# Animal Research Protocol Guide (IACUC RAP Manual)

## *Introduction*

This comprehensive, illustrated manual details requirements to create an animal research protocol at UC and navigation and use of UC's animal research protocol website, IACUC Research Administration Portal (RAP). If you are viewing this document electronically, you can click any title in the Table of Contents to quickly jump to a specific section.

## *Table of Contents*

## *Welcome to the UC Animal Care and Use Program*

The University of Cincinnati Animal Care and Use Program (ACUP) is responsible for the regulatory oversight and veterinary care of all research activities that involve live, vertebrate animals at the University of Cincinnati. The program is comprised of 2 units: the Animal Regulatory Compliance Office (IACUC office), and Laboratory Animal Medical Services (LAMS).

## *Getting Started*

### Get Your Training and IACUC/AOPS RAP Access

ACUP onboarding training includes both IACUC and LAMS trainings, as well as IACUC/AOPS RAP and facility access.

**ACUP Onboarding Steps**

1. Principal Investigator (PI) or PI proxy must complete ACUP Training Request form (trainee M# needed). This form is a "one-stop shop" that collects information needed to assign appropriate training, create an IACUC/AOPS RAP profile, and provide protocol and facility access. It is important that this information is filled out completely and accurately. **Incorrect or incomplete information may result in delays in starting your research.**
2. Once Animal Training receives the form, an IACUC/AOPS RAP profile will be created and an email will be sent to schedule required training. Training requirements are briefly summarized below and additional details are provided in the ACUP Training Policy and on Bearcats Landing.
    a. Requirements prior to joining and IACUC protocol:
        - **Online Training Courses via Collaborative Institutional Training Initiative (CITI):** The modules in CITI give an overview of how to work with an IACUC basics on what you need to know to work with your species; the three R's-replacement, reduction, and refinement; identifying and reducing pain and distress; and surgery.
        - **IACUC Orientation**: This session is typically scheduled every other Wednesday alternating morning and afternoon and will familiarize you with your roles and responsibilities as an animal researcher.
        - **Occupational Health and Safety for Animal Handlers:** This program applies to all faculty, staff, and students who have direct or indirect contact with research animals. The species of animal and associated hazards encountered in the workplace determine what type of health assessment and safety training each person will receive. You will be sent a link to Compliance Training website (CPD) to complete the Health Surveillance Assessment. **You must have occupational health clearance prior to working with/or near animals. Must be completed prior to LAMS facility orientation and LAMS animal skills.**
        - **LAMS Facility, Satellite, or Field Orientation:** This session is an introduction to animal facilities and laboratories where animal use occurs, including introduction to animal care and use Standard Operating Procedures.
        - **LAMS Animal Skills (all species except USDA large animals):** This hands-on class includes training on the handling and restraint of rodents, basic injections and euthanasia methods.
    b. After joining the protocol, before performing specific procedures
        - CSI/LAMS USDA Large Animal Procedure/Surgical Training
        - Principles of Surgery
        - LAMS Hazard Training
        - Animal Acquisition
3. Training renewal (every 3 years)
    a. **Occupational Health and Safety for Animal Handlers:** Enrollment in Occupational Health and Safety Program for Animal Research requires renewal every 3 years. You must complete the Health Surveillance Assessment in CPD before your occupational health clearance expires.
    b. **CITI training:** Working with the IACUC

## Prepare an IACUC Protocol

Preparing a research project submission for IACUC review can be a complex process. In order to streamline the process and hopefully avoid any undue burden, it is helpful to review a couple of basic steps:

1. **Consult the Laboratory Animal Medical Services (LAMS) and the Attending Veterinarian.**
   The IACUC strongly recommends that applicants consult with LAMS and Veterinarian prior to application submission. LAMS staff will be able to walk you through what is available to you in our facilities and how we may be able to accommodate your study.

   The Attending Veterinarian is responsible for oversight of the well-being and clinical care of the laboratory animals. The veterinarian will review with you the design of your study, and assist you with information regarding animal care, housing, animal procedures and surgery, pain and distress, anesthesia and analgesia, euthanasia and any other questions that you may have.

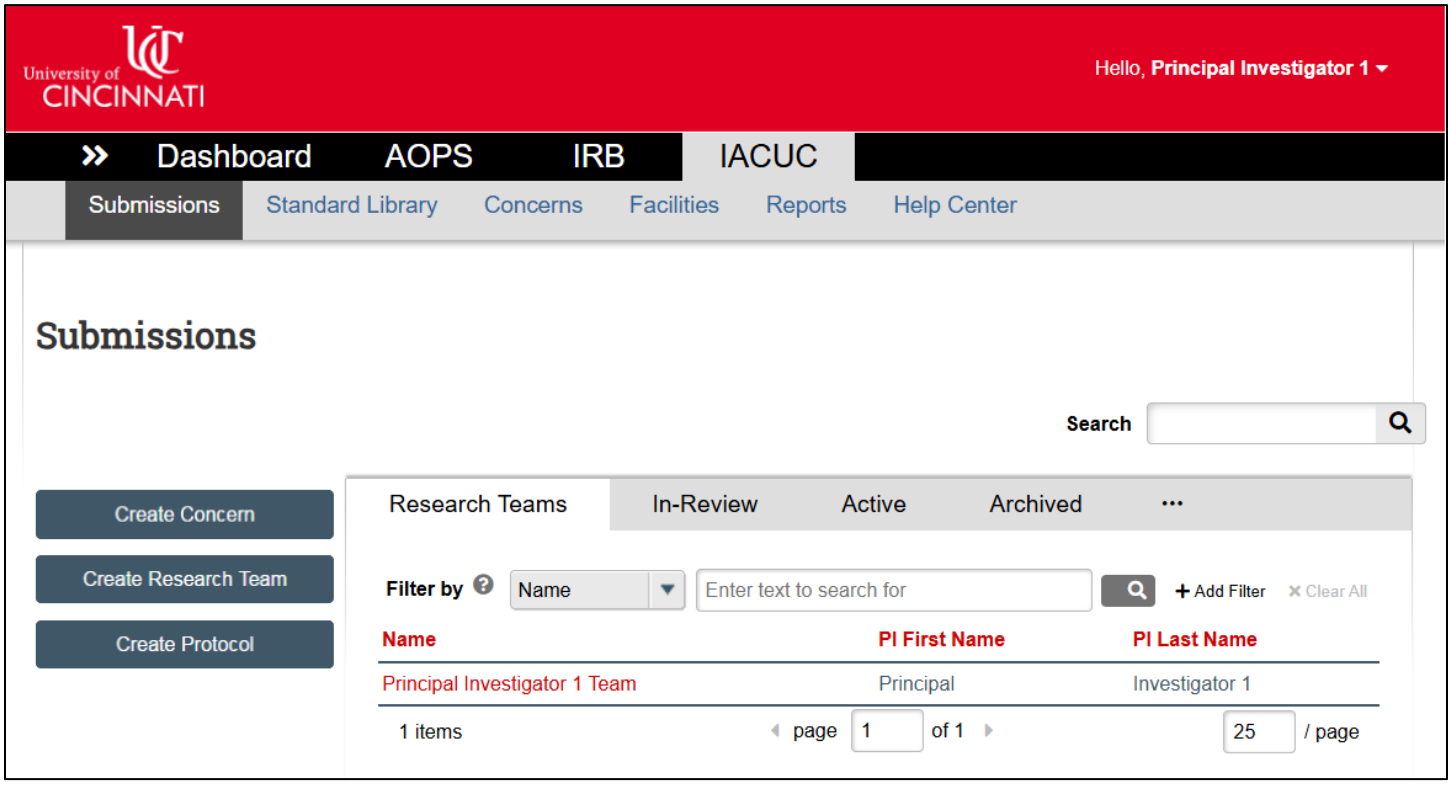
2. **Begin the process to training completion.**
   Direct all personnel listed to make sure that all mandatory training has been completed. Please contact the IACUC office for guidance on specific required training. This is important to complete at the time of protocol submission. Incomplete training can hold up study approvals.

3. **Write your Animal Research Protocol in IACUC RAP.**
   Design your study and enter it in RAP.

   The protocol form template includes questions on:
   a) Project title, Principal Investigator, key personnel
   b) Project information and specific aims, including lay summary and harm/benefit
   c) Justification for why live animals must be used and justification for the species
   d) Literature search and consideration of alternatives to animal research (3Rs-replace, refine, reduce)
   e) Experimental/study design: a complete, detailed description of all procedures including timelines
   f) Animal number justification
   g) Pain and distress information as well as measures to minimize pain and distress
   h) Animal husbandry (how animals will be cared for) and housing of animals
   i) Anticipated effects of procedures or administered substances
   j) Treatments, exposures, and biosafety levels
   k) Clear and concise humane endpoints and euthanasia

## *IACUC RAP Navigation*

Log in to the IACUC Research Administration Portal (RAP) website (https://acup.uc.edu/IACUC/) using your UC credentials. **The most compatible web browsers are Firefox or Google Chrome.**




Use the primary navigation options (black) at the top of your screen to switch to different areas of the website:

**>> (double arrow):** use this to find your location on the website, or navigate back 1 or more pages
**Dashboard:** see all pending items assigned to you that are awaiting review/action
**IRB:** human research protocol submission and management (separate log in)
**IACUC:** animal research protocol submission and management (the focus of this tutorial)
**AOPS (Animal Operations):** LAMS vivarium operations and services

Use the secondary navigation options (light grey) at the top of your screen to access different sections:

**Submissions:** a list of all your IACUC protocols
**Standard Library:** a list of UC IACUC pre-approved substances and procedures
**Concerns:** review all concerns relating to your IACUC protocol(s)
**Facilities:** a list of all UC facilities (including closed/retired sites)
**Reports:** administrative reports for IACUC Office use only
**Help Center:** All ACUP policies and guidelines, forms and signs, and IACUC RAP tutorials

Finally, there are 3 action buttons (dark grey) on the left side of your screen:

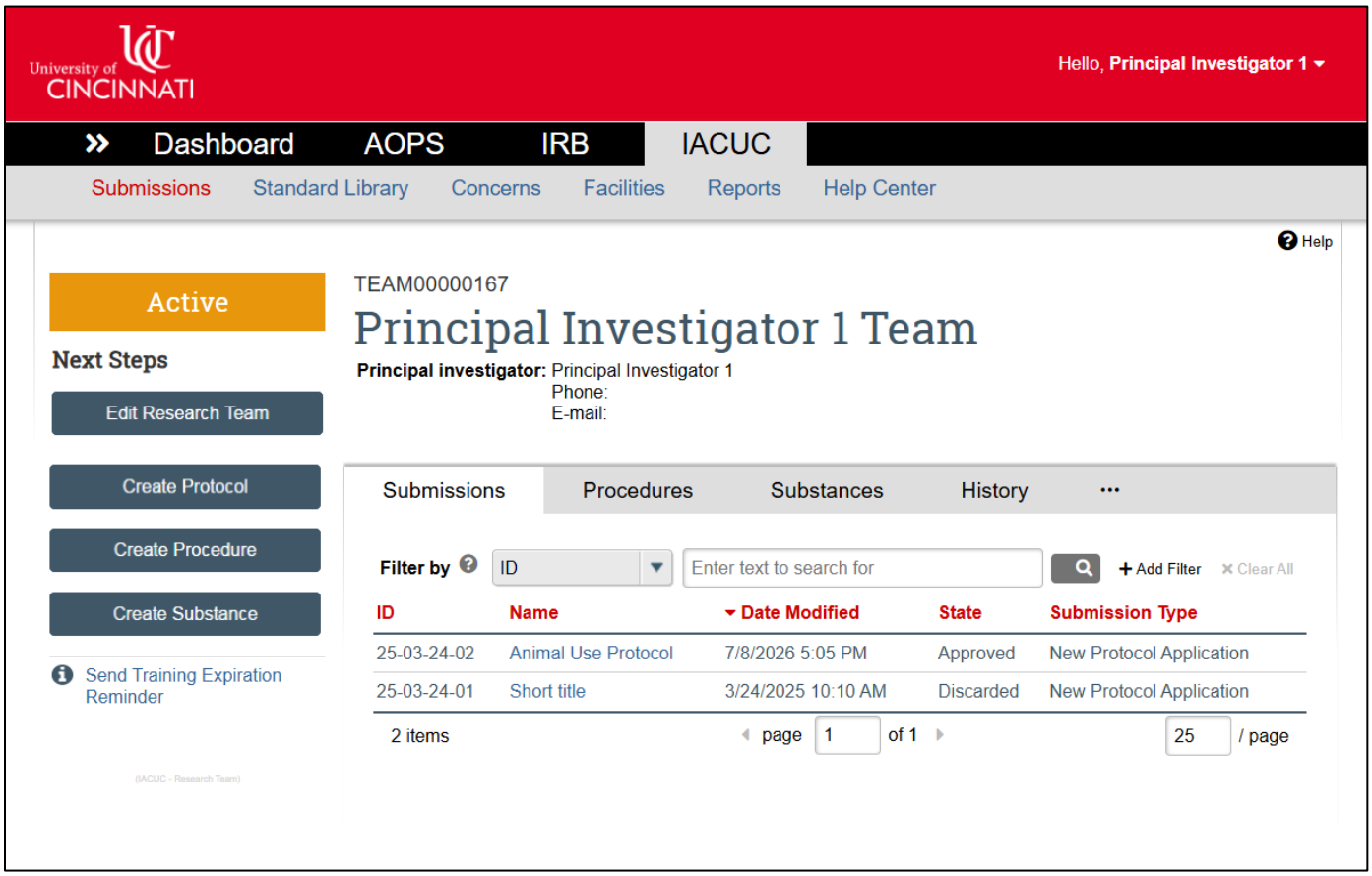
**Create Concerns:** review concerns for all of your IACUC protocols. Not currently in use.
**Create Research Team:** create a new list of researchers involved with your IACUC protocols
**Create Protocol:** create a new IACUC protocol

## *Research Teams*

The Research Team space belongs to your lab and is where all of your documents can be found. You will need to create a Research team prior to drafting any protocols, procedures and substances.

A Research Team is a list of personnel who have permission to read on the IACUC protocol when logged into the RAP website. The research team **must** include all personnel that will have an active role on your protocol, but can also include internal collaborators, administrators, lab managers who may not have an active role on the animal use protocol.

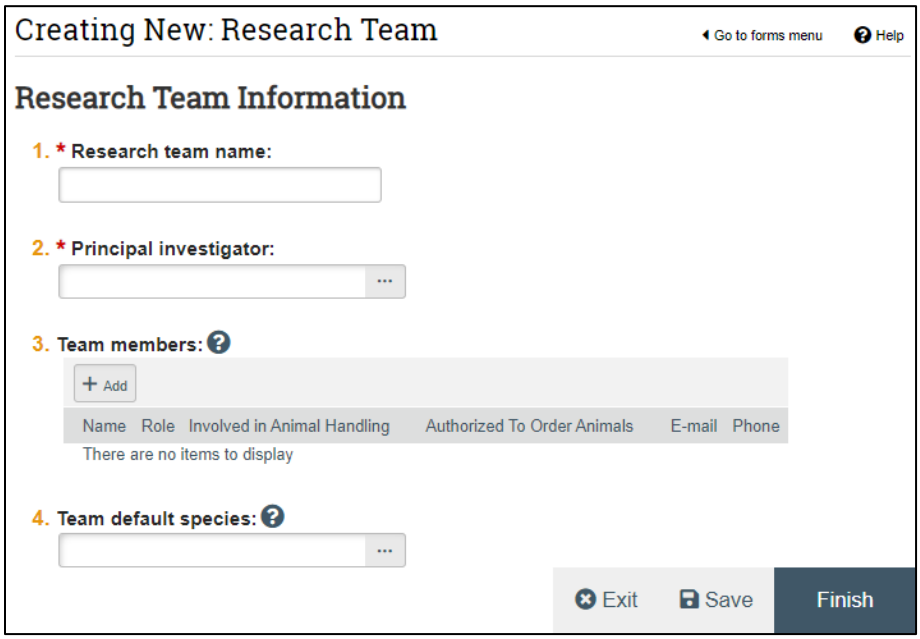
Principal Investigator (PI) or approved PI proxy have the responsibility of managing the Research Team by ensuring the list is current (see Edit an Existing Research Team).




In contrast, the Protocol Team Members is a specific list of personnel in the IACUC protocol who are approved to perform hands on animal work and/or order animals. Protocol team members must be reviewed and approved on the IACUC protocol and can only be edited by submitting a protocol amendment, which is subject to IACUC review and approval. More information on this process can be found in the Protocol Team Members section of this tutorial.

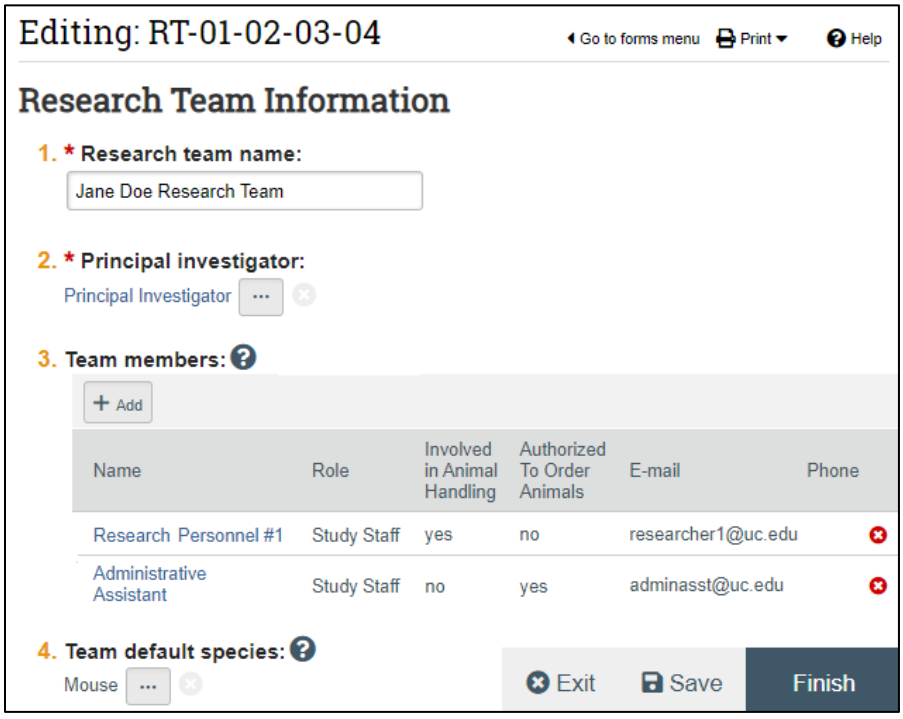
## Create a New Research Team

1. Click on the “IACUC” tab in the top navigation menu, then click the “Research Teams” sub-tab.
2. Click the “Create Research Team” button.
3. Answer all form questions. Research Team names usually include PI’s last name (e.g. Doe lab).
4. Select the “+ Add” button on Question 3 to add personnel. **Do not add PI to team members list.**
5. If your research group works with more than 1 species, do not add a default team species.
6. Select the “Finish” button to save your changes and close the form.




## Edit an Existing Research Team

1. Click on the “IACUC” tab in the top navigation menu, then click the “Research Teams” sub-tab.
2. Select the name of your Research Team, then select the “Edit Research Team” button.
3. Edit the Research Team name in Question 1 and add/remove Research Team members in Question 3.
    a. Use the +Add button to add a team member
    b. Use the red circle with x to remove a team member
4. Select the “Finish” button to save your changes and close the form.

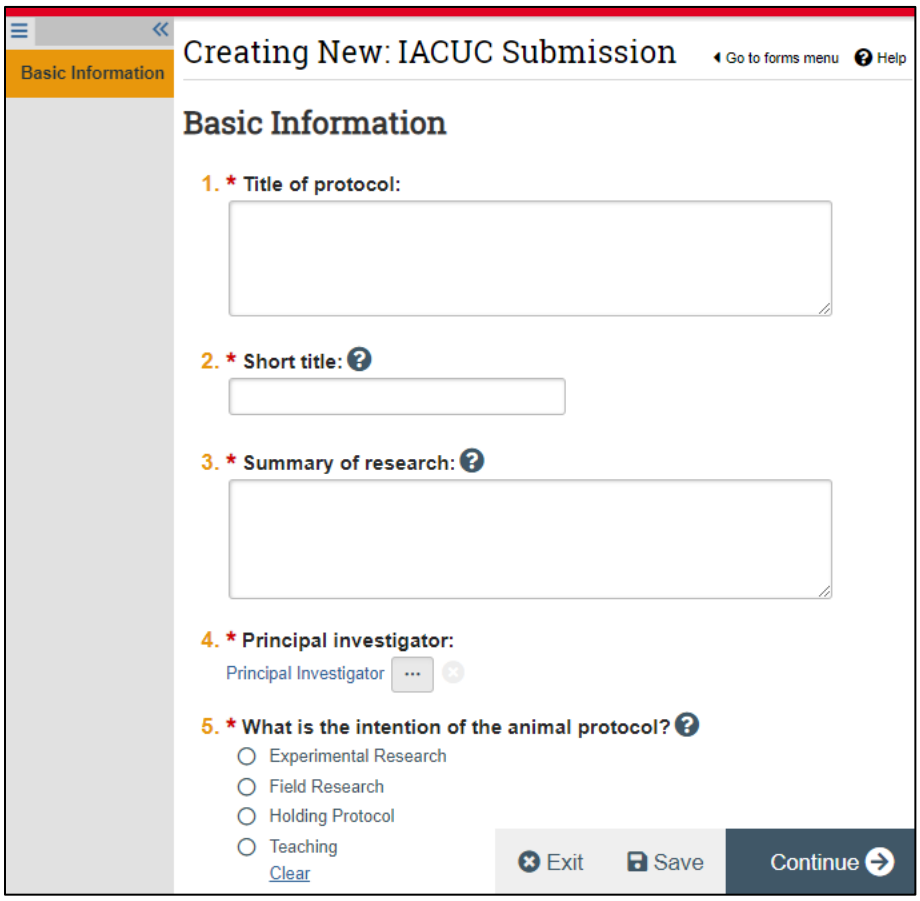


## *Create a New or Triennial IACUC Protocol*

We strongly recommend following these basic guidelines when creating an IACUC protocol:

- All required form fields are denoted by a **red asterisk (*).**
- Complete each form going page by page using the "Continue" button, to ensure no section is missed.

### Basic Information




Most questions in this section of the form are self-explanatory except for:

**Question 3 (Summary of research):**

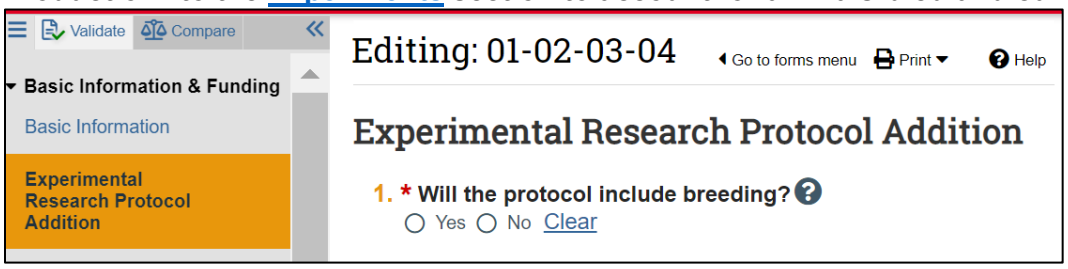
- Provide a short project description using non-technical/lay terms.
- Write this section as though you are providing a press release to a newspaper.
- Include the following information:
  - What central question is the protocol answering?
  - What is the value to humans, animals, the environment, or advancement of knowledge?
  - **Triennial submissions:** provide a brief 1-3 sentence summary of project progress over the last 3 years.

**Question 5: Protocol Intention**

- If your protocol includes both field and experimental research, select "Experimental Research" then create a "Field Research" experiment (see Experiments).

