Subject: eIACUC Form Preparation Checklist & Detailed Instructions

Version: 12/20/2018

Executive Summary

Provided are instructions for completing the new eIACUC form. As the research community transitions fully to the use of eIACUC, be aware that these instructions are a living document subject to regular revision by the IACUC as greater community experience with eIACUC informs on how to continually improve guidance to users. As such, whenever preparing or amending a protocol, contact your RPA or check the IACUC web site for the most recent version. These instructions are provided in two sections. First is an "Overview" to provide an introduction to the concept of the Procedures and Experiments components and a caution to investigators who have had their Topaz protocol content migrated by the IACUC office into eIACUC. The Procedures and Experiments form the main body of reviewable material in eIACUC. Reliance upon them, however, differs significantly from the Topaz Enterprise and Elements forms. The second section of "Detailed Instructions" provides section-by-section directions for completing the form. Understanding the Procedure and Experiment approach and following the most contemporary version of the instructions will enable greatest efficiency in preparation of protocols or amendments and the speediest IACUC review. Lastly, use these instructions and not those embedded in the eIACUC form except for specific situations identified below. Investigator and protocol form preparer feedback in improving these instructions is encouraged.

OVERVIEW:

While a lot of information is required within the eIACUC form (see Detailed Instructions below), the "meat" of the application involves providing a detailed description of the experiments to be performed on the animals in your studies. This is broken down into 2 parts, Procedures and Experiments, which are briefly described below.

Procedures: The eIACUC protocol submission form is organized around Procedures. As such, the first thing you should do when generating a new/renewal eIACUC protocol is to determine the procedures that will be required for your studies [e.g., intraperitoneal injection of a drug(s), blood collection, CO2 euthanasia, etc.]. The next step should be to determine which, if any, of the procedures you will need exists in the library of Standard Procedures (these are procedures that have been pre-approved by the IACUC and, if appropriate, can be used by any investigator – streamlining subsequent review of your protocol). Note, however, that if you choose a Standard Procedure, you will not be able to edit the procedure and will be required to follow the procedure as written. Also note that the IACUC is working to increase the number of Standard Procedures available in eIACUC. Those procedures that you will need that do not currently exist as a Standard Procedure, will need to be written by you (these are referred to as Team Procedures – and they will be reviewed along with the rest of your protocol following submission of your protocol to the IACUC). These Team Procedures can be: (i) *de novo* created; (ii) copied from another PI that has developed the same team procedure; or (iii) generated from an established Standard Procedure that has been edited by you to tailor the procedure to your specific experimental requirements. The logical first step in preparing your protocol is to write all the Team procedures that you will need.

Try to streamline your procedures as much as possible. One issue repeatedly encountered is the generation of multiple team procedures which could have been pooled together in a single procedure. For example, if you are planning to intraperitoneally inject a number of drugs, antibodies, etc., these can be written as a single procedure for intraperitoneal injection of a substance – listing the substances that will be introduced via this route (as opposed to writing a different procedure for each substance). In this example you would simply need to identify the

range of volumes to be injected and then list the substances along with the concentration and volume to be injected for each (and, in this specific case, you may find the you can create the Team SOP using the IACUC-approved Standard Procedure for IP injection as a template). This general approach will hopefully decrease the number of Team Procedures that you will need to generate.

Experiments: The next step will be to determine the "Experiments" to be carried out. Depending on the complexity of your research, it may be easiest to consider developing each "Experiment" as you would a Specific Aim in a research grant. You can structure experiments that span multiple funding sources for mice, rats, fish and birds as long as the details of the experiment are logical and can be followed during review. For each "Experiment" you will be required to write an over-view of the experiment (i.e., what is to be done to the animal subjects) in Q3. The regulatory requirement here is for a clear and concise sequential description of the procedures involving the use of animals that is easily understood by all members of the IACUC (Guide for the Care and Use of Laboratory Animals, 8th ed., p 25). In general, 3- 5 sentences (100-150 words) should suffice.

Thing to do and NOT to do:

(1) Do NOT describe procedures in Experiment section 3 – the Team and Standard Procedures in columns 6 and 7 provide this detail. In each case of a procedure or administration of a substance as a component of an experiment, there should be a corresponding Standard or Team procedure in the Common Procedure column. As the Variable Procedure column is the source of much confusion and not essential to IACUC review at Emory, a future change in the form will be to remove it.

