guide"	X			
All studies involving exemptions or exceptions from established IACUC policy.	X			
Addition of faculty collaborator (co-PI) in protocols involving USDA regulated species		X		

Addition of animals in protocols involving USDA regulated species		X		
Addition of a minor surgery in protocols involving USDA regulated species		X		
Addition of a minor surgery in protocols NOT involving USDA regulated species		X		
Reducing or eliminating previously approved water or feed restrictions in protocols not involving USDA regulated species			X	
Addition of or change in dosage of an experimental drug in the same class as one previously approved in protocols NOT involving USDA regulated species			X	
Addition of non-invasive sampling in protocols involving USDA regulated species			X	
Addition of another strain of the same species in protocols involving USDA regulated species		X		
Addition of another strain of the same species in protocols NOT involving USDA regulated species			X	
Change of sex in the animal to be used in protocols involving USDA regulated species			X	
Change of sex in the animal to be used in protocols NOT involving USDA regulated species			X	
Addition of sample collection times in protocols involving USDA regulated species			X	
Addition of sample collection times in protocols NOT involving USDA regulated species and not exceeding standard limits			X	
Addition of non-invasive sampling (i.e. feces collection, saliva, imaging, etc.) in protocols NOT involving USDA regulated species and not exceeding standard limits.			X	
Reducing or eliminating previously approved water or feed restrictions in protocols involving USDA regulated species			X	
Addition of or change in dosage of an experimental drug in the same class as one currently approved in protocols involving USDA regulated species			X	
Deletion of animal usage location approved in protocols involving USDA regulated species			X	
Substitution of one AVMA acceptable euthanasia method for another acceptable euthanasia method in protocols involving USDA regulated species			X	
Substitution of one AVMA acceptable euthanasia method for another acceptable euthanasia method in protocols NOT involving USDA regulated species			X	

Adding an amendment to allow additional perimortem tissue collection when the animal is under terminal anesthesia; pertains to protocols involving all species			X	
Substitution of one accepted biopsy method for another for tissue or DNA analysis in protocols involving USDA regulated species			X	
Substitution of one accepted biopsy method for another for tissue or DNA analysis in protocols NOT involving USDA regulated species.			X	
Changes to the PI		X		
Changes to funding (addition or deletion) in all protocols				X
Changes to contact information or training updates of the PI or study personnel for all protocols				X
Addition of faculty collaborator (co-PI) in protocols NOT involving USDA regulated species				X
Addition of <10% of the number of animals over the original authorized number in protocols NOT involving USDA regulated species				X
Deletion of animal usage location approved in protocols NOT involving USDA regulated species				X
Changing the title of a protocol approved in protocols NOT involving USDA regulated species				X