### Experimental Research Protocol Addition

Select "Yes" or "No" based on your research needs. **If you answer "Yes", you must add "Animal Production" to the Experiments section to account for animals bred and culled.**

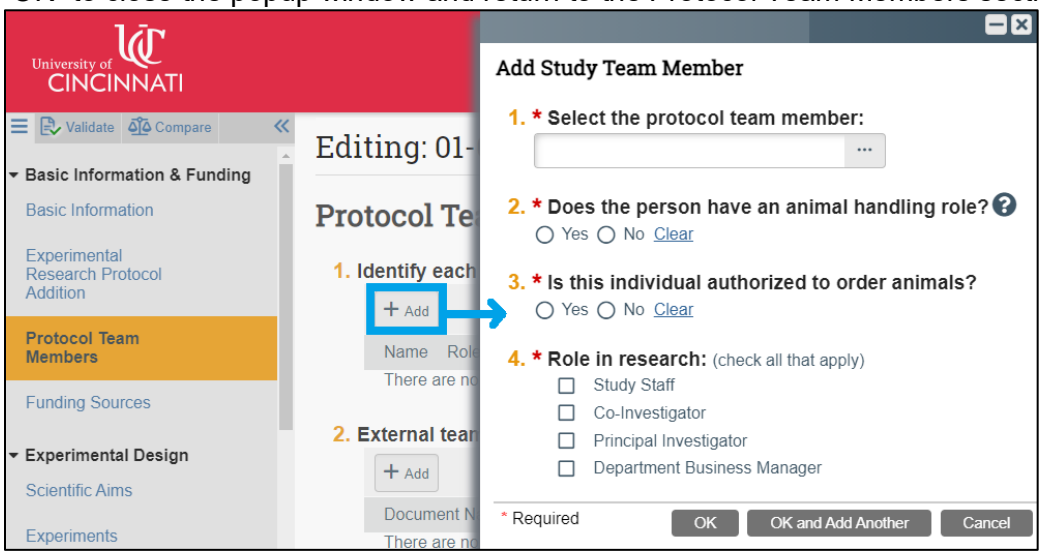



### Protocol Team Members

Protocol Team Members should include all personnel who are performing hands on animal work and/or ordering animals for the IACUC protocol. The list automatically populates from your Research Team List, but you can add or delete personnel as needed. All protocol personnel must complete training outlined in the ACUP Policy 101 (also accessible in IACUC RAP on the Help Center tab).

## Add Personnel to the Protocol Team Members List

1. Select the "+ Add" button to open the Add Study Team Member form in a popup window.
2. Begin typing the first or last name of the individual you wish to add. You may also press the ellipsis "…" button to scroll through a list of personnel in the RAP database. See Viewing and Scrolling Lists Using Ellipses (…) for more details.
    a. If you cannot locate an individual in the RAP database, send an email to animaltraining@uc.edu with the individual's UC username (6+2) and M#.
3. Provide answers for Questions 2 through 4 based on the individual's responsibilities on the IACUC protocol. Select "OK and Add Another" to add additional personnel. When you are finished, select the "OK" to close the popup window and return to the Protocol Team Members section of the protocol form.

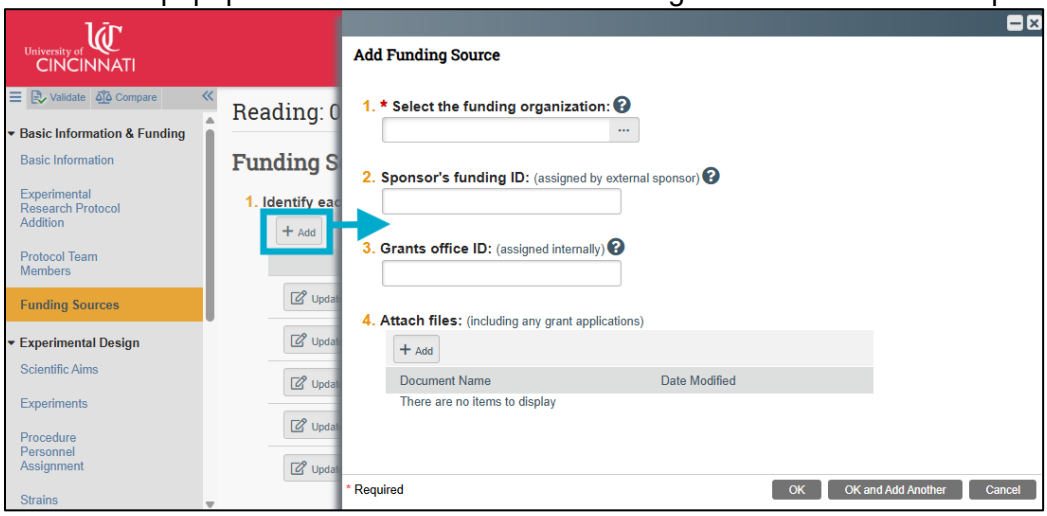



## Funding Sources

This section helps the IACUC associate protocols with specific grants. You should list all external and internal funding sources (e.g. industry sponsors, government agencies, departmental funds).

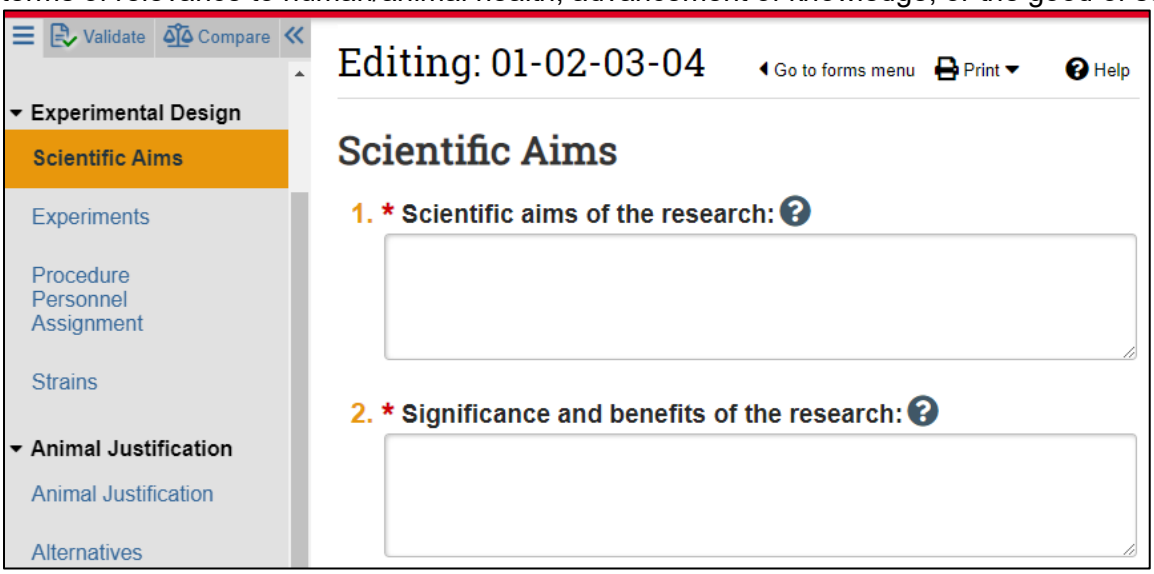
## Add Funding Sources to the IACUC Protocol

1. Select the "+ Add" button to open the Add Funding Agency form in a popup window.
2. Begin typing the full name (not acronym) of the funding agency. You may also press the ellipsis "…" button to scroll through a list of funding sources in the RAP database. See Viewing and Scrolling Lists Using Ellipses (…) for more details.
    a. To perform a partial search, use % as a wildcard (takes the place of 1 or more letters).
3. **If you can't locate the funding agency in this section, email the IACUC Office with details.**
4. Sponsor's funding ID and Grants office ID leave blank. They will be completed by the Grants office.
5. Select "OK and Add Another" to add additional funding sources. When you are finished, select the "OK" to close the popup window and return to the Funding Sources section of the protocol form.



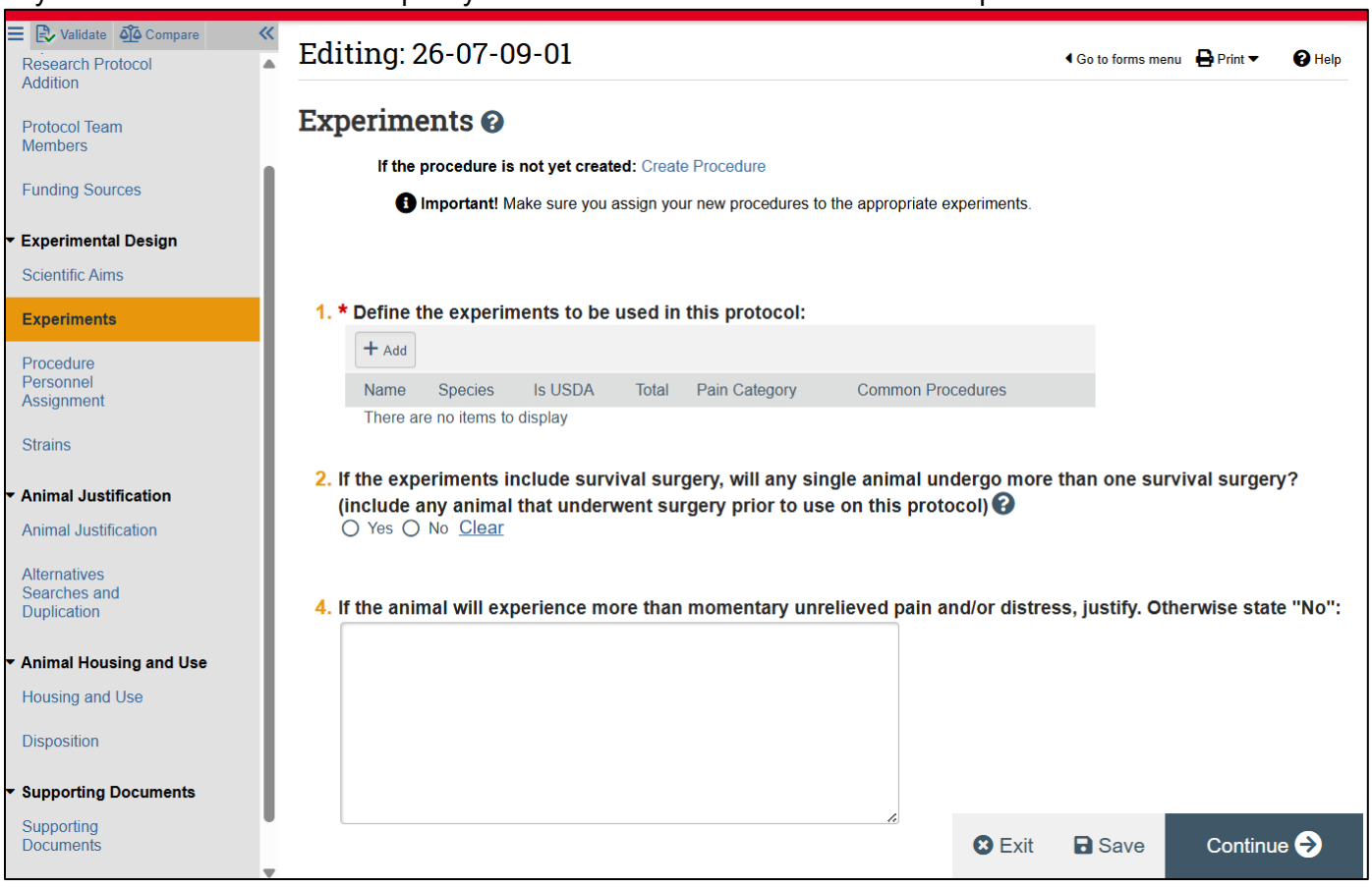
## Scientific Aims

1. **Scientific aims of the research:** goals of the research (recommend bullet point list).
2. **Significance and benefits of the research:** justify the benefits to society (humans, animals, the environment, advancement of knowledge) in relation to the potential detrimental impact on the animals.
    a) This is frequently justified from an ethical cost-benefit perspective: any animal pain, morbidity and mortality must be outweighed (or at least balanced) by the potential project benefits in terms of relevance to human/animal health, advancement of knowledge, or the good of society.



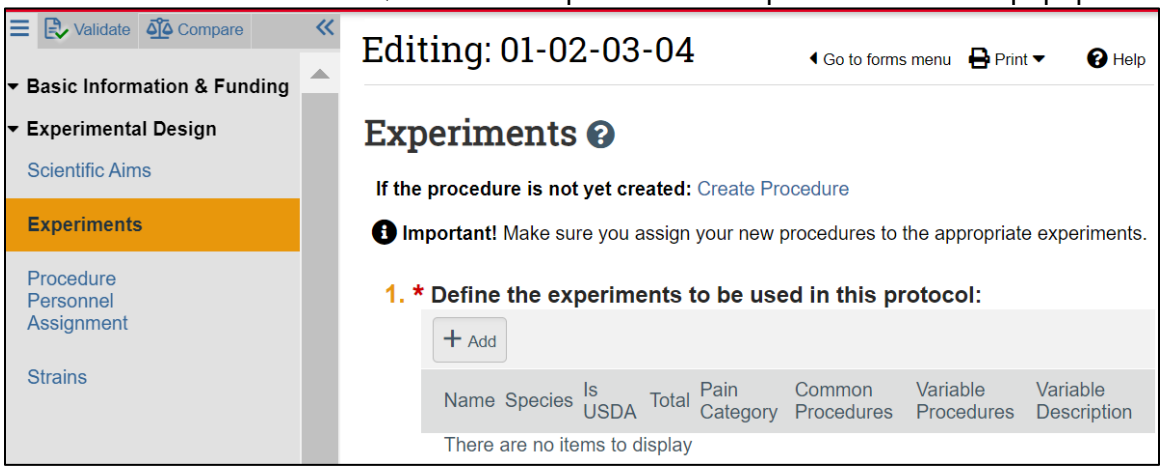

## Experiments

Add all protocol experiments to this section; experiments should be separated by specific aims/goals of the research. When you add an experiment (Question 1), you must select the applicable procedures and identify any variations. You must also specify the number of animals used in each experiment.



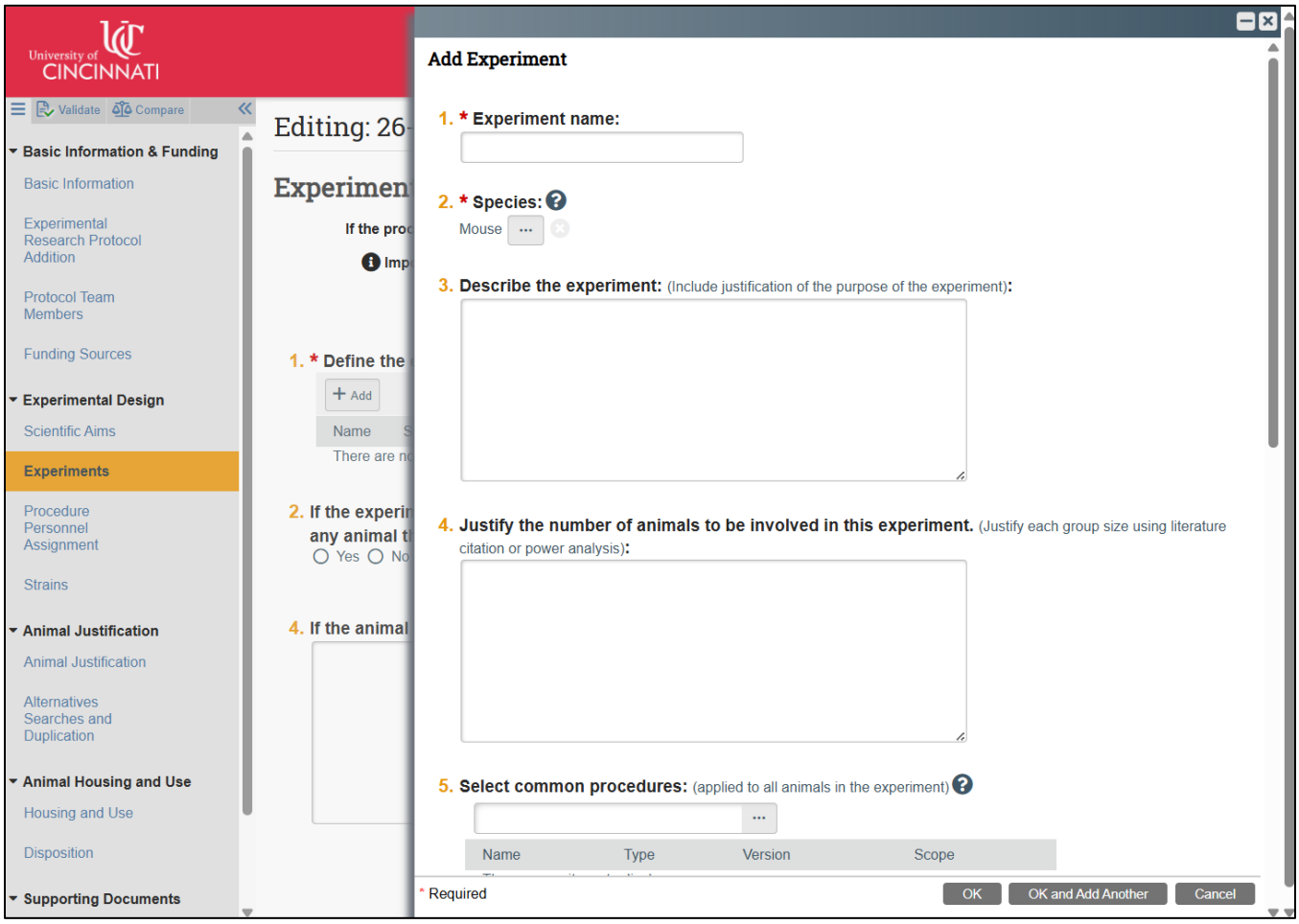
**Experiments Question 1: Add an Experiment to an IACUC Protocol**

Select the "+ Add" button in Question 1 to open the Add Experiment form in a popup window.




If you answered "Yes" to the breeding question in the Experimental Research Protocol Addition section, your first experiment should be "1-Animal Production/Breeding" experiment to account for animals bred/culled.

There are 10 questions within the Add Experiment form.



1. **Experiment name:** provide a short title of the experiment. Experiments should be separated by specific aims/goals of the research and numbered to facilitate cage card labelling.

2. **Species:** select the species involved in the experiment.

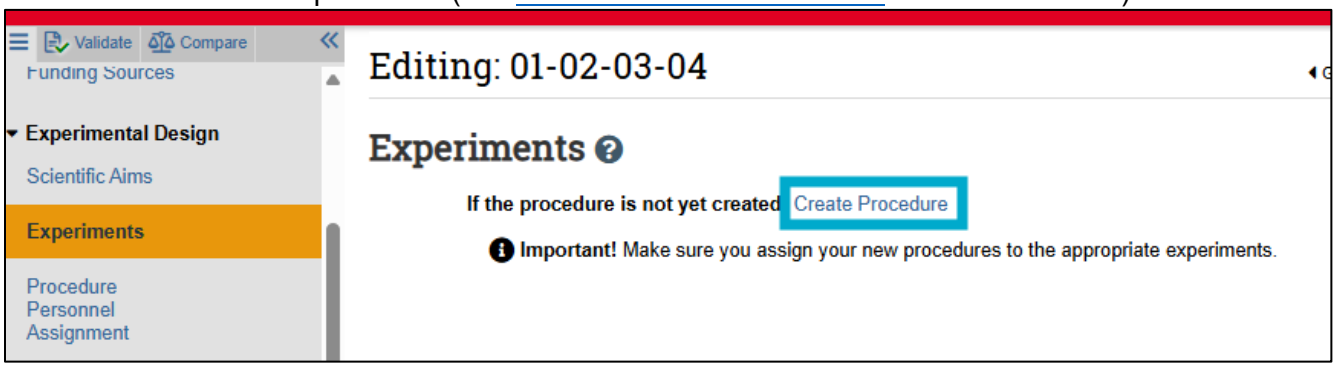
3. **Describe the experiment (Include justification of the purpose of the experiment):** You must provide enough information so that protocol reviewers understand what is happening to each animal.
    - See Appendix 1: Protocol Writing Examples for well-written study design examples.
    - Specific details of the individual procedures should be provided in the procedure form.

    This section must include the following study design information:
    - A clear, concise, sequential description of what is happening to each animal.
    - Outline of the procedures/manipulations performed on each experimental group including timing and frequency.
    - List the number of animals per group and number of groups per study. Include positive and negative controls, and if sex differences are being measured.
    - Timeline, including maximum duration of the experiment.
    - Only include animal numbers/experiments that can reasonably be performed in the next 3 years.

4. **Justify the number of animals involved in this experiment (justify each group size using literature citation or power analysis).** Justify each group size using literature citation or power analysis. Justify quantity of tissue used and/or need for pilot study (the "N").
    - Taconic Biosciences: Animal Research Sample Size Calculation
    - Animal Research Reporting of In Vivo Experiments - Sample Size

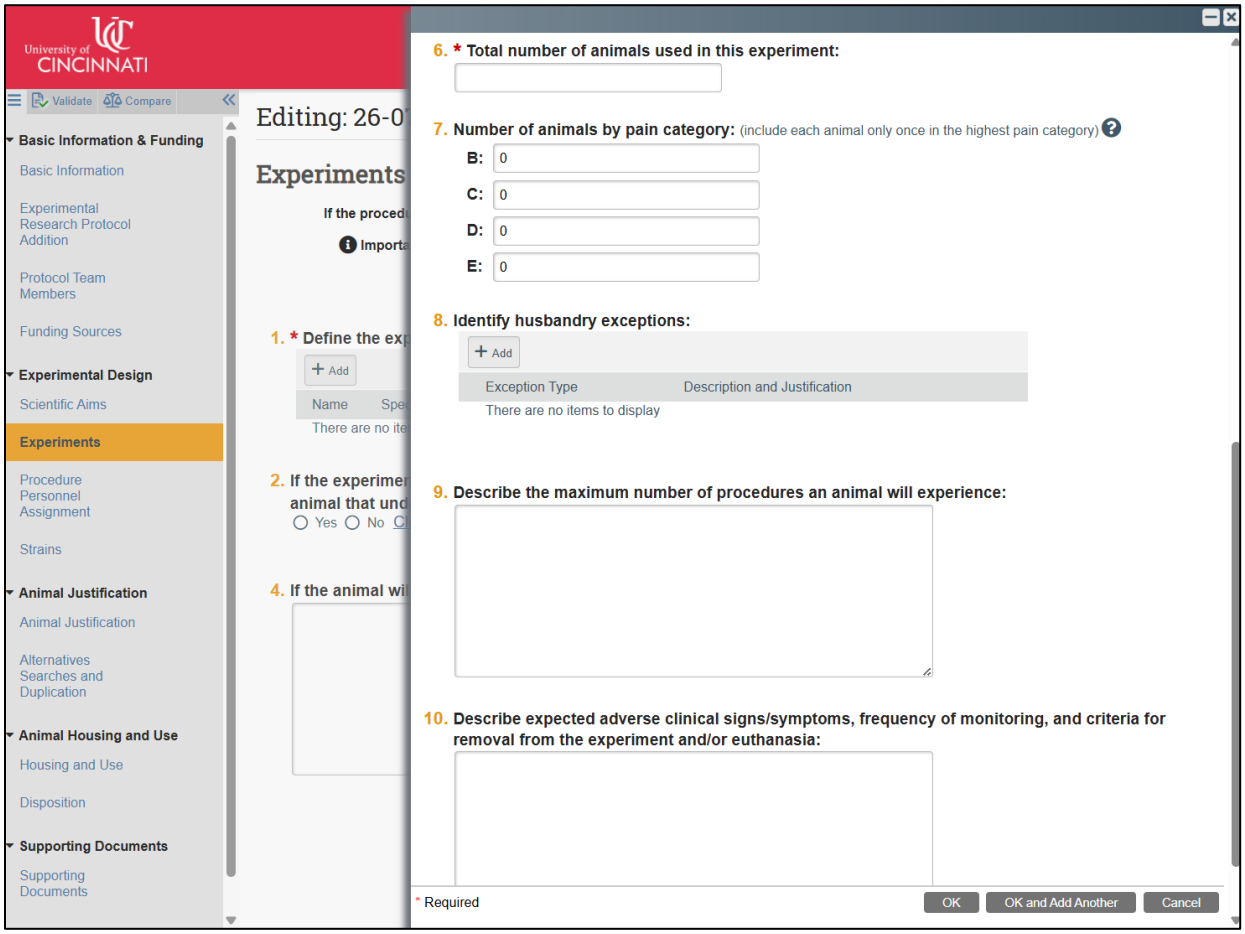
5. **Select common procedures: We have a library of over a hundred commonly used procedures that are available as IACUC approved standards.** Begin typing the procedure name to view a list of available options. You may also press the ellipsis "**…**" button to scroll through a list of procedures in the RAP database. See Viewing and Scrolling Lists Using Ellipses (…) for more details. You can also use the % as a wildcard to search for key words (see Easy Filtering and Searching for details).