(2) It is critically important that you provide: (i) clear endpoints for your experiments; (ii) the specifics of how often animals will be monitored and what criteria you will use to euthanize experimental animals that are doing poorly; and (iii) what pain the experimental animals may experience and how you will treat this [if experimental animals are likely to experience more than momentary discomfort, then analgesics will usually be required – unless withholding analgesics can be scientifically justified (e.g., their use would interfere with one or more parameters being measured by the proposed experiment)]. With few exceptions, statements such as "analgesics will be administered if the experimental animals appear to be in pain" will NOT be accepted since it is often difficult to assess how much pain animals are experiencing (e.g., prey animals frequently mask overt signs of pain). Rather, the working standard is that if a similar procedure would cause more than momentary pain in humans, then the expectation is that the procedure will cause more than momentary pain in the experimental animals.

(3) Do NOT cut and paste long rationales for experiments from your grant into the Experiment description – rather, as indicated above, keep this description very focused detailing only the overall goal, numbers of animals required, what procedures will be done on specific groups of animals (particularly important if you are including variable procedures within an experiment).

Other important considerations: Approval of your IACUC protocol will likely require additional approvals from other university committees, and these approvals will need to be attached to your protocol:

- Biosafety approval (if you are treating animals with any biologics)
- Chemical safety approval (if you are treating animals with any toxic chemicals)
- Radiation safety approval (if you are treating animals with any radioactive substances)
- Laser safety approval, if applicable.
- Cell line testing (if you are injecting cells into experimental animals)

Cautionary Note Regarding Migration Protocols:

Please note that migrated protocols present a unique challenge for subsequent review. These are protocols where the IACUC office personnel, in their best guess about how your research is conducted, transferred all content from the IACUC-approved Topaz predecessor into eIACUC for you. Differences between the obsolete Topaz forms and the eIACUC replacement made this a complicated endeavor. The migration was performed using a cut and paste approach under a "best-fit" methodology. The resultant eIACUC protocol contains all the information previously approved, however it does not conform to the requirements and structure of the new system and is thus an incomplete and possibly inaccurate conversion. There are many questions in eIACUC that do not have a specific singular correlate in the previous formats, and therefore this detail could not be accurately addressed during the migration process by the IACUC office staff. This presents itself in multiple sections of the form, but is most evident as a complicating factor within the Team Procedures.

The IACUC does not require that PI's revise the migrated protocol prior to three-year renewal, however at renewal all protocols must be fully converted to the new format. The IACUC does strongly encourage researchers to submit a revision amendment to fully convert the protocol into the eIACUC format prior to submission of subsequent amendments. We strongly believe that this is in everyone's best interest. In our experience, review of amendments to migrated but unconverted protocols can result in significant delays in approval and multiple rounds of review to answer all questions and concerns. This of course increases burden to all and runs the risk of scientific delays which none of us want. If you have questions or need assistance in this regard, please reach out to the IACUC office for assistance prior to submitting an amendment. They can assist you in determining the best course of action and in modifying the migrated protocol to aid subsequent review. This generally includes replacing team procedures whenever possible with pre-approved standard procedures, which greatly accelerates review and streamlines effort moving forward.

DETAILED INSTRUCTIONS:

Please note that to enable expeditious review and minimize complications in maintaining a protocol, such as when amending it, entries in each section of the form should be unique and not repeated in other sections. Cutting large sections from a grant application usually complicates review, potentially leading to delays in approval. This also often leads to inconsistencies, as well as repetition, in the approved IACUC protocol.

Note that for some sections there are no instructions as input of material is self-explanatory (e.g., instructions are not provided here for what to enter for "Title of Protocol" or "Principal Investigator" or similar simple fields.

BASIC INFORMATION

Q4. Lay Summary.

1. Briefly describe the potentially painful techniques and procedures performed on the animals and why they are necessary.
2. If there are more than momentary painful or stressful procedures, address whether or not anesthetic or analgesic agents are required.
3. A scientific abstract copied from the grant application using highly technical terms is NOT acceptable.
4. Use simple terms understandable to high school science students.
5. Scientific objectives, significance/benefits of the research, and justification for the use of animals and species are addressed in the "Scientific Aims" section and thus do not need to be added here.

EXPERIMENTAL RESEARCH PROTOCOL ADDITION

Will the Protocol Include Breeding?

Indicate if the protocol will include breeding. The answer you specify here will affect the remaining pages that appear for this protocol.

PROTOCOL TEAM MEMBERS

1. Provide emergency phone numbers (i.e., cell, home) for at least two persons in the event DAR needs to make contact off-hours in the case of a physical plant or animal welfare emergency.
2. The External team member information section is for addressing students that may rotate through the lab, visiting scientists or scholars from outside Emory who may engage in the research.