    If a procedure does not appear in the list, go back to the Experiments section, and select the "Create Procedure" link at the top to add it (see Substances and Procedures section for details).



Each procedure is categorized into 1 of the following types:

- **Survival surgery:** Animals are allowed to recover from anesthesia.
  - **Major** - any surgical procedure that penetrates and exposes a body cavity or has potential to produce permanent/significant physical or physiological impairment.
  - **Minor** – any surgical procedure that does not penetrate or expose a body cavity or produces permanent/significant impairment of physical or physiological function.
- **Non-survival surgery:** Any surgical procedure in which animals are euthanized prior to recovering from anesthesia.
- **Tissue/Blood Collection:** Any tissue or fluid collection while the animal is still alive.
- **Behavioral:** Behavioral procedures are those in which animals have a conscious choice to participate (e.g. CPP, open field, running wheel without forced exercise.
- **Non-Surgical:** Any procedure that does not fit in any other category. Non-surgical procedures may have a behavioral component, but animal does not have a conscious choice to participate (e.g. forced exercise, Hargreaves, burn).
- **Substance Administration:** Any substance/agent administered to animals-including chemicals, biologicals, radioactive materials, diluents, etc.
- **Physical Restraint:** More than momentary physical restraint of an awake animal. Separate procedure is required for physical restraint greater than 10 minutes. Otherwise, the restraint must be described in its associated procedure and/or experiment.
- **Food and Fluid Restriction/Regulation:** Withholding of all or some food or water for a specific time period. Separate procedure is required for 16 or more hours of food restriction and 8 or more hours of water restriction. Otherwise, the restriction must be described in its associated procedure and/or experiment.
- **Imaging:** Separate procedure is only required if you will be performing the imaging or irradiation. Separate procedure is not required if the procedure is performed via temporary transfer.
- **Euthanasia:** Procedure that results in the humane death of an animal.



6. **Total number of animals used in this experiment:** provide a total count.

7. **Number of animals by pain category:**
   - USDA species: report each animal into the highest pain category of all performed procedures within each experiment.
     - e.g. an animal undergoing both category C and E procedures is reported in category E, but is not counted in both categories.
   - Non-USDA species: report all animals in the highest pain category listed on the protocol.
     - e.g. if a protocol lists 2 experiments (pain categories D and E respectively), then all protocol animals are reported in category E regardless of performed procedures.

8. **Identify husbandry exceptions: Refer to Husbandry Exception Guidelines.**
   - Include the exception type, description, and justification.
   - Satellite locations that store special diets must be listed in this section.
   - Some behavioral procedures/stressors (e.g. chronic stress paradigms) exceptions can be combined (e.g. non-standard caging can include large, small, tilt, wet, empty, etc.).
     - Acclimation Waiver
     - Altered Light Cycle Duration
     - Enrichment Policy Waiver
     - Medicated Water
     - Observation Frequency
     - Sanitation Frequency
     - Special Diet
     - Other
     - Altered Room Temperature
     - Do Not Disturb Post-birth
     - Extended Weaning
     - Non-standard Caging
     - Social Housing Policy Waiver
     - Solid Bottom Cage (no bedding)
     - Wire Bottom

   - Metabolism cages-IACUC Approved standard procedure is available for Q5: multiple exceptions are needed (non-standard caging, wire bottoms, withhold enrichment, single housing, if rat >250 gm guide exception to size may be required-see cage manufacturer and *Guide for Care and Use of Laboratory Animals* to confirm size requirements)
     **Note: This is where LAMS looks to confirm exceptions to standard practice.**

9. **Describe the maximum number of procedures an animal will experience.** Provide the maximum number of procedures per procedure type (Questions 5 and 6 above) to be performed on each animal. This should appear as a list (similar to the ingredients for a recipe).
   - Example: each animal may undergo up to 5 behavioral procedures, 1 major and 2 minor survival surgeries, 6 tissue collections, and 1 euthanasia.

10. **Describe expected adverse clinical signs/symptoms, frequency of monitoring, and criteria for removal from the experiment and/or euthanasia.** Include a detailed description of **ALL** humane endpoints for each experiment, including procedures within the experiment. If none, state "none expected". For frequency, provide details e.g. instead of 2 times/day, state 2 times per day-am and pm at least 4 hours apart.
    **Note: Remember to include how frequency of monitoring may change as clinical signs become apparent.**

    When you are finished adding experiments, select the "OK" button to close the Add Experiment form and return to the Experiments section of the new protocol form. **IMPORTANT: Use the "Save" and "Continue" buttons often to save the data that you have entered and not lose progress!**

- **If you have multiple similar experiments, save time by creating 1 experiment, copying the experiment, and making changes to the resulting copy.**

- **If your protocol includes both field and experimental research, you must select "Experimental Research" for Question 5 in the Basic Information section, and add a "Field Research" experiment that answers the following 3 questions:**

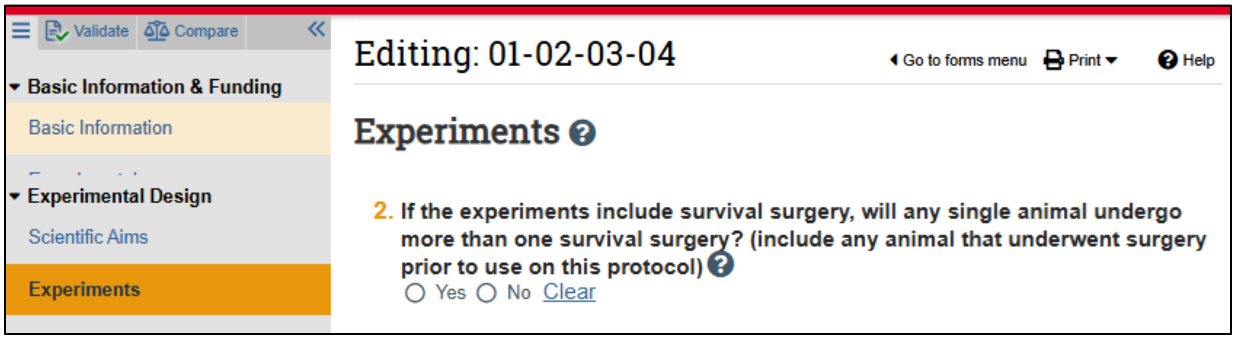
    1. **Where will these studies take place?**
    2. **Describe your plan if animals become injured during procedures.** Include the anesthetic, analgesic, or euthanasia procedures in the associated question.
    3. **List the required permits to conduct the field research.** Include permit number/oversight agency. Approved permits must be uploaded to the protocol.

**Experiments Questions 2 & 3: Multiple Survival Surgeries**

If an animal will undergo more than 1 survival surgery (minor or major), select **Yes** for Question 2.

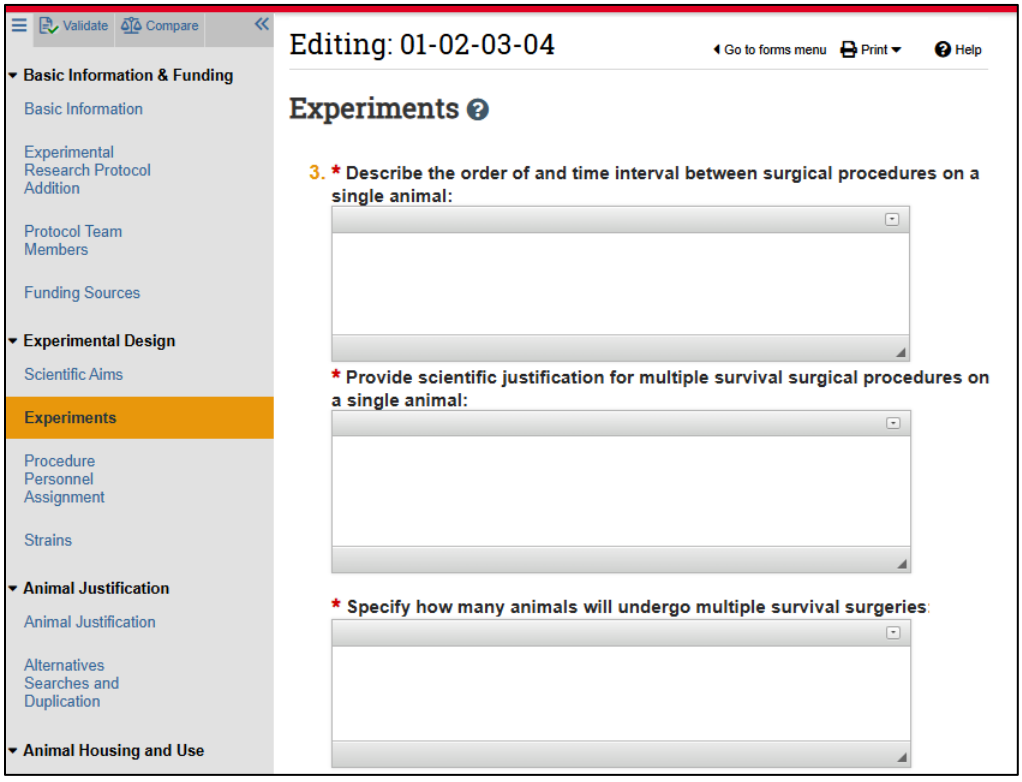
**Survival surgery includes both minor and major procedures.** Surgical procedure examples include:

- Major survival surgery: myocardial infarction, ovariectomy
- Minor survival surgery: subcutaneous minipump implantation, castration




The form will update to display Question 3, where you must provide the following information:

- Describe the order of and time interval between surgical procedures on a single animal.
- Provide scientific justification for multiple survival surgical procedures on a single animal.
- Specify how many animals will undergo multiple survival surgeries.



**Experiments Question 4: Momentary Pain/Distress**

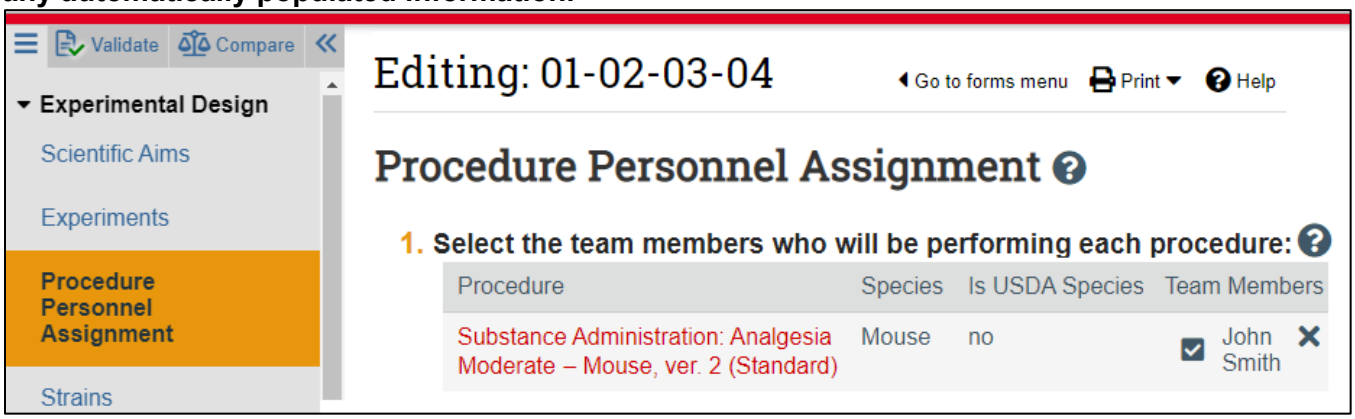
You must tie unrelieved pain and distress to the associated procedures and experiments.


Describe and justify more than momentary pain and distress if your protocol:

- Withholds analgesics, anesthetics, or tranquilizers.
    - Provide additional justification for the three classes of analgesics (opioids, NSAIDs, topical/local), related to each specific model; as well as when you can give one and not another e.g. can give opioids but not NSAIDs. Include literature citations.
- Contains any pain category E procedures.
    - Any procedure that results in pain/distress that is not relieved e.g. forced swim, noxious stimuli that the animal cannot avoid/escape, exposure to extreme environmental conditions, use of paralytics without anesthesia.
- Toxicological, microbiological, or infectious disease research that requires continuation after clinical signs are evident without medical care or that requires death as an endpoint.
- Refer to USDA/APHIS Animal Care Tech Note: Categorizing Animal Pain or Distress in Research Facility for additional information and examples.

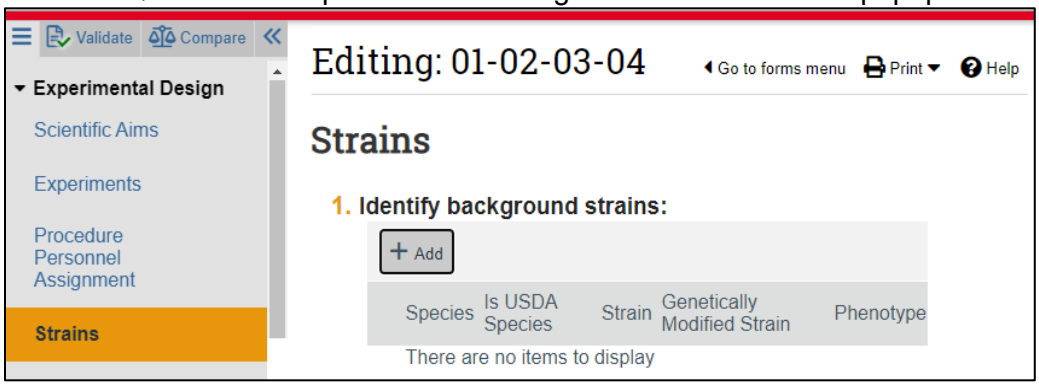
## Procedure Personnel Assignment

This section should automatically prefill with all team members performing all procedures. **Do not add or edit any automatically populated information.**



## Strains

Only list a strain if it has a spontaneous adverse phenotype that requires special care or observation (e.g. strain that develops tumors or develops multiple sclerosis without additional intervention). Click the "+ Add" button in Question 1 to open the Add Background Strain form in a popup window.

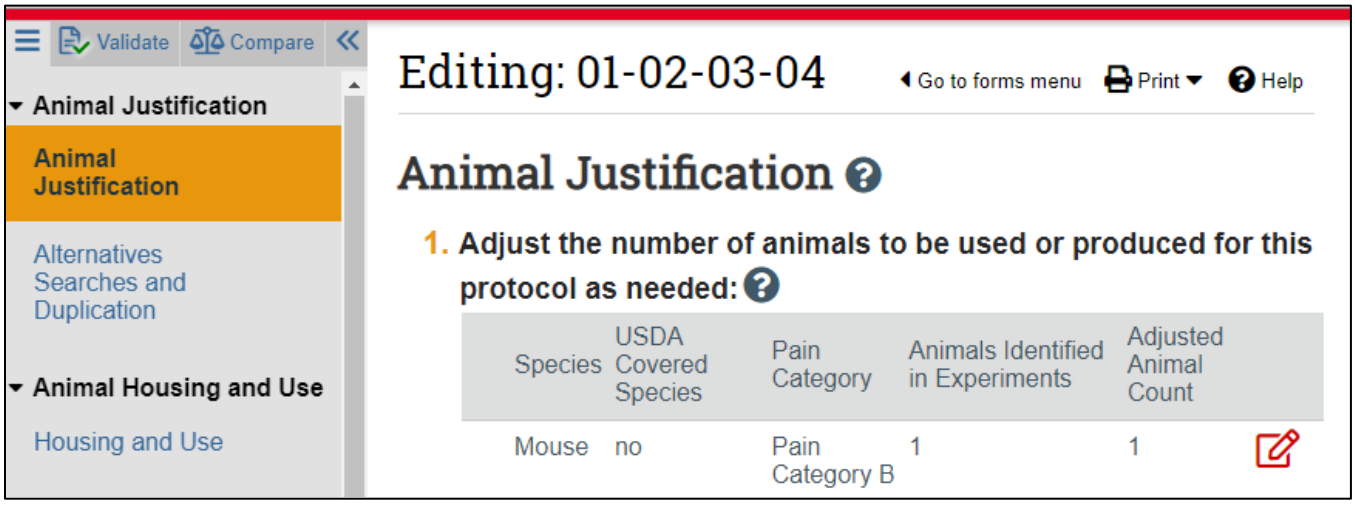



## Add Background Strains Form

There are 5 questions within the Add Background Strain form.

1. **Strain:** leave first field blank and skip to next 2 fields.
    - **If other, identify here:** type strain information in the text box (e.g. B6SJL.SOD1-G93A).
    - **Species:** select applicable species.
2. **Genetically modified strain:** select "Yes" or "No".
3. **Phenotype:** provide an ID or description.
4. **Percent of animals with the phenotype:** consider using Punnett squares or Hardy-Weinberg equilibrium calculators to assist with completing this field.
5. **Describe how animals will be managed if the phenotype causes welfare issues.** Include information regarding monitoring frequency, what will be monitored, and endpoints. Details should be provided relative to the impact of the phenotype on animal welfare – small impacts require few details, and large impacts require extensive details.

## Animal Justification




1. **Adjust animal numbers:** section is prefilled by the number of animals that are in your experiments.
2. **Explain animal number adjustment:** leave this question blank.
3. **Rationale for animal use:** Animals should be used only when necessary and only when their use is scientifically and ethically justified. Explain why computers, *in vitro* systems, invertebrates, or human subjects cannot be used in place of animal experiments in this protocol. For additional information, see Speaking of Research: The Animal Model.

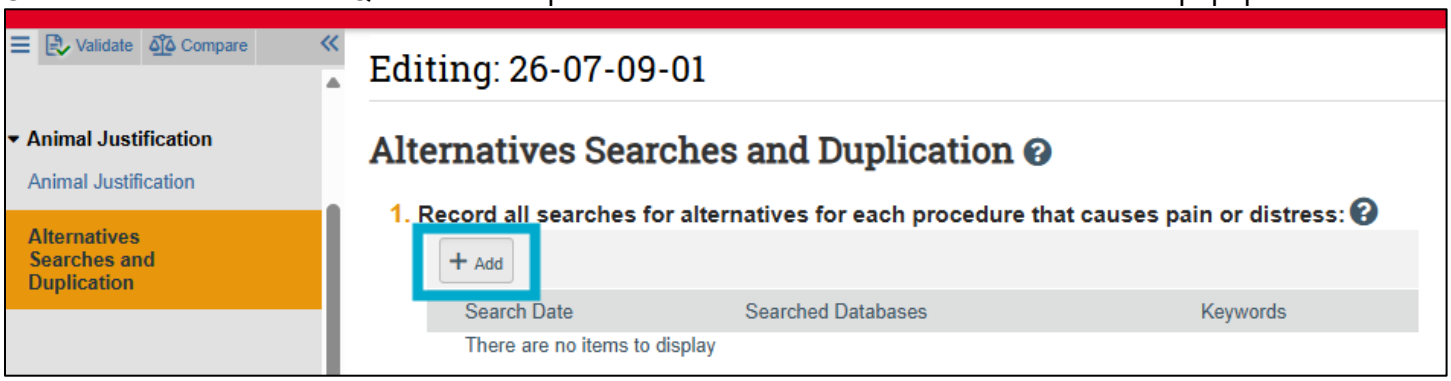
4. **Animal number justification:** write “Refer to each associated experiment for details”
5. **Animal species justification:** justify the use of each specific species listed on the protocol. Animals should be suitable for the purpose and of an appropriate species and genetic background to ensure scientific validity and reproducibility. For additional information, see Understanding Animal Research by Species.
6. **Supporting documents:** Do not use.

## Alternatives Searches and Duplication

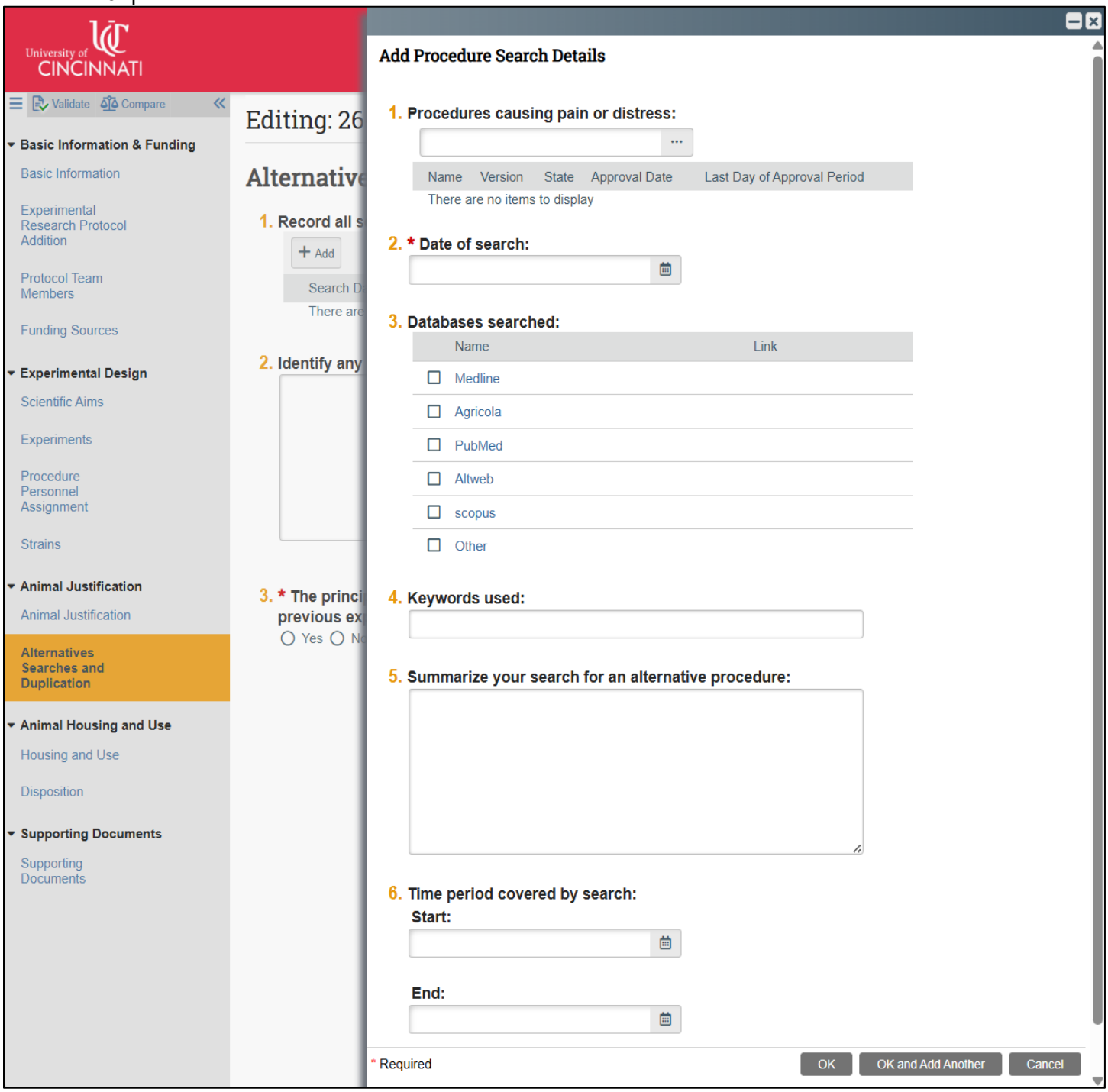
**For each procedure listed on your protocol that causes pain or distress, you must document a recent literature search.** If your procedure does not cause pain or distress, you may still be asked to complete this section by the IACUC or Attending Veterinarian in some circumstances. The search should look for animal alternatives, ways to reduce pain/distress, and methods to reduce the number of animals needed for the study. See also: USDA Guidance and literature search strategies.

### Alternatives Question 1: Add a Search for Alternatives

Click the “+ Add” button in Question 1 to open the Add Procedure Search Details form in a popup window.

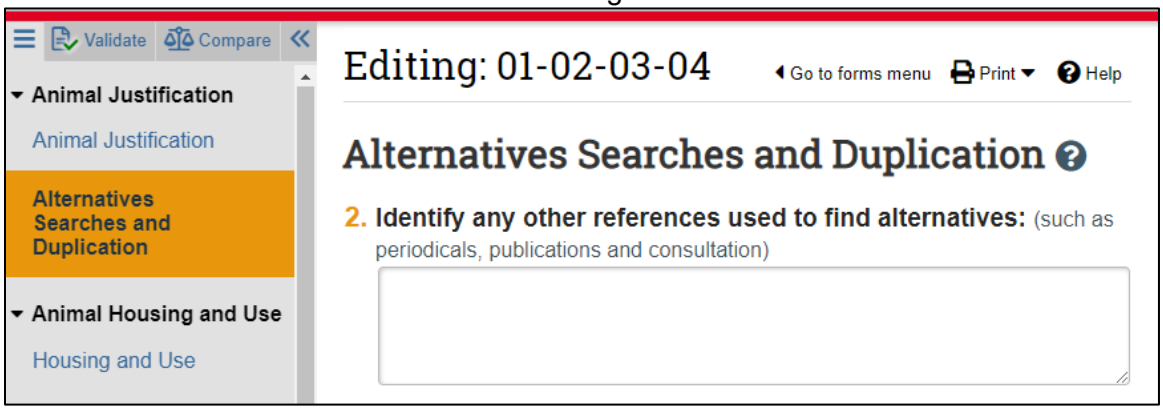


There are 6 questions within the Add Alternative Search Details form:




1) **Procedures causing pain or distress:** select 1 or more procedures that you are performing the literature search for. Begin typing the procedure name to view a list of available options, or press the ellipsis "**…**" button to scroll through a list of procedures found in the Experiments section of your IACUC protocol that cause pain or distress.
2) **Date of search**
3) **Databases searched:** check all that apply **(minimum of two)**.
4) **Keywords used:** words likely to be found in the title, abstract, and descriptor fields of the publication.
    - Use words included in specific aims, species, anatomy, and systems studied.
    - Use Boolean search strategies (e.g. cardiac AND rat OR mouse AND myocardial infarction).
5) **Summarize your search for an alternative procedure.**
6) **Time period covered by search:** each search must cover a minimum span of the last 10 years.

**Alternatives Question 2: Identify Other References**
Examples of other references include scientific meetings and outside collaborators.




**Alternatives Question 3: No Unnecessary Duplication of Previous Experiments**
Select the "Yes" option to confirm that the activities described in the protocol do not unnecessarily duplicate previous experiments, and that you will not unnecessarily duplicate other animal research.

## Field Research Details

This section contains 3 questions and only displays if you selected "Field Research" for Question 5 in the Basic Information section.

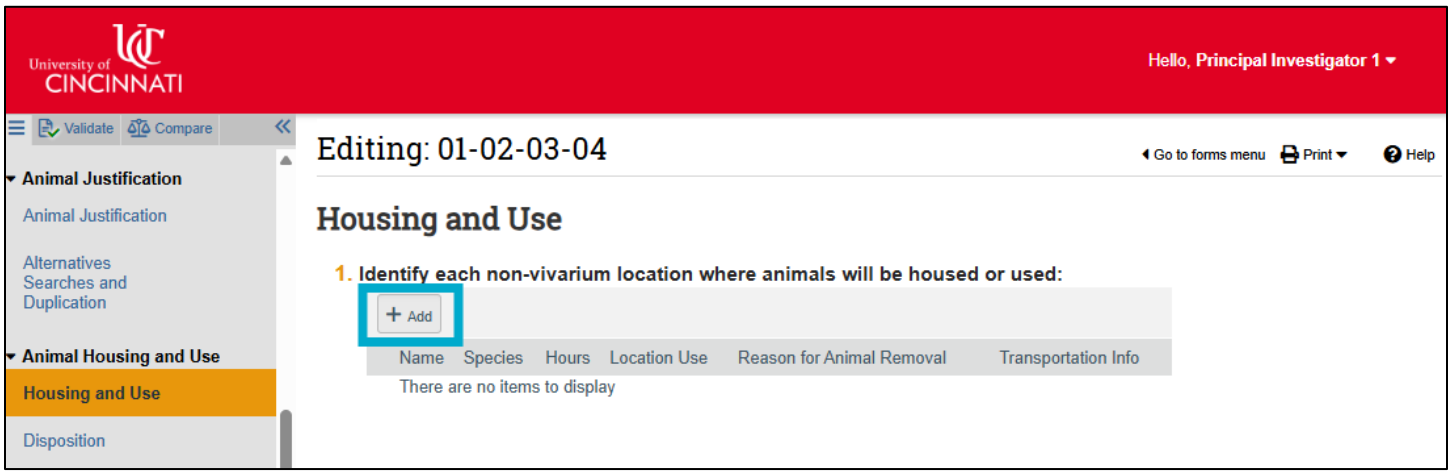
If your protocol includes both field and experimental research, you should instead select "Experimental Research" for Question 5 in the Basic Information and create an experiment in the Experiments section called "Field Research" that includes answers to the following 3 questions:

1. **Where will these studies take place?**
2. **Describe your plan if animals become injured during procedures:** Include the anesthetic, analgesic or euthanasia procedures in the associated question.
3. **List the required permits to conduct the field research.** Include permit numbers/oversight agency. Approved permits must be uploaded to protocol.

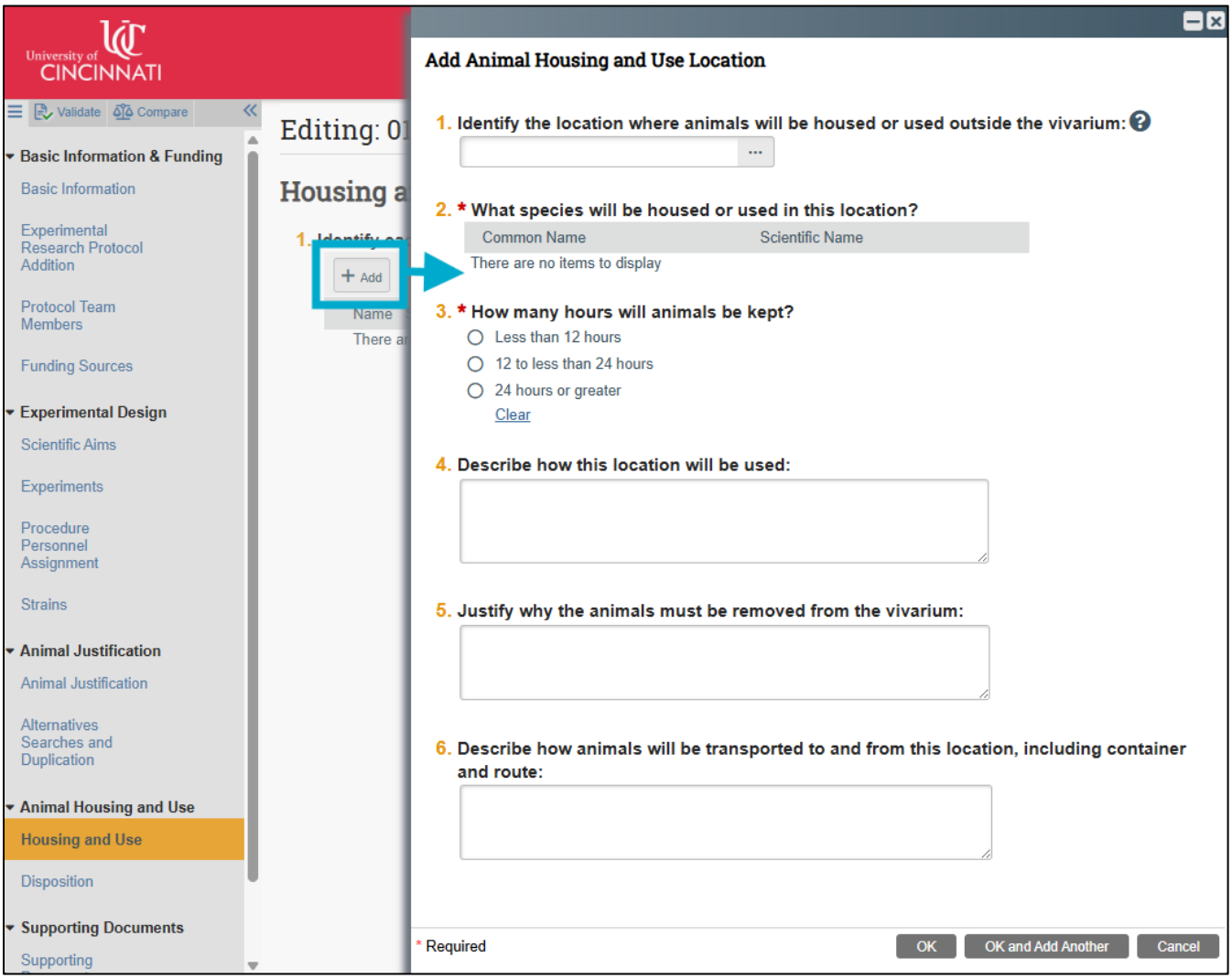
## Housing

Include all satellite locations where you are housing animals, using live animals, and/or storing diet outside of the vivarium. Refer to ACUP Policy 109 and Satellite Animal Use Areas and Diet Storage Locations Guidelines.

1. **Identify non-vivarium housing/procedural locations:** click the "+ Add" button in Question 1 to open the Add Animal Housing and Use Location form in a popup window.



There are 6 questions within the Add Animal Housing and Use Location form:




1. **Identify the location where animals will be housed or used outside the vivarium:** Begin typing the room number to view a list of available options. You may also press the ellipsis "**…**" button to scroll through a list of existing satellite locations found in the RAP database. See Viewing and Scrolling Lists Using Ellipses (…) for more details. If you cannot find the location, or it is not in the system, you will need to complete the New Satellite Location form to have the location added to the system.

2. **What species will be housed or used in this location?**

3. **How many hours will animals be kept?** Areas in which non-USDA covered species (e.g. mice, rats, ectotherms, avian) are held 24 hours or longer, or USDA covered species (e.g. guinea pigs) are held 12 hours or longer are considered housing areas. Use of a satellite housing location requires the PI to include a standard operating procedure (SOP) detailing animal husbandry and care with their protocol.

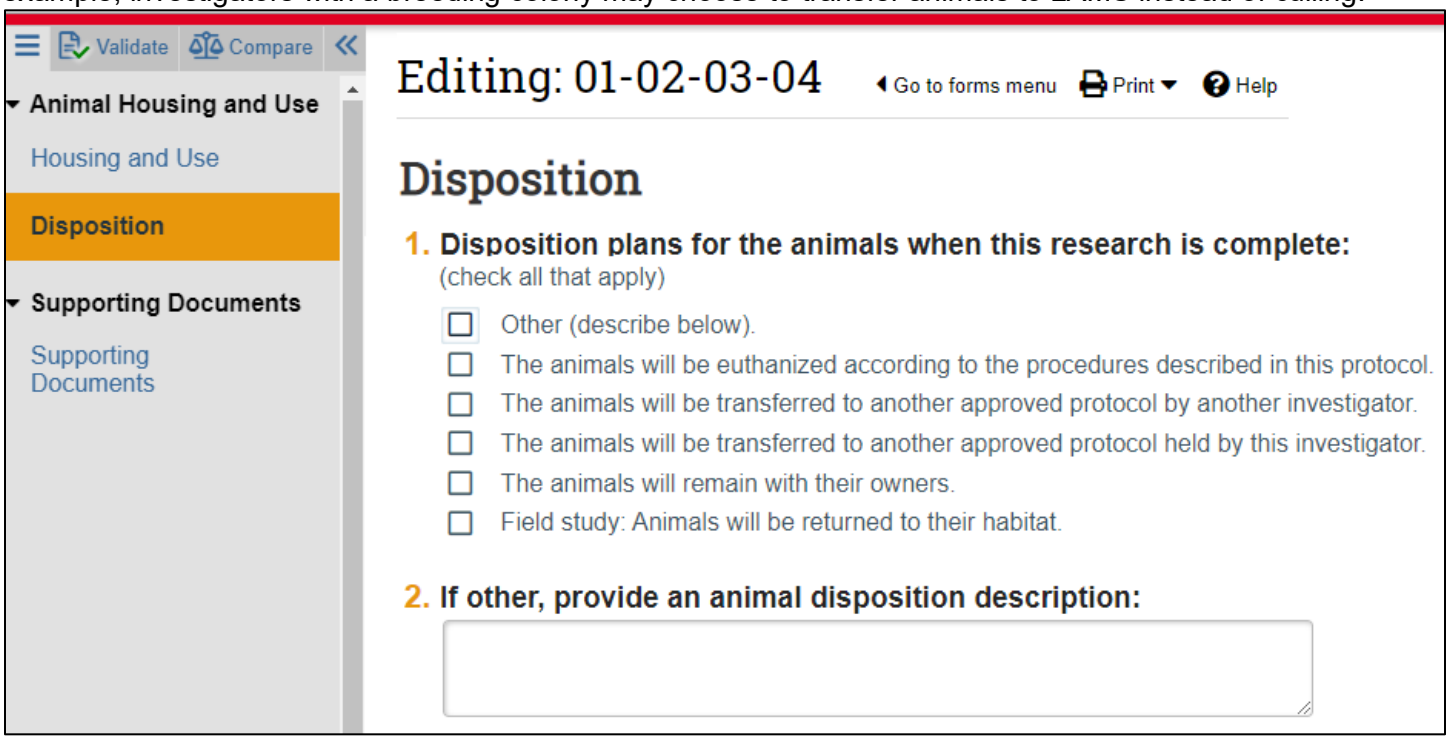
4. **Describe how this location will be used.**

5. **Justify why the animals must be removed from the vivarium:** provide justification (for example, research equipment cannot be moved).

6. **Describe how animals will be transported to and from this location, including container and route:** Refer to ACUP Policy 108 for specific requirements. Describe specific details regarding safe animal transportation including containers, routes. A Personal Vehicle User Form must be completed if transporting with a personal vehicle.

## Disposition

Check all options that apply. If you intend to transfer animals to LAMS for training purposes, be sure to check the box indicating that animals will be transferred to another approved protocol by another investigator. For example, investigators with a breeding colony may choose to transfer animals to LAMS instead of culling.




## Supporting Documents

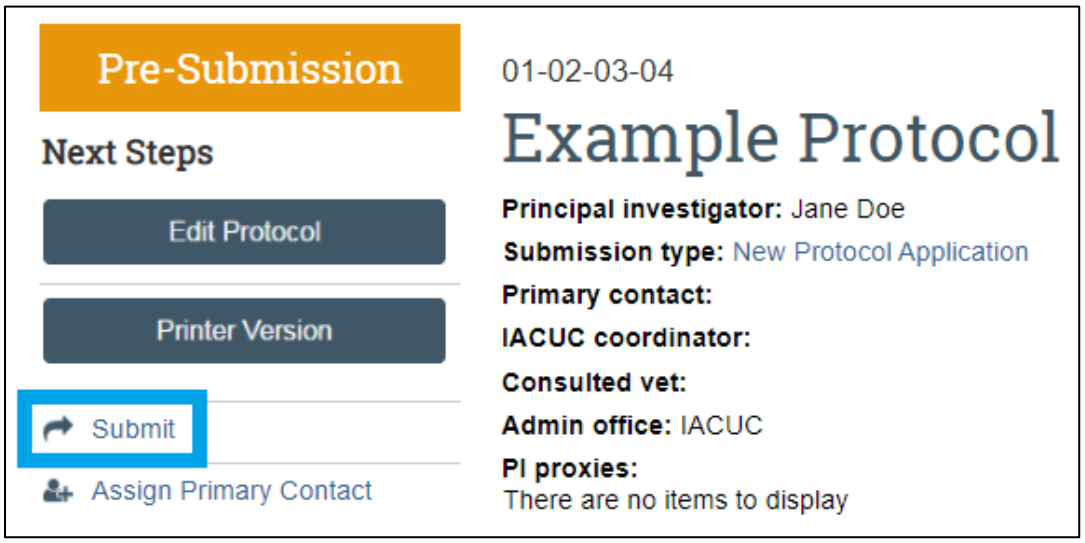
In this section, you may attach any relevant protocol documentation to help with IACUC review. Documents may include but are not limited to: cleaning/hazard SOPs, literature citations, grant congruency reviews, MOU documents, field permits.

**This is the last section of a new protocol form.** Press the “Finish” button in the bottom right corner of your screen to save your changes and return to the main protocol workspace.

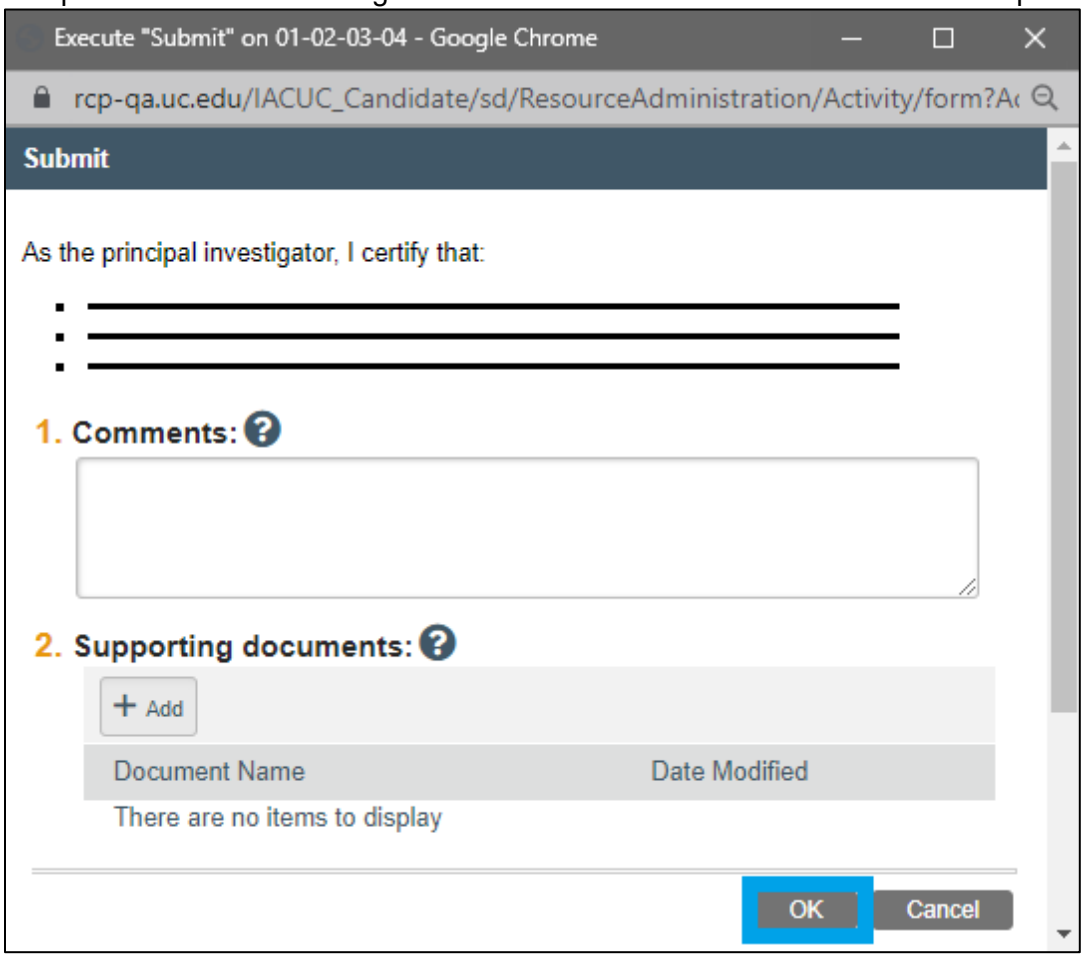
## *Submit an IACUC Protocol for Review*

As you create content in your draft IACUC protocol, the status will display as “Pre-Submission”. Use the following process to submit your protocol draft for IACUC review:

1. On the protocol workspace, click the “Submit” button on the left side of the screen to open a popup window.




2. Carefully review each confirmation statement and provide comments or supporting documents if necessary. Press the “OK” button to submit the protocol for review and close the popup window. The protocol status will change from “Pre-Submission” to “Pre-Review” on the protocol workspace.



## *Substances and Procedures*

There are 2 types of substances and procedures found in IACUC RAP.

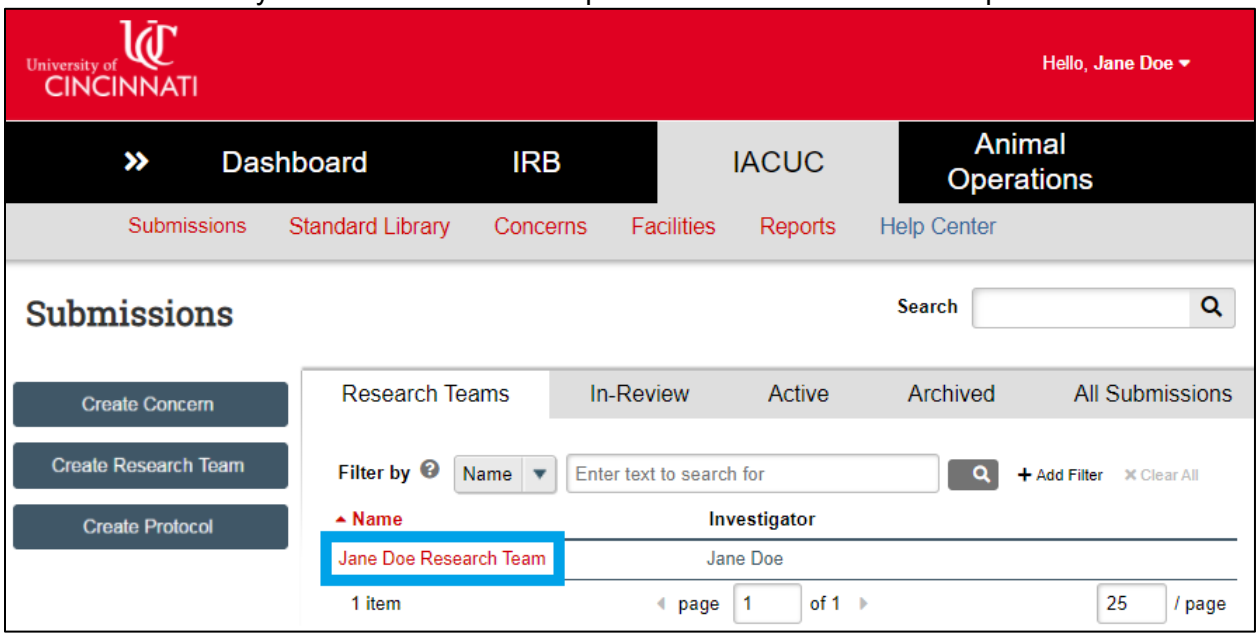
- **Standard**: these have been pre-approved by the appropriate safety office(s) and IACUC
- **Team**: these are subject to review and approval by the appropriate safety office(s) and IACUC

When creating an experiment for your IACUC protocol, you should always use existing RAP substances and procedures if they meet your research needs. You can perform a Search for Existing RAP Substances and Procedures to View Substance or Procedure Details and compare them to your research needs.

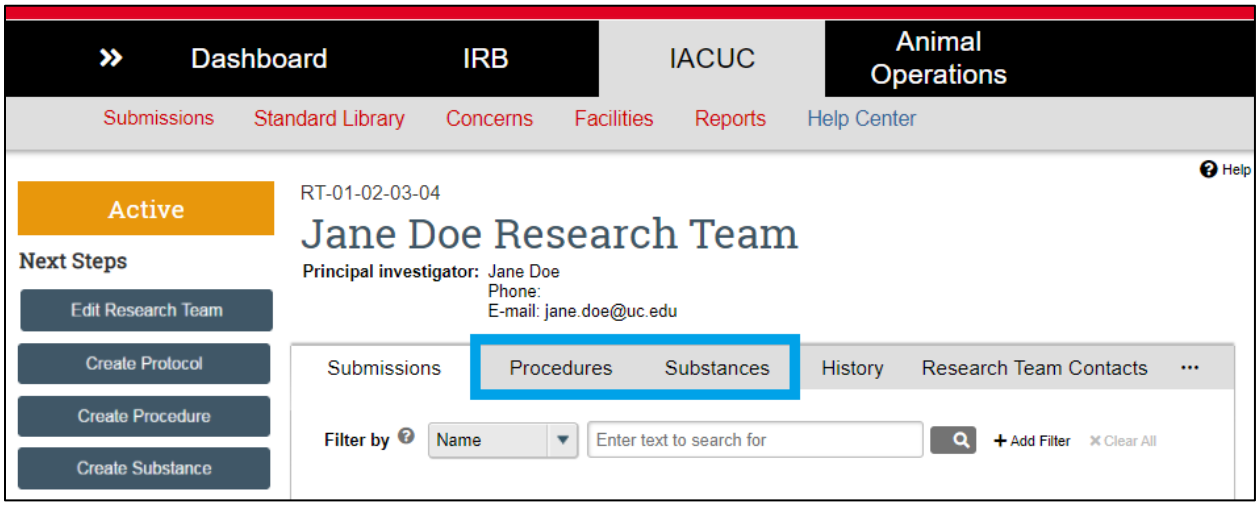
If a substance or procedure does not meet your research needs, you must Create a New Team Substance or Create a New Team Procedure.