FUNDING SOURCES

Identify all external funding sources, such as industry sponsors and government agencies. The main purpose is to help the IACUC identify all protocols associated with particular grants. If funding comes from a specific internal funding program, also identify that funding source. For this section, the instructions revealed by selecting the link at "For Emory specific guidance on Funding Sources, click here" Are applicable.

For protocols involving species regulated under the federal animal welfare act (i.e., species other than rats, mice, birds or fish), the IACUC requires a protocol for each grant.

SCIENTIFIC AIMS

Q1. Specific Aims.

1. Provide a description of the scientific goals and objectives of the study as a broad overview.
2. Be brief. Do not include the entire research methods section.
3. A scientific abstract copied from the grant application using highly technical terms is NOT acceptable.

Q2. Provide justification for the use of animals and for the species to be used in these studies.

1. Provide the reason animals are necessary, and why alternatives such as computer modeling, tissue culture, organ preparations or organs on a chip; or invertebrate model systems cannot be used.
2. Explain why the species chosen is necessary and, if multiple species are intended for use, why each is necessary.

Q3. Significance and benefits of the research.

Identify the significance of the research as applied to the area of interest (e.g., quantification of the economic cost or consequences for patients of the disease, condition or lack of knowledge) and the overall benefit (e.g., in improved patient care, cures or treatments, or advancement of new knowledge and its potential applicability) in light of any pain or stress caused to experimental subjects.

Q4. Describe the potential for pain and/or distress to animals in this study.

1. Identify the probability and characteristics of each element of harm or cost to the population in use or under study, including that which is unrelieved and/or may result in death, and balance them against the potential benefit.
2. If there are adverse effects or events possible or likely with the model or model systems

please identify these with a prediction of incidence and severity, if possible.
3. Include supportive care to be provided to prevent, minimize or intervene with respect to pain, distress, disability or impairment.
4. Identify the general schedule for monitoring animals for wellbeing and adverse effects, including any measurements to be obtained as baseline and through the course of the study (e.g., periodic body weight, CBC, etc.).

Q5. Detail all humane endpoints used in this study indicating the criteria utilized and the frequency and timing of observations.

1. Detail criteria that will be used to remove subjects from study, require euthanasia, or allow for veterinary medical or nursing care.
2. If the protocol will follow the guidelines as specifically outlined under IACUC policy 357 'Humane Endpoints" or specific guidelines for other models as referenced (IACUC Policy 304 "Tumor Burden Scoring Guidelines" or IACUC policy 363 " MPTP Guidelines") then those can simply be referenced here.
3. If other criteria are utilized, they should be described in detail.
4. Investigators, as subject matter experts for their model, are encouraged to propose measurable or assessable parameters for removal of animals from experiment for consideration by the IACUC that are more conducive to their research purposes and different from the IACUC default sets.
5. Disclose the schedule of monitoring of the study subjects for well-being.
6. Where the research is not expected to cause discernible harm, provide assurance that IACUC endpoints will be used in cases where subjects develop unexpected or spontaneous conditions.

EXPERIMENTS

1. Each experiment may only be associated with a single species.
2. For each column 1 experiment:
    a. Q3. Describe the experiment
        i. Provide a 3-5 sentence overview of how the experiment has been organized and will be conducted and done.
            1. Specifically, disclose the associated hypothesis or aim(s) for the experiment and explain how experiments are organized in terms of variables controlled and measured, the number of experimental groups, their sizes and differentiating characteristics (including genetic composition, gender(s), age(s), chemical, physical and/or biological agents administered; and surgical induction) up to, and including, euthanasia. If the experiment is supported by one or more rat, mouse, fish or bird breeding colonies maintained under this protocol, provide the number and direct reviewers to the Breeding section.
            2. Disclose if experiments will be repeated and, if so, the total number of repeats.
            3. Identify the types of data collected (e.g., behavior, phenotypic measurements, survival, images, biological materials such as blood, and/or tissues at euthanasia).
            4. Rely on SOPs (columns 6-7) to elaborate on these procedures and for the schedule and timing of these procedures to be covered by Q7.

    b. Q4. Justify the purpose of this experiment.
        i. Provide the scientific need for the running of the experiment and identification and justification for any unrelieved pain and/or distress.
        ii.
        iii. Different from Question 3 in the Scientific Aims section, focus here on the

rationale and justification for this particular experiment, not the project as a whole.