### Search for Existing RAP Substances and Procedures

1. Select the "IACUC" tab in the top navigation menu, then select the "Research Teams" tab.
2. Select the name of your Research Team to open the Research Team workspace.



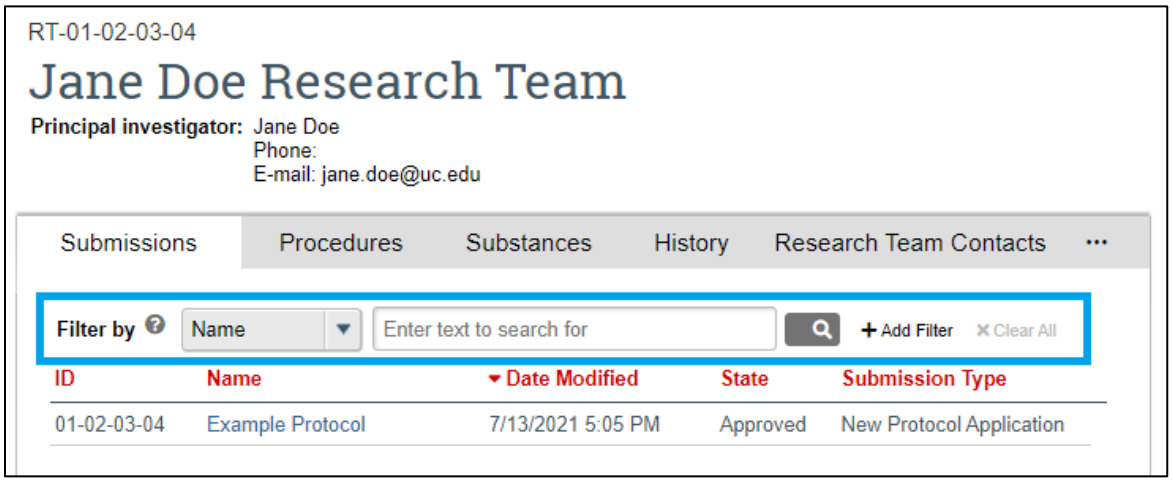

3. By default, the Research Team workspace opens with the "Submissions" tab displaying.
   a. select the "Procedures" tab to view a list of all RAP procedures
   b. select the "Substances" tab to view a list of all RAP substances



**Use the Filter to Search for Specific Criteria**

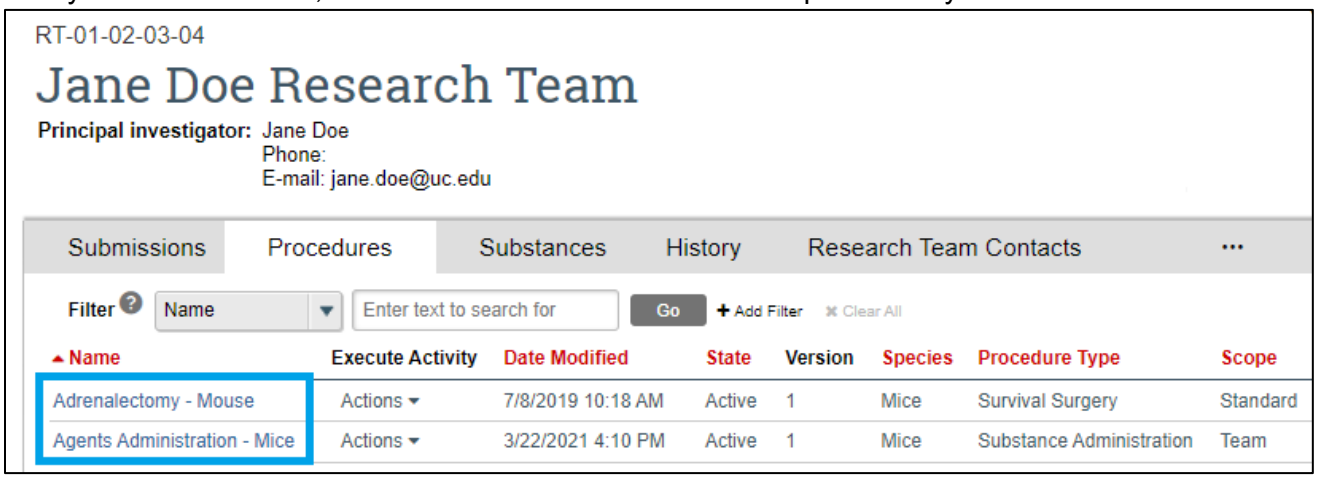
Almost every tab on the Research Team workspace has a filter to search for specific criteria or view specific results. To perform a partial search, use % as a wildcard (takes the place of 1 or more letters in a search).

- **Example**: searching for %glu will result in a list of results with "glu" anywhere in the name
  e.g. glucose, L-glutamine, monosodium glutamate, fluoro-2-deoxyglucose

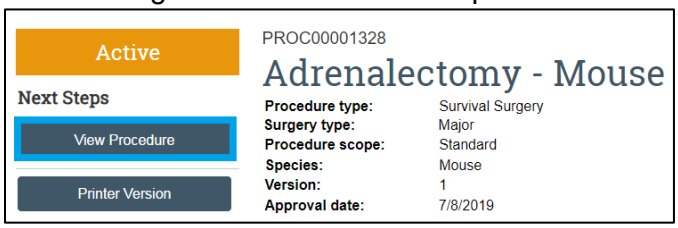


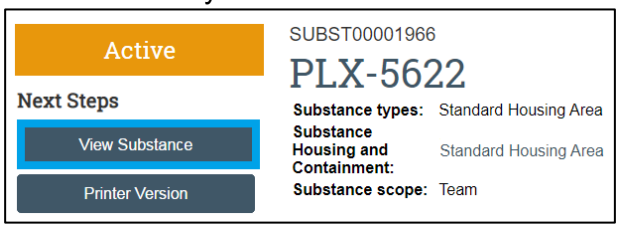

View Substance or Procedure Details

1. In your search results, select the name of the substance or procedure you want to view details for.




2. Select the "View Procedure" or "View Substance" button on the left side of your screen for details. Scroll through and review the entire procedure and check if it meets your needs.




If the standard procedure or substance meets your needs, then no further action needed. The standard will be available when you need to add it to the experiment. If the procedure or substance does not meet your needs, you must Create a New Team Substance or Create a New Team Procedure.

3. When you are done viewing procedure or substance details, click the "Exit" button on the bottom right of your screen to close the form.

## Create a New Team Substance

From the Research Team workspace, select the “Create Substance” button on the left side of your screen to open a “Create New Substance” form. There are 5 questions within this form:

1. **Name:** follow the guidance below for substance name requirements
    - use generic name instead of trademarked name
        - e.g. “acetaminophen” instead of “Tylenol®”
    - add substance abbreviations in parenthesis
        - e.g. “dimethyl sulfoxide (DMSO)”
    - if radiological agent, identify the radionuclide
        - e.g. “uridine triphosphate S-35 (UTP S-35)”
    - use the compound class to group similar substances together (must provide 1 or 2 examples)
        - e.g. “topical antibiotics (e.g. neomycin, bacitracin)”
        - Only chemicals with the same hazard profile can be grouped. Biologicals and radioisotopes must be separated.

2. **Substance Types:** select all that apply, including at least 1 of the following types
    - Biological Agent
    - Chemical Agent
    - Radioactive Agent

3. **Is this a hazardous agent?** Select “Yes” or “No”. You can confirm the hazard status of a substance with the appropriate safety office:
    a. Biological agents: UC Biosafety Office
    b. Chemical agents: UC Environmental Health & Safety (EH&S)
    c. Radioactive agents: UC Radiation Safety Office

4. **Supporting Documents.** Attach a Safety Data Sheet (SDS) or white paper for any created substance.

5. **Substance Housing and Containment:** select all that apply to the housing and containment of animals after administration of this substance.
    - Non-hazardous substances are typically used in a “Standard Housing Area”.
    - Hazardous substances must typically be used in at least 1 of the following areas:
        - Biocontainment Room (biohazards)
        - Chemical Containment Room (chemicals)
        - Radiation Commissioned Room (radioactive agents)

Select the “Finish” button to finish creating the new team substance and close the form.

## Create a New Team Procedure

From the Research Team workspace, select the “Create Procedure” button on the left side of your screen to open a “Creating New Procedure” form. If multiple species on your protocol undergo similar procedures, use the Copy a Procedure technique to quickly duplicate a procedure and change the species.

There are 5 questions on the first page of this form:

1. **Name:** create a name for the procedure with enough detail so that you can easily search for and add this procedure to a protocol experiment later on (e.g. administering inflammatory agents, TAC surgery).

2. **Procedure Type**: choose 1 of the categories below. Your answer to this question will determine the questions populated on the next page of the form. Each category is defined in Appendix 2: Preferred Language and Definitions.

   - Survival Surgery (major/minor)
   - Substance Administration
   - Food and Fluid Restriction
   - Non-survival Surgery
   - Behavioral
   - Non-Surgical
   - Physical Restraint
   - Tissue/Blood Collection
   - Euthanasia

3. **Species:** select 1 species per procedure.

4. **Admin office:** defaults to IACUC.

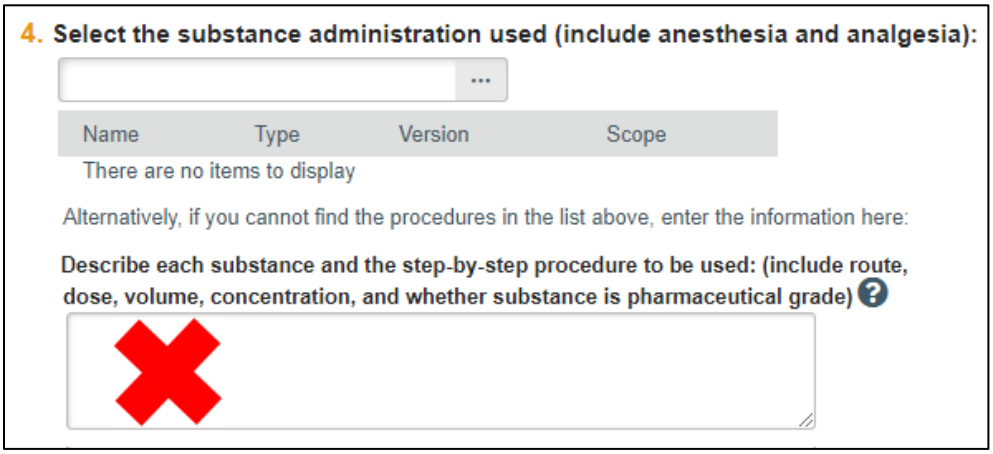
5. **Will administering this procedure cause any more than momentary pain and distress?** Consider both the immediate procedure and intended, downstream effects of this procedure in your answer. For example, you should answer "Yes" for a procedure administering Lipopolysaccharide (LPS), bacteria, or tumor cells with the intention of making the animal sick, grow tumors, cause inflammation, etc.

   Another example: you should answer "No" for a substance administration procedure where a substance that does not cause pain/distress (e.g. insulin, saline) is administered by a route that does have associated pain/distress (e.g. surgical minipump implant). In this example, the pain/distress description is provided in the surgical implant procedure instead of the substance administration procedure, because the surgery is the source of the pain/distress.

   If yes, provide the following response to the following questions:
   a. **Identify expected symptoms from administering this procedure**
   b. **Identify criteria under which animals will be removed from research**

Press the "Continue" button to move forward to the next page(s) of the form. Use the following guidelines to complete the remaining procedure form pages.

- Textbox questions: if there is no appropriate response, type "N/A" (do not leave field textbox blank).
- Use the word "animal" instead of the species name when providing descriptions (facilitates the Copy a Procedure technique).
- See Appendix 2: Preferred Language and Definitions for writing examples and specific details.
- Forms for all procedure types EXCEPT Substance Administration will ask you to identify substances administered during the procedure. This includes anesthesia and/or analgesics administered.
  - **Add related substance administration procedures for all non-variable substances.** For example, for a Survival Surgery you would include analgesics and anesthetics, but would not include experimental substances (e.g. LPS, biological and chemical agents).
  - **Leave the "Describe each substance" textbox blank.**

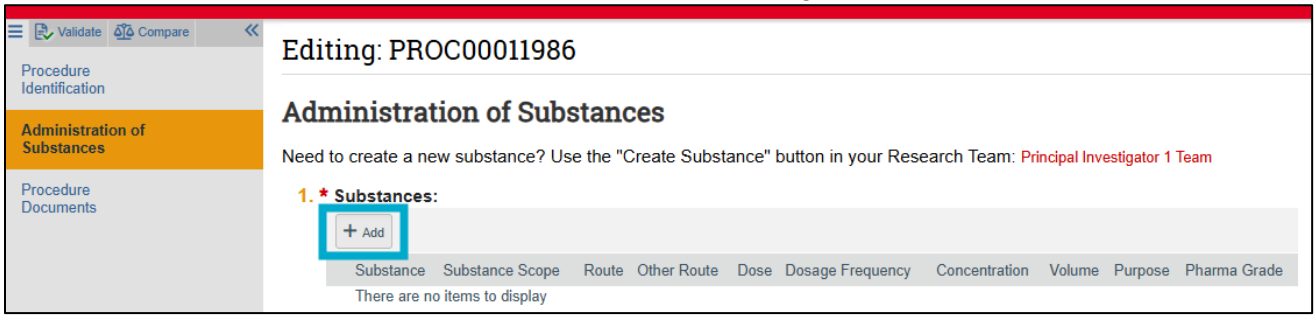


## Substance Administration Team Procedure

If you selected “Substance Administration” as the procedure type, this is the second page of the form. Group substances based on use.

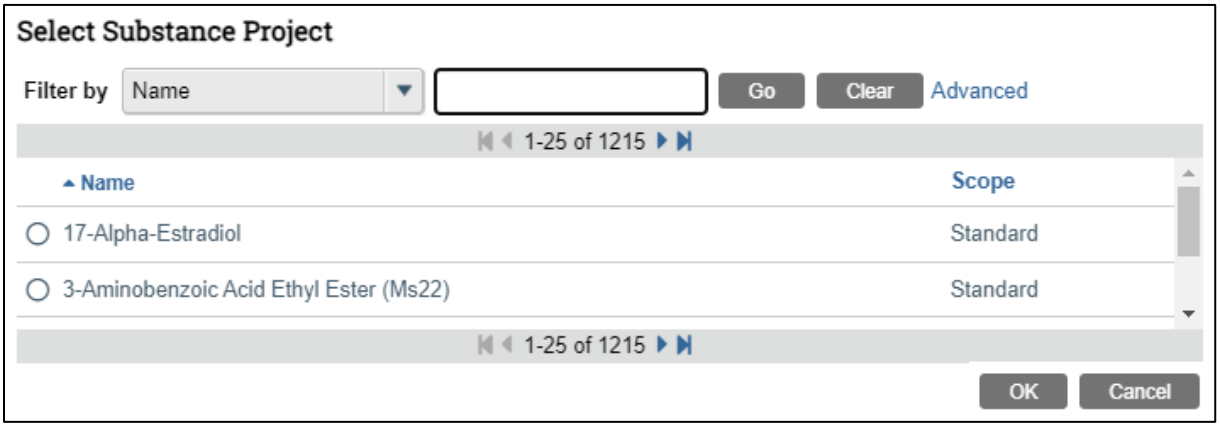
For example, if you have an induction of tumor substance administration that would include all of your tumor cells, and a separate treatment of tumor substance administration that includes all of the agents that you would use to stop tumor growth.

1. **Substances.** Click the “+ Add” button to add substances using a “Add Substance to Procedure” form.

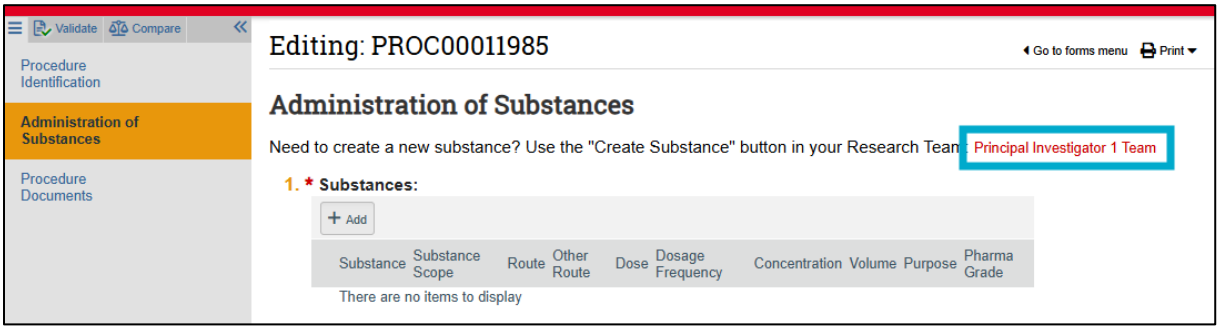



2. Complete all 8 questions on the Add Substance for Procedure form:

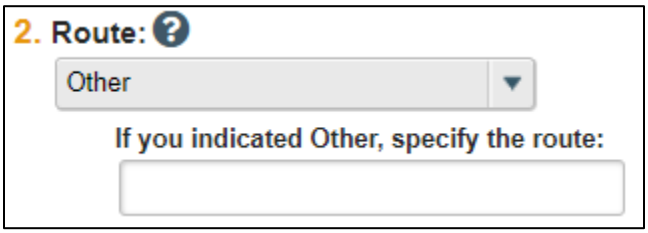
   a) **Substance.** Use the filter feature to search for a substance. You can use % as a wildcard (takes the place of 1 or more letters in a search) to perform a partial search.




**If you do not find a substance that you are looking for, click “cancel” and on the previous screen you will see the prompt to Create a New Team Substance.**



b) **Route.** Select the route of administration from the dropdown menu. If using multiple routes of administration OR the route of administration is not listed, select "Other" from the dropdown menu, and describe in the provided textbox:




c) **Dose.** Provide a dose and units of measurement.
   i. Units of measurement can be specific (e.g. mg/kg) or general (e.g. number of cells).
   ii. Provide a dose range or use flexible language (e.g. up to 5 mg/kg).
   iii. Distinguish between multiple administration routes (e.g. 5 mg/kg PO, 2-6 mg/kg IP).

d) **Frequency of dosage.** Distinguish between multiple routes of administration if applicable (e.g. PO administered 1x/week, IP administered 2x/month).
   i. If 1 substance has several administration routes and frequencies, consider adding the substance with a different administration route and frequency multiple times, instead of adding too many details to 1 substance. **Information must be clear to the reviewer.**

e) **Concentration.** Typically provided in mg/mL. This field is not required if your provided adequate details in the "Dose" question.

f) **Volume**. Provide the maximum volume/route.

g) **Purpose.** Provide a reason for substance administration (e.g. induce inflammation, treatment, antibiotic).

h) **Is substance pharmaceutical grade?** Answer using 1 of the following options.
*Note: most biological agents are not pharmaceutical grade.*
   - Yes
   - No (not available)
   - No (incorrect formulation)
   - No (other) – *provide a description/justification in Q4a*

Select either the "OK" (closes form) or "OK and Add Another" (keeps form open) button to finish adding your substance.

3. **Describe step by step the procedure for administering the substances.** See Appendix 2: Preferred Language and Definitions to see examples of responses to this question.

4. **Describe any anticipated adverse reactions to administering the substances.** Do not leave this question blank. If no adverse reactions are expected, you must state this.

5. **Are all substances being administered in this procedure pharmaceutical grade?**
If you listed multiple substances, be very clear about which specific substances are non-pharmaceutical grade and provide detailed responses to subsequent questions. For details and definitions, see ACUP Policy 105.

If you answer “No”, the following questions will display:

a) **If you answered "No-other" above, please provide justification for not using pharmaceutical grade.** Otherwise state "N/A".
b) **For each non-pharmaceutical grade substance, describe the procedures to be used to ensure the sterility, purity, stability, and physiologic pH of the compound.** Provide detailed formulation information including vehicles, including sterile filtration through 0.22 micron filter if applicable.
c) **For each non-pharmaceutical grade substance, describe storage method, if any.** e.g. substance frozen at -80°C, then thawed at room temperature for before administration.

6. **Select the anesthesia and analgesia procedures to be used.** Add ONLY if required for the act of substance administration (e.g. retroorbital injections). Anesthesia and analgesia administered during surgery must be listed in the surgical procedure (e.g. craniostomy, minipump) and should not be included here.

7. **Describe the monitoring of the animal during the procedure.**

8. **Describe post-procedural care and monitoring.**

Press the “Finish” button in the lower right corner of your screen to finish creating your new team procedure.

## Copy a Procedure

Copying a procedure is a quick and easy technique to use similar language, descriptions, and substances. Standard or team procedures can be copied from a research team or from the procedure workspace.

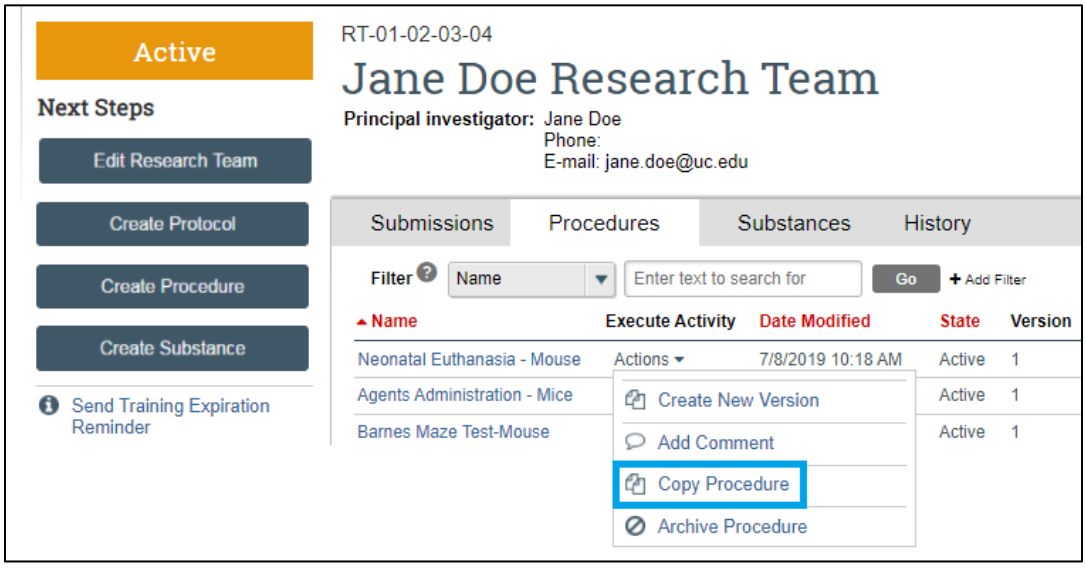
Examples of why you might want to copy a procedure include:

- Modifying a standard procedure to meet your research needs
- Applying similar procedures to multiple species

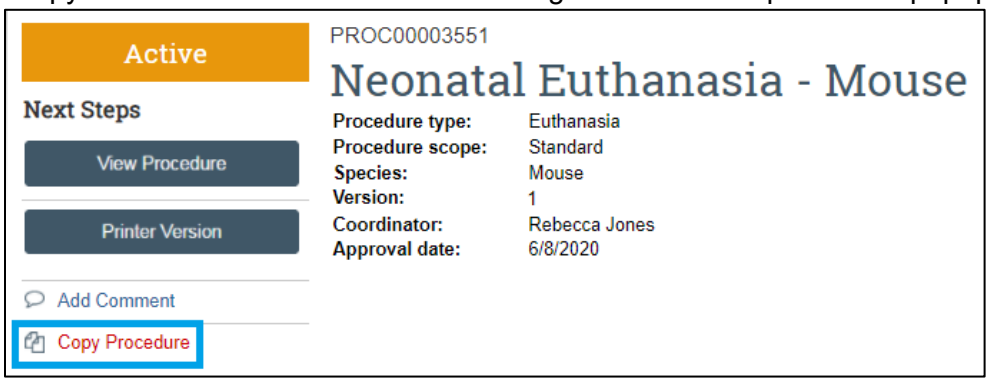
When you copy a procedure, it may take a few minutes before the copied procedure associated with your research team displays in RAP. You may need to refresh your page a few times.