c. Q7: Procedure Timing.
    i. Provide the relationship of procedures for the experiment to each other and the overall schedule of the experiment, the frequency of each (e.g., hourly, daily, weekly, once at euthanasia, etc.) and duration of the period of time in association with the procedure (e.g., up to 6 months, once at euthanasia, etc.).
    ii. The rich-text field allows the use of tables, flow charts, and other diagrams or pictures and these are encouraged

d. Q8: Total Number of animals used in this experiment.
    i. Note Act-species animals require a breakdown by USDA pain category, non-Act species (i.e., rats, mice, birds, fish) do not. For these species, select “NA”.
    ii. This table question generates based on the species indicated within the experiment.

e. Q9: Housing Conditions.
    i. Identify any and all special housing requirements needed for the experiment (e.g., ABSL2, ABSL3, single housing, sterile housing, food restriction, water restriction, environmental alteration, chemical containment, lab-provided care, delayed weaning, etc.).
    ii. In many cases (i.e. “No Specialized housing-standard care only”) very little description or justification would be required, whereas in other situations more details would be required.

PROCEDURE PERSONNEL ASSIGNMENT

Q1. Select the team members who will be performing each procedure: Note that this table will prepopulate with all of the procedures defined in the last section and will originally default to having all staff listed as performing all procedures. To delete a team member from any given procedure simply click on the icon out to the right of the row (pencil icon). You can then unselect any given team member by unclicking their name.

Note that where veterinary and other specialized staff associated with the animal resources programs will be participants in the research, they can be added by selecting options such as “Managed Breeding Service DAR”, “Imaging Personnel Yerkes”, “Behavioral Management Yerkes” and “Res_Reources Yerkes”

Q2. Team member Training: This field should auto-populate for all team members. Please note all training and if you feel that any is missing please contact the office for assistance in having this updated.

STRAINS

1. Q1. Respond “yes” to this query if there are any genotypes associated with adverse phenotypes. Disregard the reference to “strains”.
2. Q2. List any “Genotypes with Adverse Phenotypes” rather than “Identify Background Strains”.

ANIMAL JUSTIFICATION

Note that this section is to add animals other than those justified for specific experiments such as breeders, those for training, unforeseen losses, and possibly high mortality models and to explain why.

1. Q1. Click Update to add additional subjects above those carried-over from the experiments

section.
2. Q2. If you update the animal numbers in Q1, identify the reason. Common purposes to increase animal numbers above those necessary for experiments are breeding colonies that generate experimental subjects or to compensate for expected mortality or complications, unforeseen losses, to train new personnel and/or learn new techniques.
3. Q3. Justify the number of animals.
    a. For each of the reasons necessary to increase animal numbers sum the head-count for each purpose and provide reasoning for arriving at that number.
    b. Specifics of breeding colonies should not be provided here as they are covered in the BREEDING section.

ALTERNATIVES

Q1. Record all searches for alternatives for each procedure that causes pain or distress, even if relieved (such as surgery, lymph node biopsy, etc.).
Click on the +add icon to populate the table with your procedures identified as having pain and/or stress. A text box will appear with a series of questions as follows:

1. Procedure causing pain or distress: use the … icon to see whether or not any procedures are listed here for your protocol. If any of the procedures you have either written (team) or chosen (standard) has the potential for more than momentary pain or distress, then those procedures will be found under the menu button for question 1 in the “Add Procedures” field. Choose **each** of the procedures that are identified here independently and complete the rest of the questions for each.
2. Date of search: Date last search performed. Note it is recommended (but not required) that search results be saved by the PI team.
3. Use at least two databases - either ALTBIB or AWIC combined with PubMed, Medline or equivalent.
4. Combine procedure key words and the species used related to the experiments with "Animal welfare" and "animal testing alternatives". There should not be any more than 3-4 key words in combination for most procedures.
5. Disclose if potential alternatives were identified. If they are not going to be used, justify as to why not.
6. Enter time period covered by search using the calendar function.

Q2. Identify any other references used to find alternatives (such as periodicals, publications, and consultation)

1. Use this section to provide references or other materials including, but is not limited to, the background and experience of the PI including participation on study section, organization of meetings, conferences and colloquia, or consultation with a bona fide expert.
2. Provide a narrative of appropriate length detailing how the principles of Reduction of animal use and Refinement of experimental methods have been incorporated into the conduct of the research.
    a. Reduction. Describe how the number of animals to be used has been minimized in this protocol and explain why further reduction would disproportionately compromise the value of the data. Reduction can be achieved, for example, by using statistical methods and power analysis to guide experimental group sizes and repeats along with rigorous control of experimental variables.
    b. Refinement. Describe the refinements that have been incorporated into this work, explain why no further refinements are feasible, and consider how future work might be refined. Refinement is often achieved through the use of state-of-the-art anesthesia, minimally invasive surgical technique, and effective pain management programs; post-op and nursing care interventions where indicated; ante mortem endpoints tailored to the specific experimental goals; dose or exposure minimization; chronological imaging protocols; use of fine needle aspirate over

biopsy; and other innovations to prevent or minimize pain and/or distress and avoid death as a routine endpoint.

c. Note that the third “R” of replacement is addressed at item Q2 of the Scientific Aims section.

DUPLICATION

1. Q2. Identify any other references used to determine that the research is not unnecessarily duplicative. Beyond literature searches, the expertise of the investigator, applicable relevant experience, such as service on study section, and competitive climate for the source of funding are welcomed.

BREEDING

1. If breeding is not a component of this project, this section will be absent.
2. If breeding is covered in a Team or Standard Procedure associated with the Experiments Section, it is not necessary to complete this section. State “refers to applicable Procedure” instead.
3. In the case of rats, mice, fish or birds, if there is not a breeding Procedure description or lab-specific SOP, at Q3 provide the attributes and necessary production from each genotype maintained to support the studies in a logical and easy-to-follow manner, including:
    a. The mean and maximum number of breeding cages of each.
    b. The male:female breeder ratio in those breeding cages.
    c. The expected production (if not known, use 0.5 pups weaned/breeding female/week for genotypes on inbred background and 1.5 pups weaned/breeding female/week for outbred, non-inbred, crossbred or early back-crossed background).
    d. The frequency of replacement of breeders (prior to senescence and at reproductive decline; usually in the 6-9 month of age range).
    e. Segregate progeny into the number of pups anticipated to be by age, genotype, gender and/or other attributes to be useful experimentally and those that will not be useful experimentally and must be culled.
    f. Please note that in-weaned pups are not tabulated on the census (i.e., only weaned animals are counted) and these should not be included in the tabular amounts.
    g. Reviewers should be able to easily link the production output here from each colony as attributed to each experiment.

HOUSING AND USE

Complete the table by entering the sites for housing and experimental use.

DISPOSITION

Q1: Disposition plans for the animals when this research is complete:
This is a multi-select box, so please check all that apply.
NOTE: If euthanasia is selected, then the procedures used for euthanasia must also be described within
the experimental section of the protocol.
Q2: If other, provide an animal disposition description:
Text box to describe any alternatives not shown in the menu above.

ALLOCATING ANIMAL COUNTS

Note that the system auto-populates a table showing each source directly funding animal expenses (from the Funding Source table) and a second set of columns indicating all species and adjusted animal counts.

Q1: Identify which animals will be covered by each funding source associated with this protocol. Use the Update icon to add and update funding sources. For each funding source the following questions are populated:
1)Species:
pull down based on the species listed on the protocol
2) Number of animals covered:
This is a text field to add the number of animals associated with each funding source. An actual number is required, not a percentage such as 50% or text such as “all”.
3) Previously assigned Segment ID:
This field refers to any segment used for this funding source under the Topaz system. If there was a previous segment (such as mouse 1, mouse 2) this is needed here so that the DAR’s can reconcile both billing and transfer of any animals from the existing protocol to the new eIACUC submission
4) Comments: This is a free text field.

SUPPORTING DOCUMENTS

1. If there are biological hazards used, attach the current letter of approval from the Institutional Biosafety Committee (IBC) for the use of biological hazards signed by Chair G. Marshall Lyon, MD, MMSc with the "Biosafety Protocol Approval Letter - Addendum" defining the conditions of approved use of the biological hazard. This document is normally identified as "Biosafety File # beginning with the prefix "HAD...". The list of biological materials requiring EHSO/IBC review can be found here: http://www.ehso.emory.edu/research-safety/biosafety-protocol.html.
2. If hazardous chemicals, radioisotopes, lasers or other hazards are used for animal research purposes, attach the appropriate review and approval documentation.
3. Immortal cell lines in research rodents must be confirmed as fully pathogen-free, particularly of viruses, by the DAR. Please review the material at http://www.dar.emory.edu/vetcare/Cell_and_biological_testing_policy.pdf for specific requirements and follow them. Attach a copy of the DAR-issued biologicals approval letter.
4. Lab-specific SOPs for breeding colony management, procedures not logically covered by Team or Standard Procedures, or publications or other documents deemed by the PI to be valuable in association with the protocol can be attached here.