### Copy Procedure from a Research Team

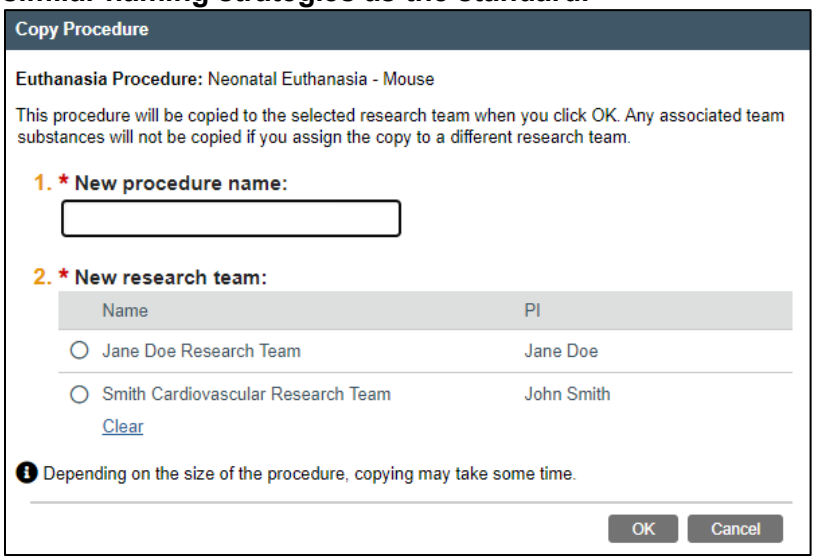
1. Select the “IACUC” tab, then click on the name of your Research Team.
2. Select the “Procedures” tab and locate the procedure you want to copy.
3. In the Execute Activity column, select the small arrow to the right of “Actions” to display a dropdown menu. Select “Copy Procedure” from the dropdown menu to open a new popup window.



4. Alternatively, you can click the procedure name to navigate to the procedure workspace. Select the "Copy Procedure" button from the left navigation menu to open a new popup window.

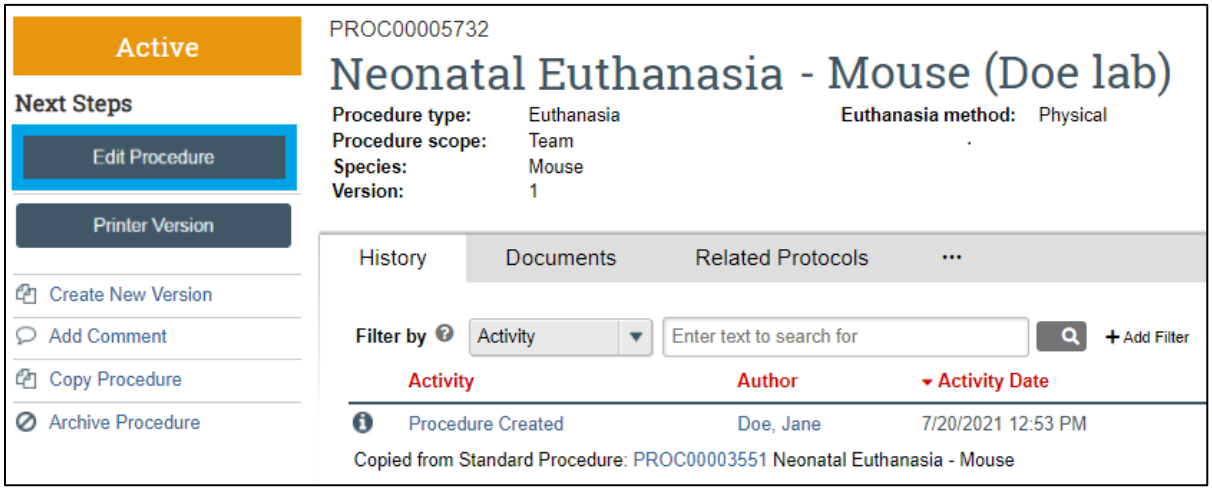



5. The "Copy Procedure" form will display in a popup window. Provide a name for the copied procedure (Question 1) and assign it to the applicable research team (Question 2). Press the "OK" button to create a procedure copy. **When copying a standard procedure: to avoid confusion, please do not use similar naming strategies as the standard.**




## Edit a Copied Procedure

1. Select the "IACUC" tab, then click on the name of your Research Team.
2. Select the "Procedures" tab and use the filter feature to search for a procedure using specific criteria. Once you locate the copied procedure you want to edit, click on the procedure name.
3. Select the "Edit Procedure" button on the procedure workspace to review and make edits/changes.



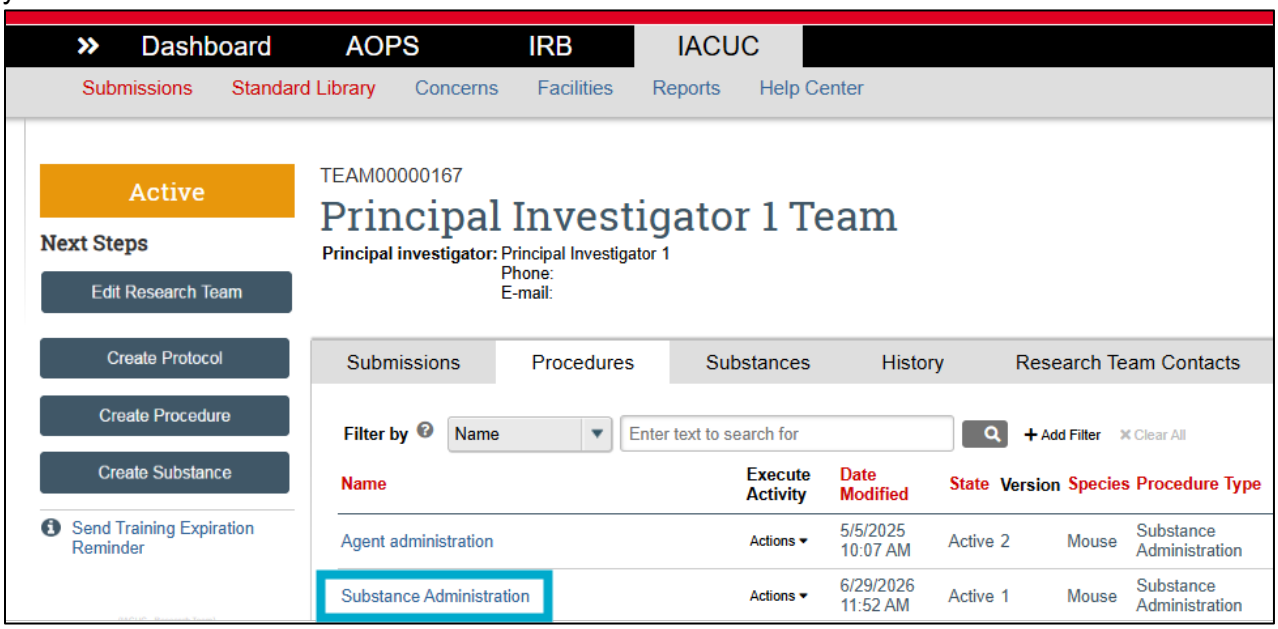
You can edit the procedure to meet your needs – for example, you may need to change the species the procedure applies to or change the type of substance administered as part of this procedure. Like other forms, press the “Continue” button to save your changes and proceed to the next section of a form. Press the “Finish” button to save your changes and close the form.

## Create a New Version of a Team Procedure

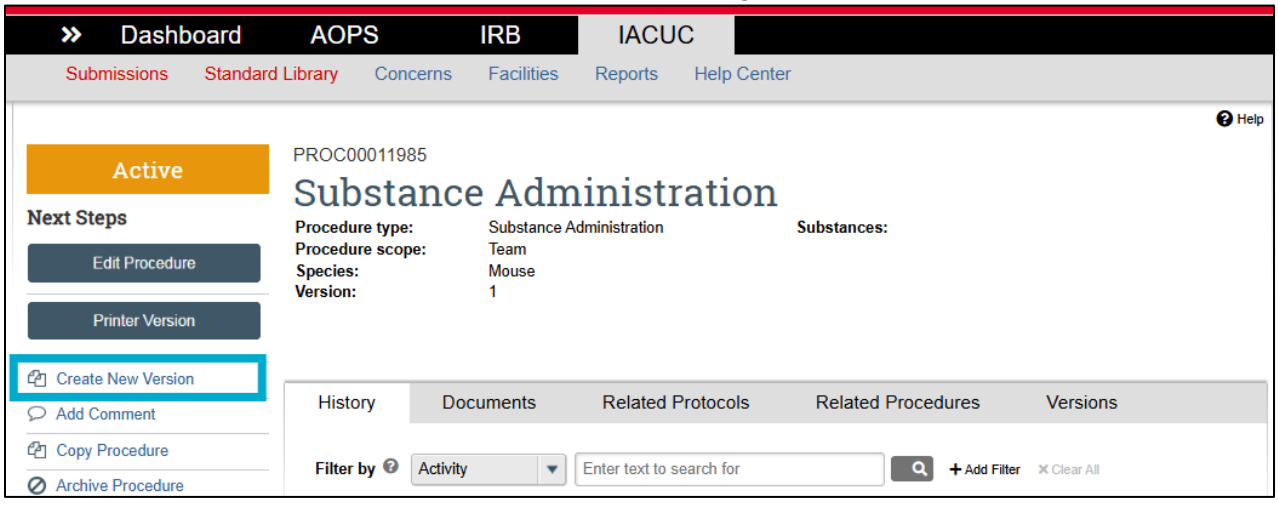
If you have a team procedure that is approved on your protocol or approved on another protocol you may want to create a new version of the procedure. Benefits of creating a new procedure version include:

- Historical tracking of procedural changes over time (allows you to keep the historical procedure in use but allows you to make changes to a new procedure version).
- Automatic archiving of previous procedure versions (will cause the system to flag archived procedures for update/replacement during triennial review). **Old versions must be replaced by the newest versions during triennial. Each procedure has an associated version number visible on the procedure workspace.**
- Designated reviewers can focus on changes between previous and new procedure versions, instead of reviewing an entirely new procedure from start to finish (decreases reviewing turnaround time).

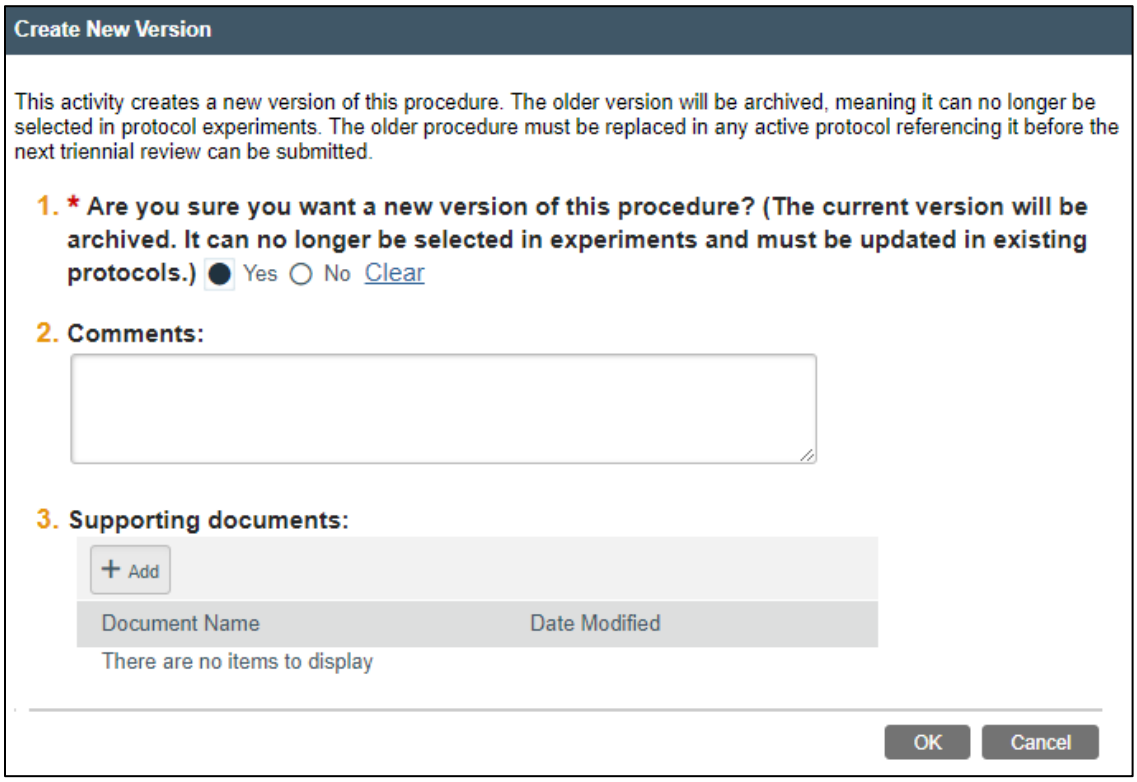
1. On your Research Team workspace, select the Procedures tab and click on the name of the procedure you want to create a new version of.




2. Select the “Create New Version” button from the left navigation menu to open a new popup window.

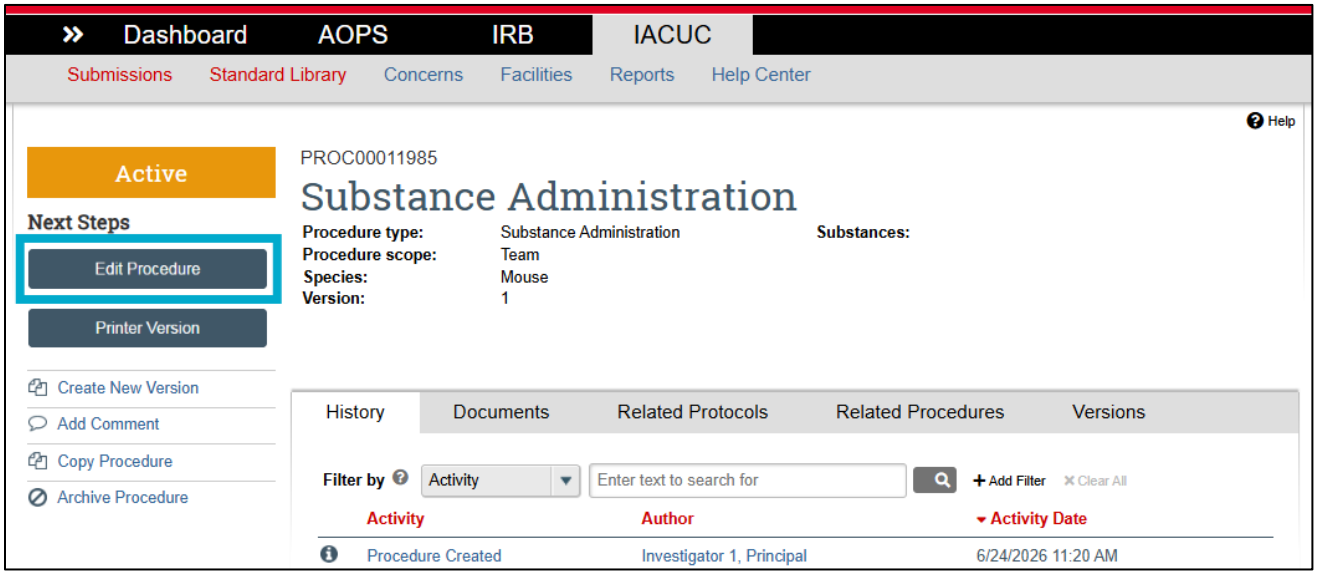


3. The “Create New Version” form will display in a popup window. Select “Yes” for Question 1, then press the “OK” button to create a new version of the team procedure. **This action will archive the prior version of the procedure and activate the new version of the procedure.**




## Edit a New Version of a Team Procedure

1. Select the “IACUC” tab, then click on the name of your Research Team.
2. Select the “Procedures” tab and use the filter feature to search for a procedure using specific criteria. Once you locate the copied procedure you want to edit, click on the procedure name.
3. Select the “Edit Procedure” button on the procedure workspace to review and make edits/changes.

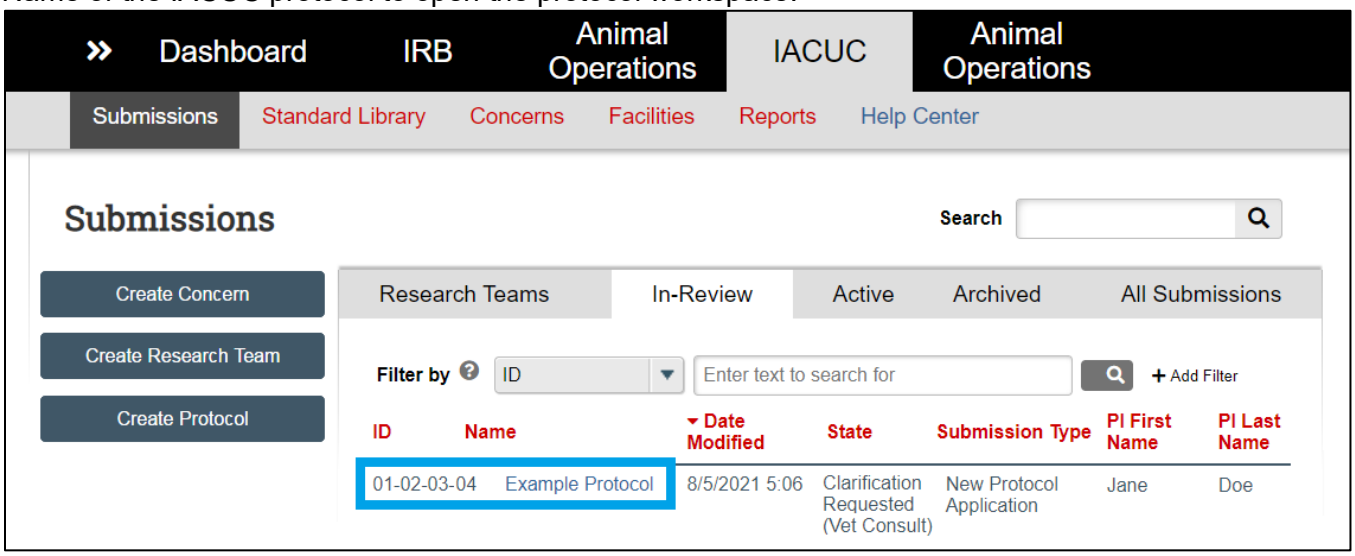



4. Press the “Continue” button to save your changes and proceed to the next section of a form. Press the “Finish” button to save your changes and close the form.

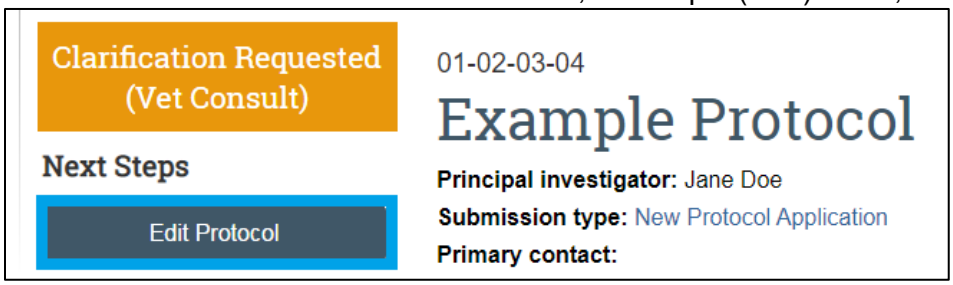
## *Responding to a Request for Clarification*

Submitted IACUC protocols and amendments are subject to review by the IACUC prior to approval. During the review process, IACUC reviewers may leave comments on the amendment summary and/or specific sections of the protocol form for many reasons, including requesting clarification or edits to your protocol or amendment. **Remember that you may use your Dashboard button on the primary navigation bar to quickly see all pending items assigned to you that are awaiting review/action.**

1. Select the "IACUC" tab, then select the "In Review" tab on your main workspace. Click on the ID or Name of the IACUC protocol to open the protocol workspace.



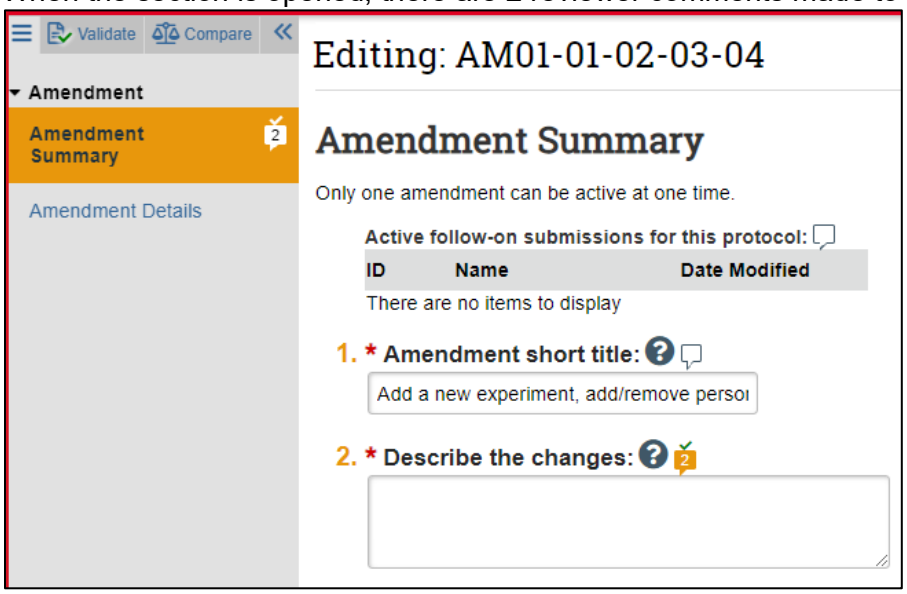

2. For protocol reviewer comments, press the "Edit Protocol" button on the left side of your screen. If you want to see amendment reviewer comments, see step 3 (next). If not, advance to step 4.




3. For amendment reviewer comments, locate and click on the amendment ID in the "History" tab to open the amendment workspace. Press the "Edit Amendment" button on the left side of your screen.

4. To locate reviewer comments, look for a numbered textbox icon on the left navigation panel. When you click and open the specific section, you will see the textbox icons next to specific questions on the form, indicating there are comments available for review.

   Example: in the image below, there are 2 reviewer comments in the Amendment Summary section. When the section is opened, there are 2 reviewer comments made to Question 2 of this form.




To ensure all reviewer comments are addressed, it is recommended to start at the top of the form and work your way down each section of the form, saving changes made to each section of the protocol form and responding to reviewer comments before switching between sections. To edit substances and procedures in response to a reviewer comment, refer to the Substances and Procedures section of this manual.

## Protocol Review Process and Timelines

Reviewers may ask questions or request clarification at any step of the process. This back-and-forth process is performed within RAP, and the IACUC Office is available to help incorporate requested changes at any time.

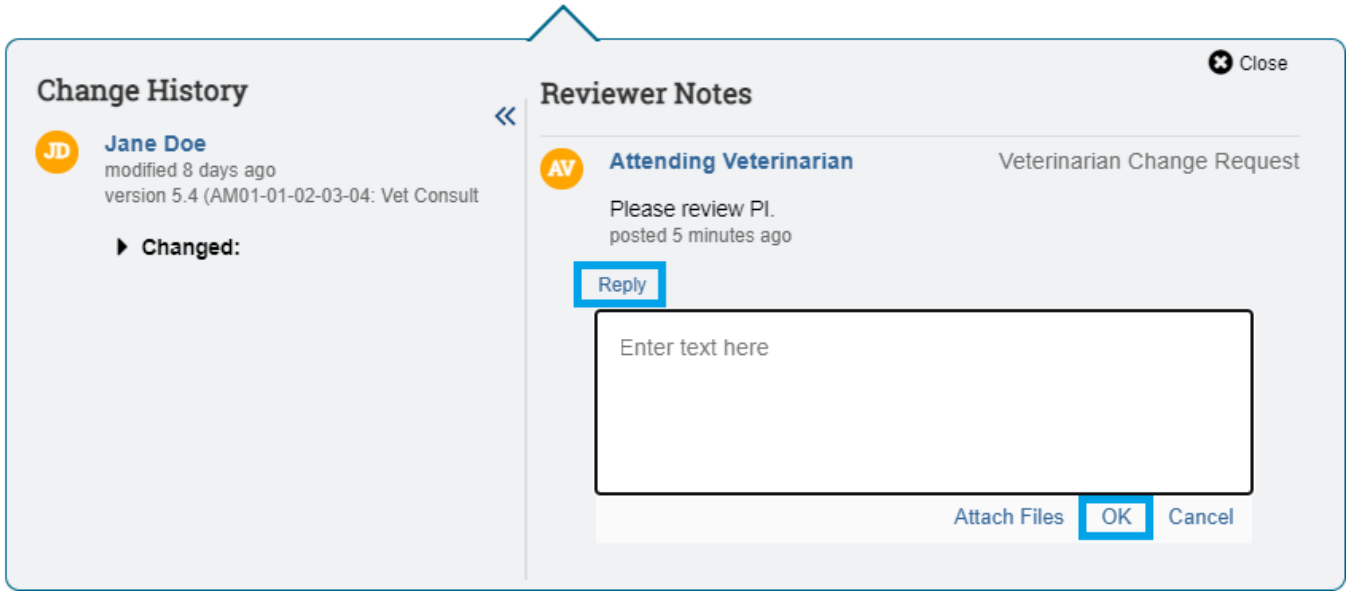
1. **Pre-review (IACUC Office):** administrative review of all protocol sections, ensuring content is clear, concise, and complete.
2. **Vet review (ACUP Veterinarian):** focuses on animal health and welfare, animal housing (satellite or within LAMS) arrangements, and husbandry considerations.
3. **IACUC review:** scientific review by either full committee (all members) or designated members (2-3 people). Review focuses on harm/benefit analysis and the 3Rs (Reduction, Refinement and Replacement).
4. **Post-review (IACUC Office):** if there are any outstanding items still needed (e.g. IBC approval, training updates), they must be addressed during post-review before the IACUC protocol can be approved.
5. **Approval:** If this is a triennial, animals active on your previous protocol will be transferred to your new protocol. Begin using the new protocol number, and discontinue using the old protocol number for all correspondence, service requests, animal orders, etc.

## Responding to Reviewer Clarifications

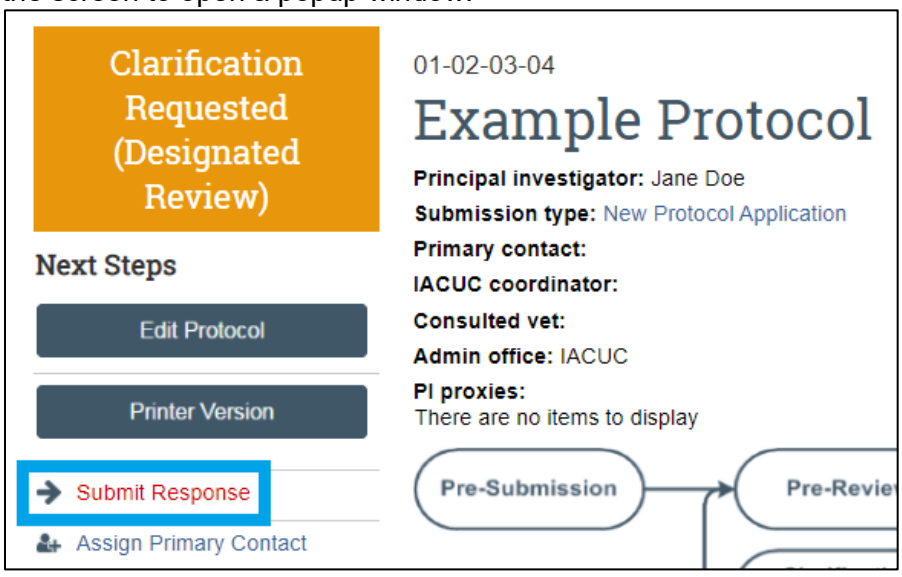
1. Click on the numbered textbox icon next to a specific question on the protocol form to open the comment in a textbox-shaped popup window. The comment popup window has 2 sections:
    a. **Change History (left side):** a history of changes made to the protocol form as a result of this comment.
    b. **Reviewer Notes (right side):** includes a history of requested changes or clarifications.

2. Make the requested changes to the protocol form. Press “Save” to save your changes.

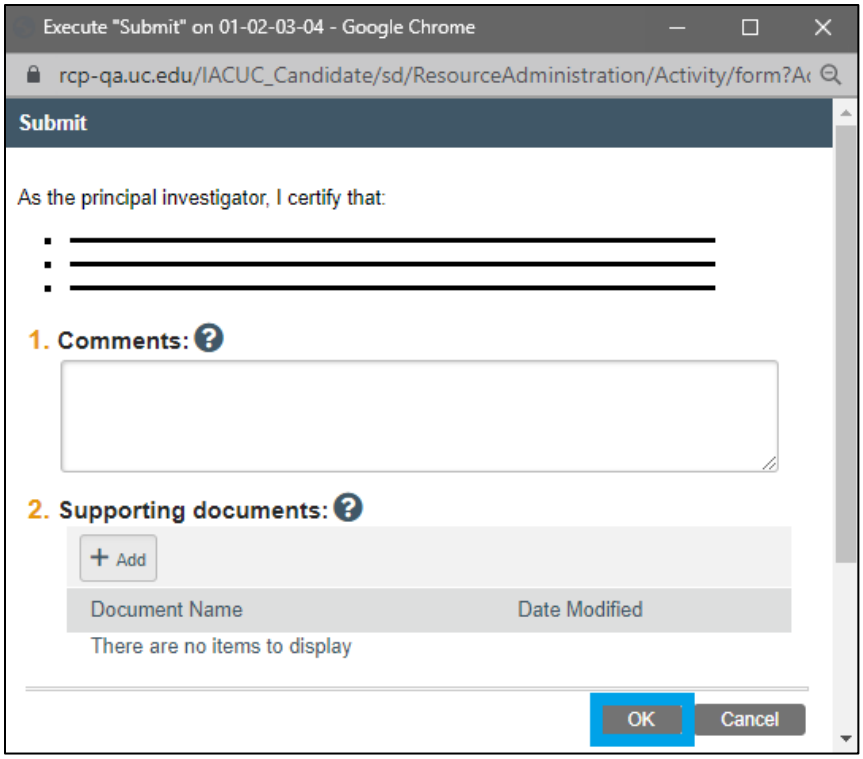
3. On the “Reviewer Notes” side of the popup, press the “Reply” button to open a textbox where you can type a response to the reviewer. Press the “OK” button to save your comment response.




4. Once all changes have been made and saved, press the “Exit” button to leave the protocol form and return to the protocol or amendment workspace. Press the “Submit Response” button on the left side of the screen to open a popup window.



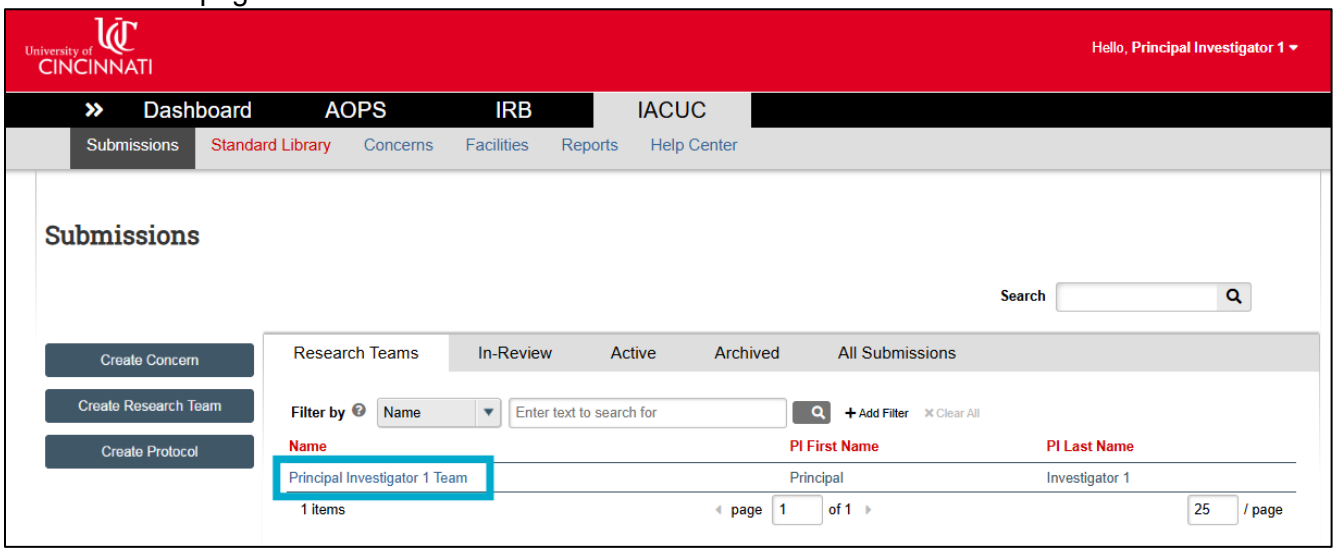

5. Provide comments or supporting documents if necessary. Press the “OK” button to submit the protocol for review and close the popup window. The protocol status will no longer contain “Clarification Requested” on the protocol workspace.



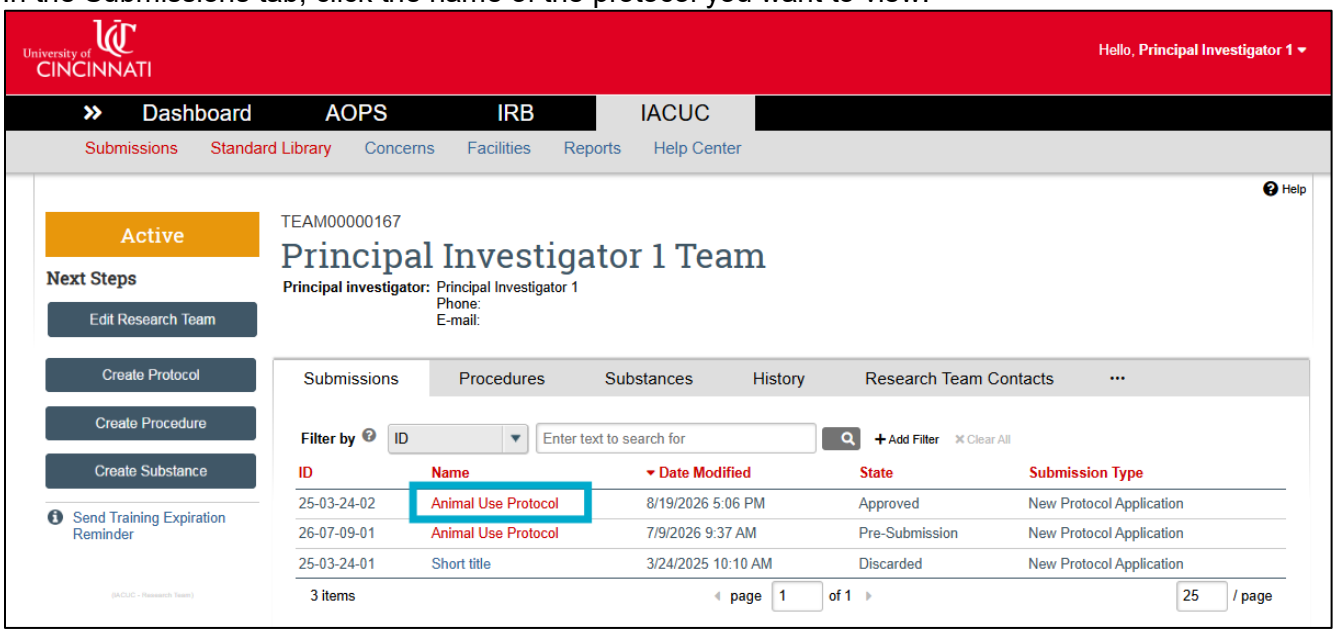

## *Protocol Maintenance*

<u>Finding Your Protocol</u>

1. Click the Submission link in the top navigation, then click the “Research Teams” tab to see a list of your research teams and the associated Principal Investigator (PI). Click the research team name to open the associated page.



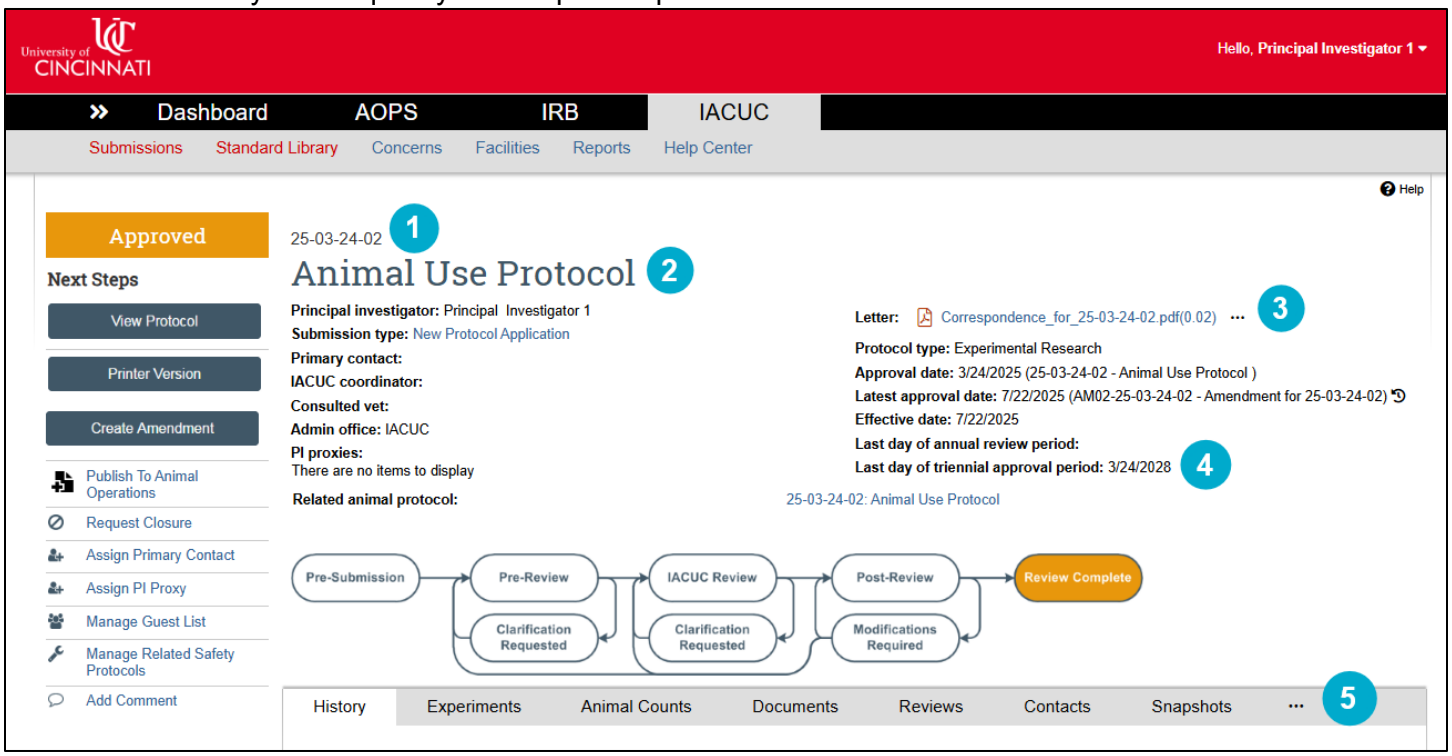
2. In the Submissions tab, click the name of the protocol you want to view.



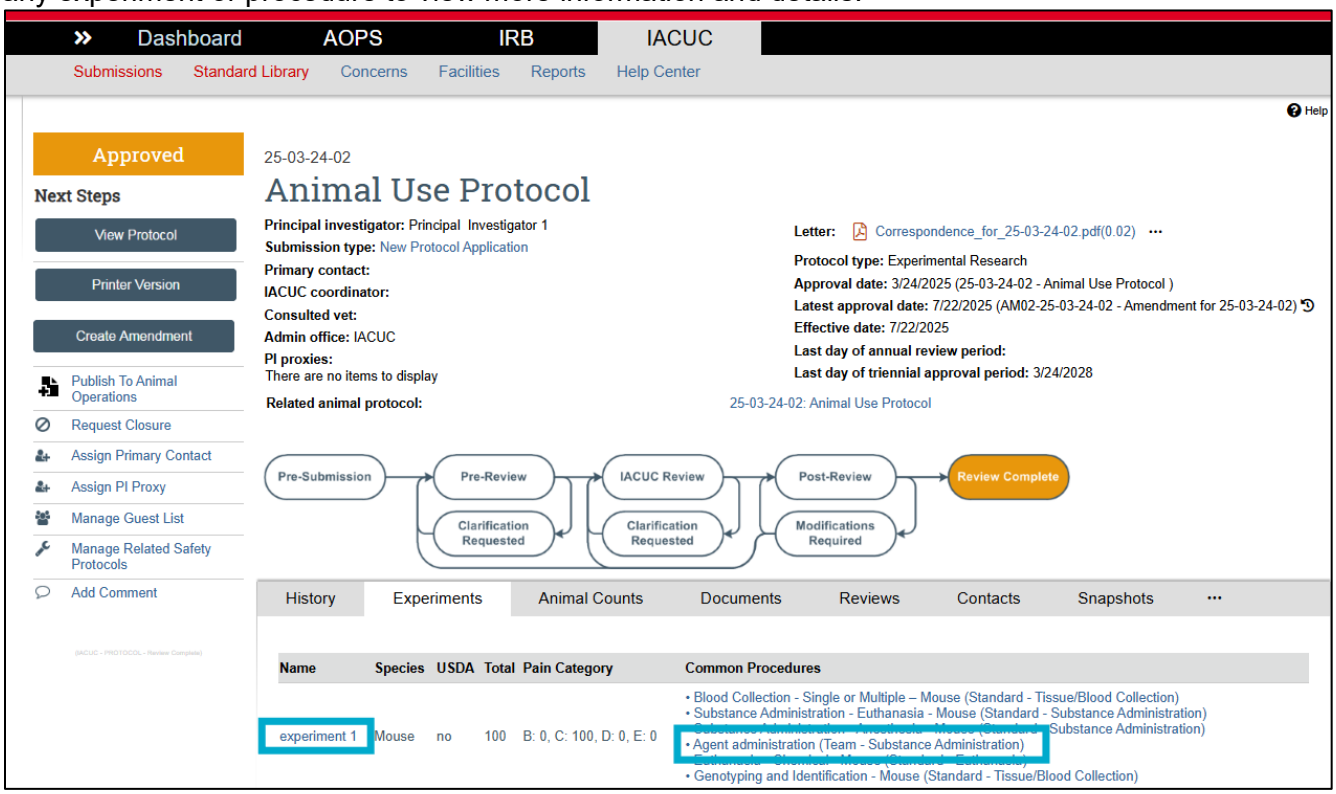

## Reviewing Your Protocol

The protocol workspace includes:

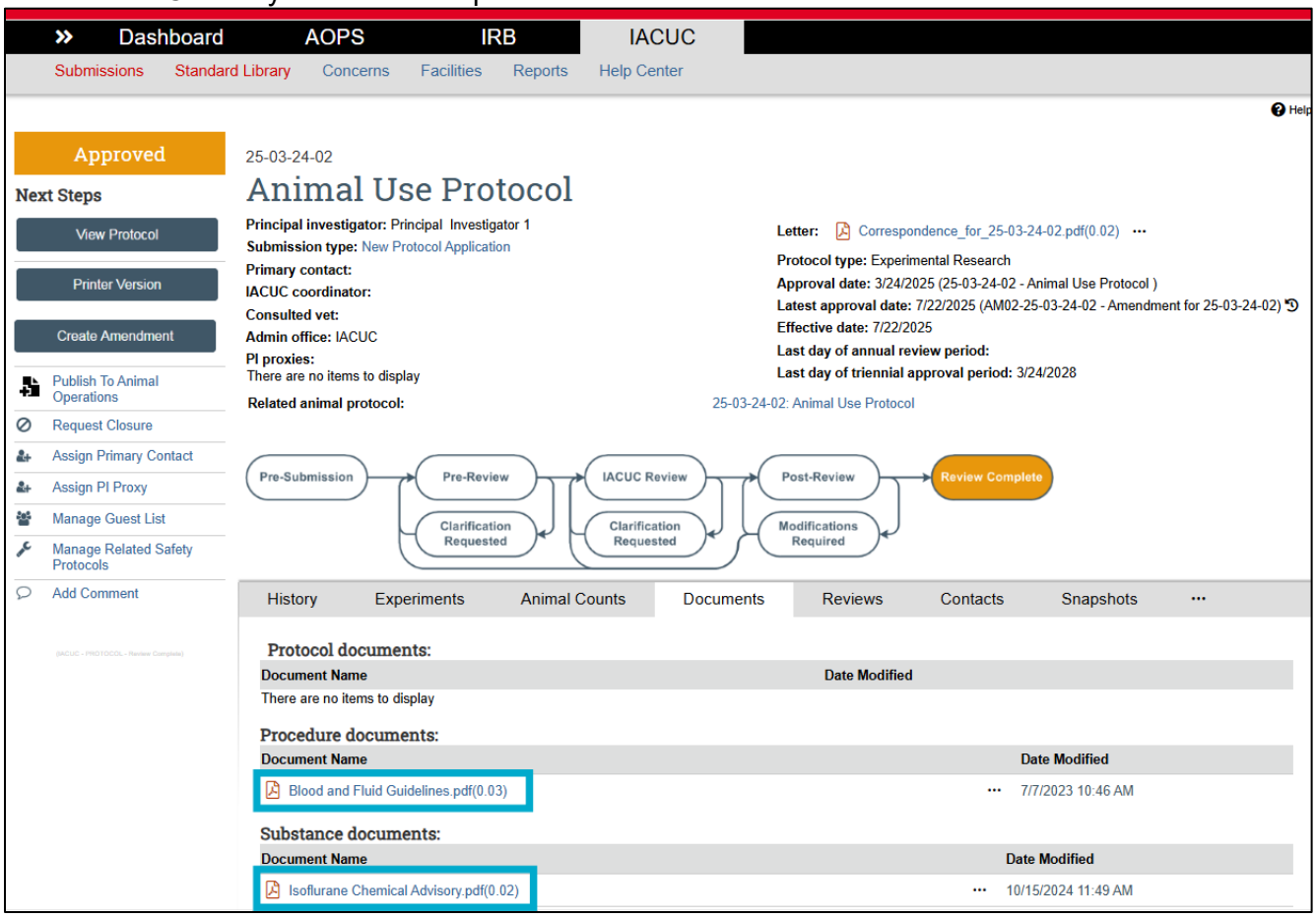
1. protocol ID
2. protocol name
3. expiration date
4. approval letter
5. tabs where you can quickly view important protocol information



1. Click the Experiments tab to quickly display experiments and procedures. You can click the name of any experiment or procedure to view more information and details.



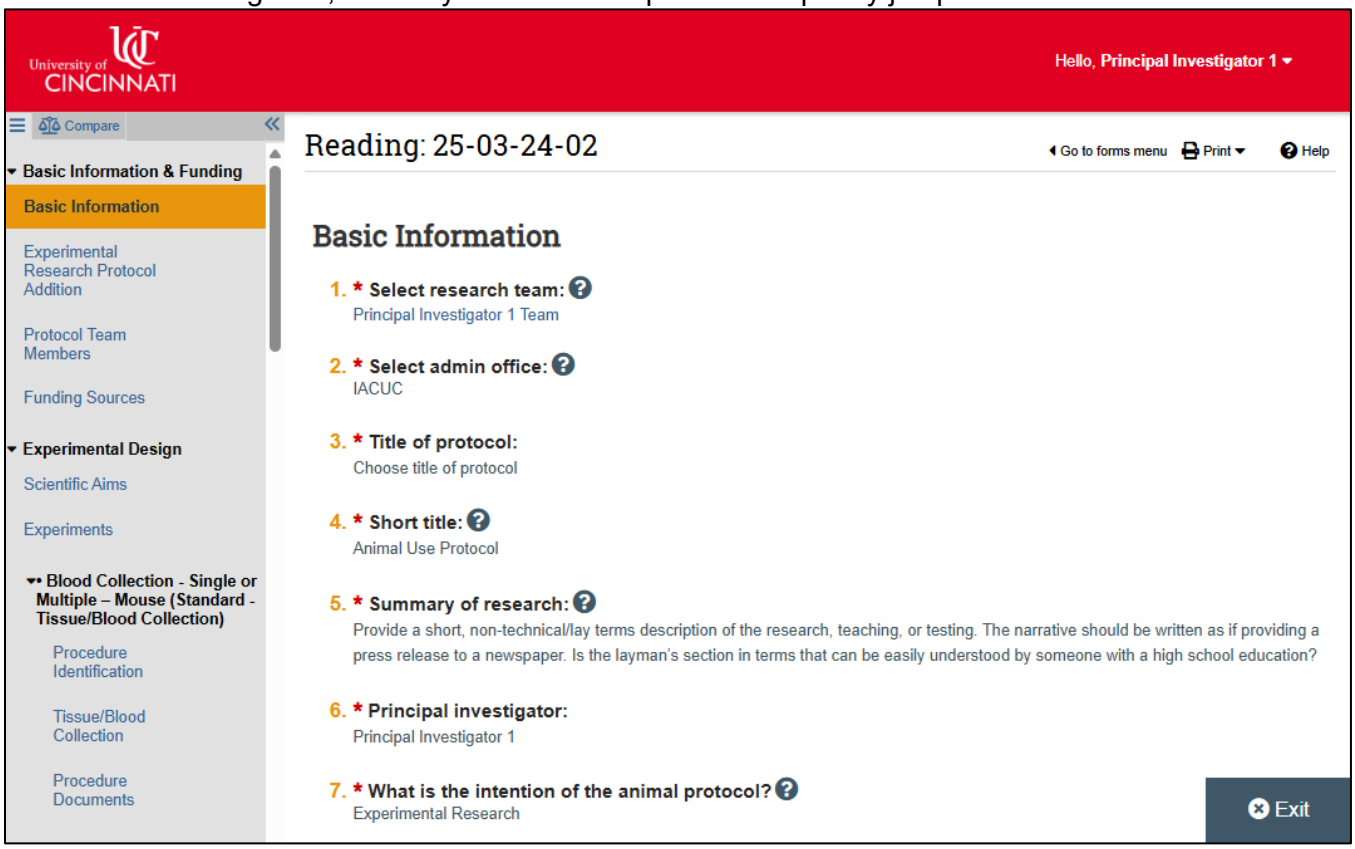

2. Click the Documents tab to quickly access any documents attached to the protocol, procedures, or substances. Click any document to open it and view its contents.



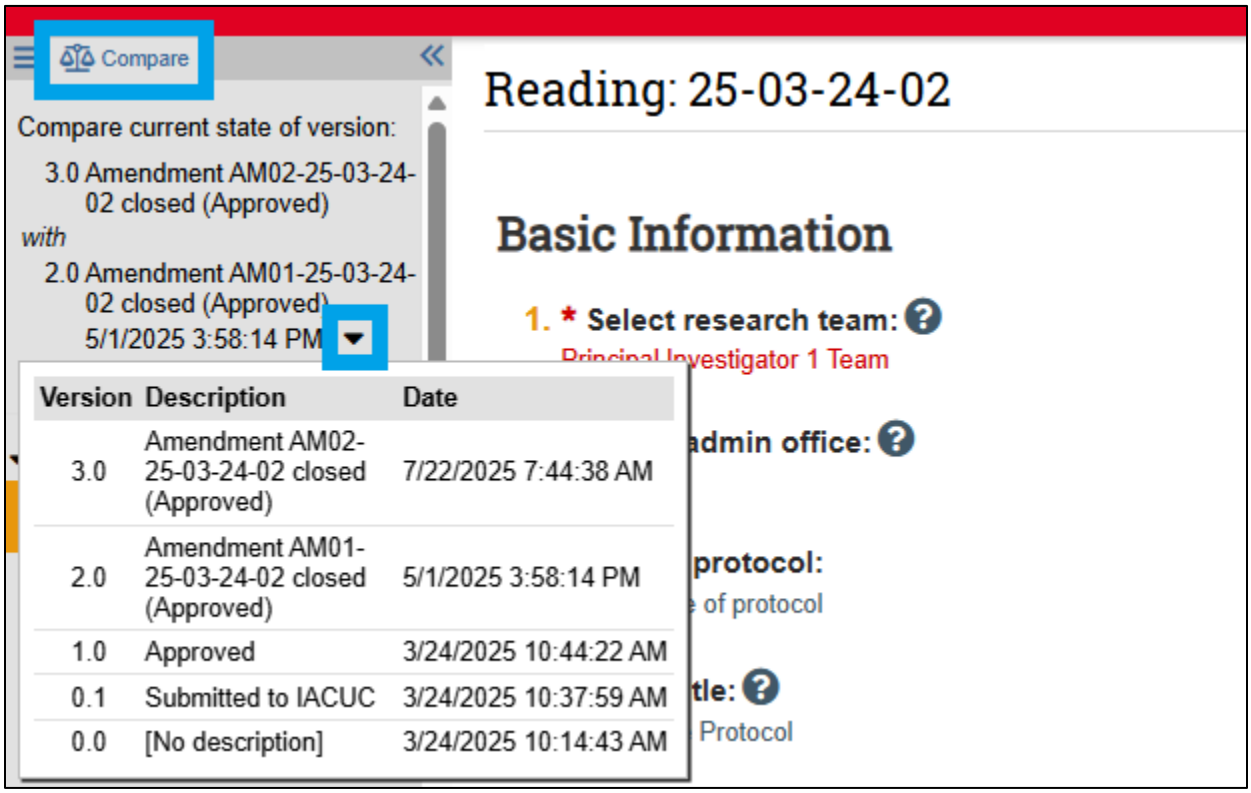
3. Use the View Protocol button or the Printer Version button on the left side of your screen to view the entire contents of your protocol.


## Reviewing Your Protocol Using the View Protocol Button

1. The right side reading pane allows you to scroll through the entire protocol.
    a. Use Ctrl + F to find specific keywords.
2. In the left side navigation, click any section of the protocol to quickly jump to its contents.

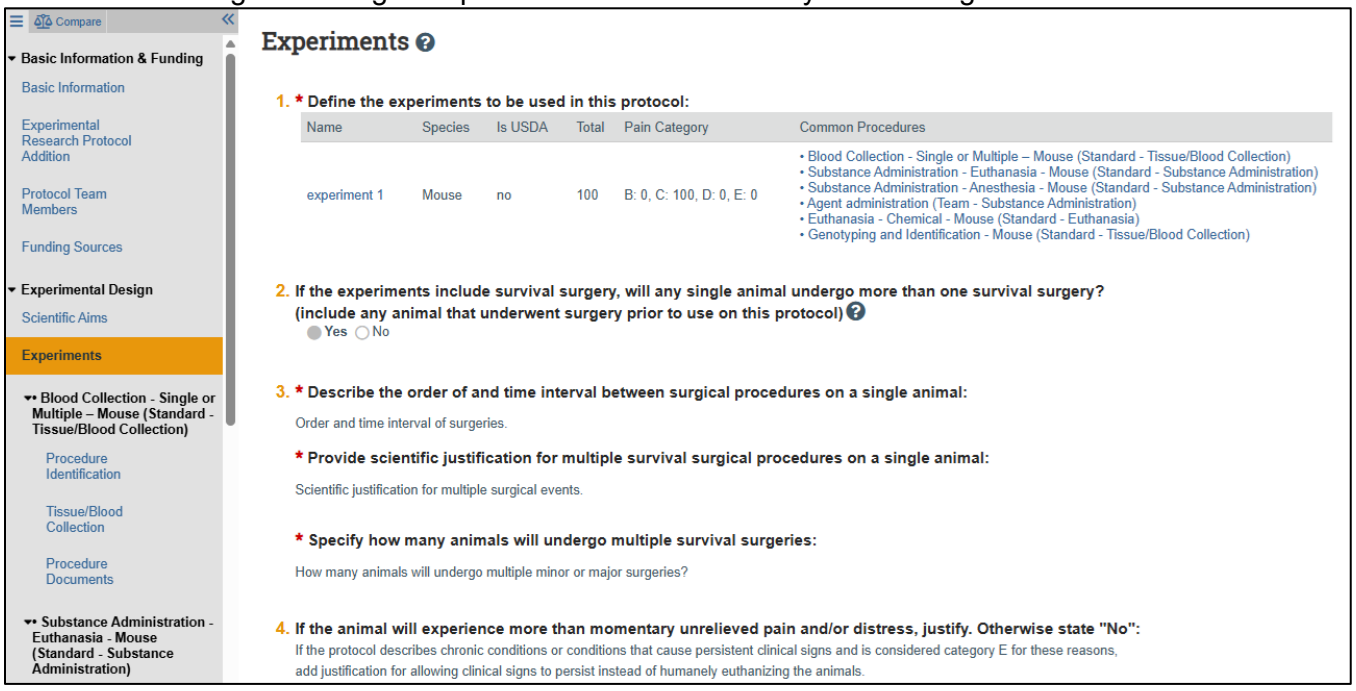


3. Use the Compare button in the top left to compare a previous version of the protocol to the current version (helpful when making requested clarifications and amendments).
    a. Click the down arrow ▼ to select the version of the protocol version that you want to compare to the current version.

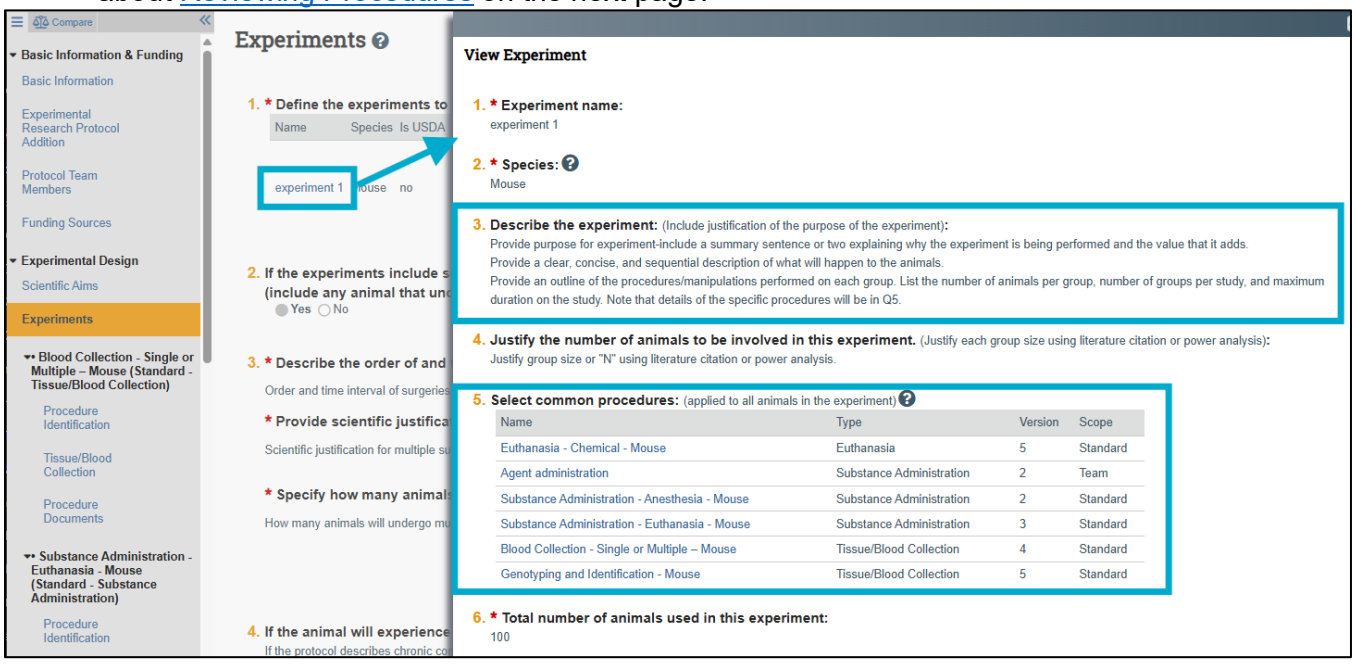



***Reviewing Experiments***

1. Click on Experiments in the left side navigation to quickly jump to that section of the protocol.
    a. Question 2 and 3 describe if there are multiple surgical events done on one animal.
    b. Question 4 describes the protocol humane endpoints. If the protocol describes chronic conditions or conditions that cause persistent clinical signs (pain category E), add justification for allowing clinical signs to persist instead of humanely euthanizing the animals.

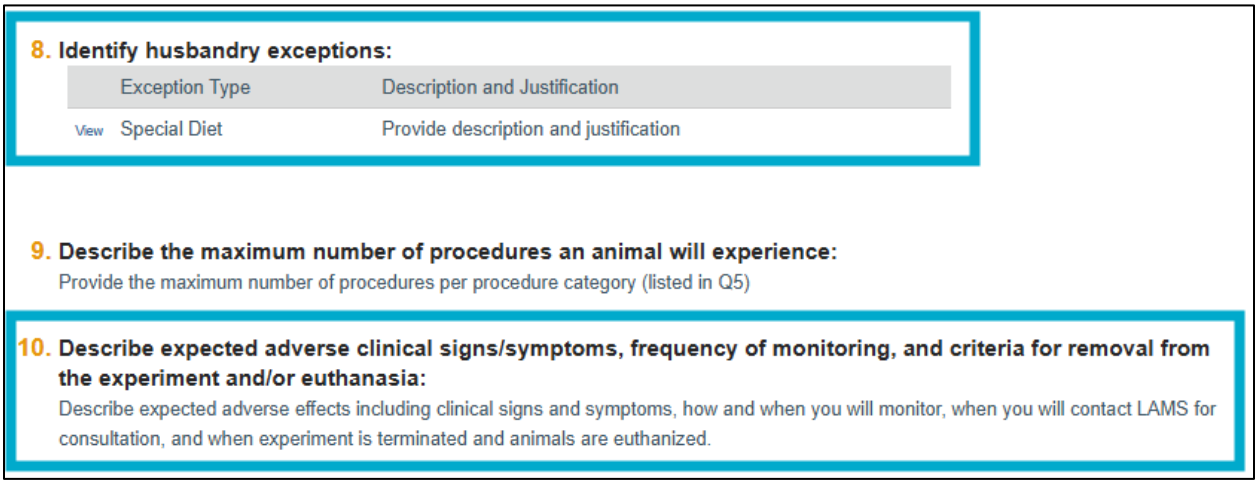


2. Click the experiment name in Question 1 to open a panel that will slide in from the right side of your screen. The slide-in panel provides further experimental details that you can scroll through.
    a. Question 3 contains a detailed description of the experiment.
    b. Question 5 provides a list of related procedures. Click the procedure name to open the procedure workspace in a new window where you can view detailed information. Learn more about Reviewing Procedures on the next page.



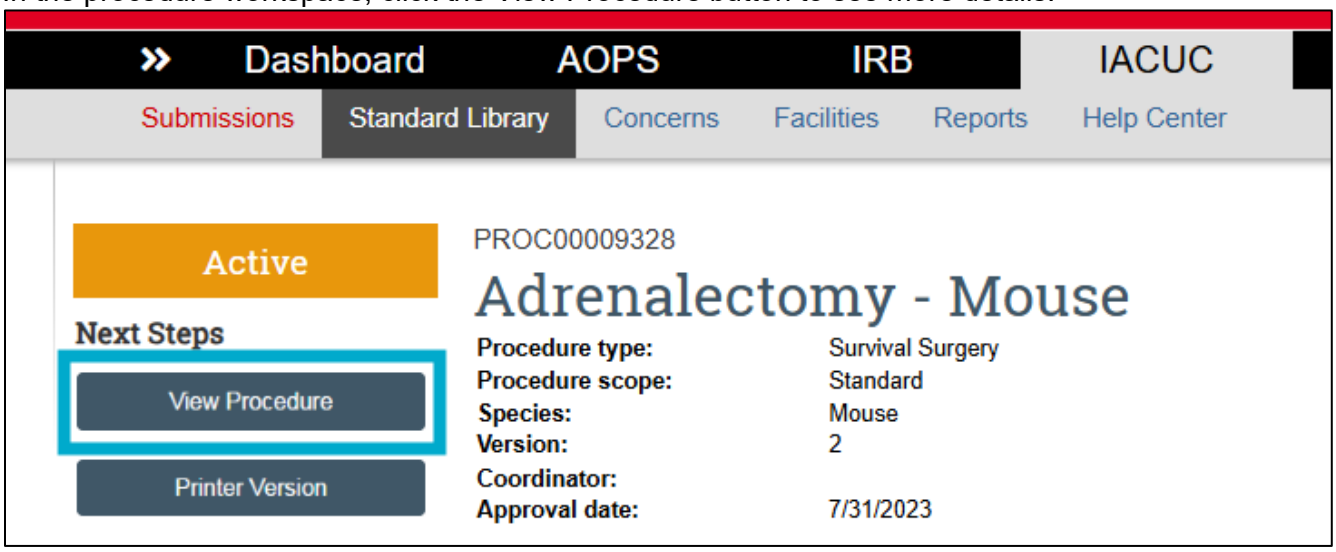

    c. Question 8 describes any husbandry exceptions to LAMS standard practices. These include single housing for social animals, non-standard caging, medicated water/special diet, withholding enrichment, acclimation waiver, do not disturb, and extended weaning.
    d. Question 10 describes humane endpoints and monitoring. This includes expected adverse effects such as clinical signs and symptoms, how and when you will monitor, when to contact LAMS for consultation, and when the experiment is terminated and animals are euthanized.

    Sometimes, questions 9 and 10 appear blank due to a system bug that will be fixed in the next upgrade. See Appendix 3: View Missing Content for Experiment Questions 9 & 10 for viewing instructions.

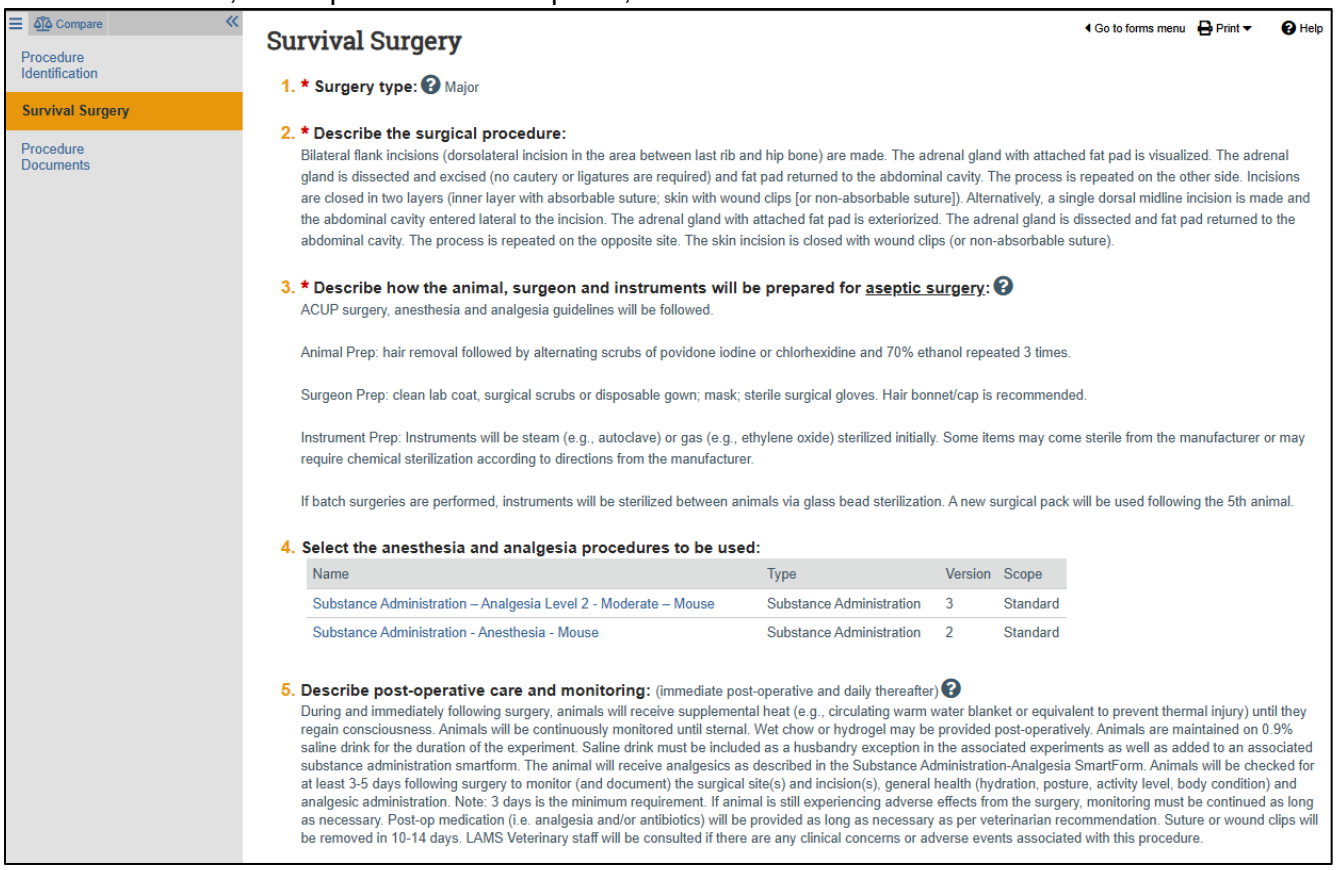


***Reviewing Procedures***

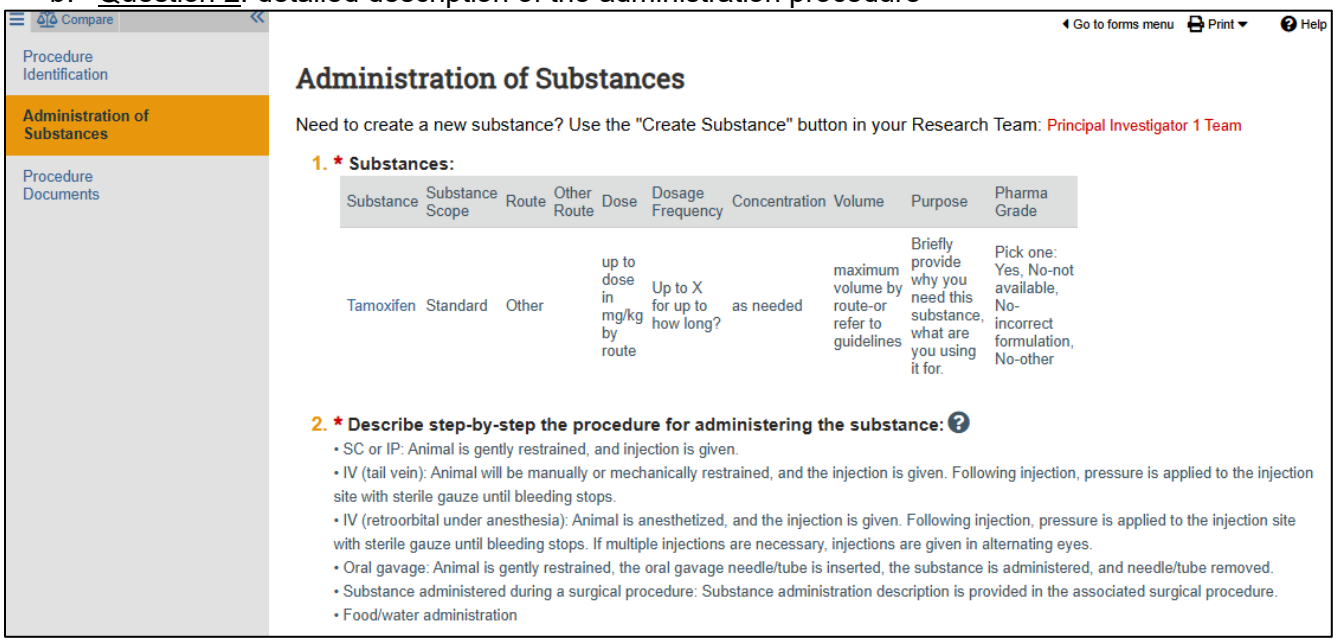
1. In the procedure workspace, click the View Procedure button to see more details.




2. Surgery procedures describe details in the Survival Surgery section of the procedure form:
    a. Question 1: procedure name
    b. Question 2: detailed description of the surgical procedure
    c. Question 3: aseptic preparation of the animal, surgeon and instruments
    d. Question 4: anesthetics and analgesics, including the level of analgesia
        i. Click the procedure name to see details (e.g. analgesia level 2 moderate)
    e. Question 5: post-operative care and monitoring, including how often animals should be monitored, what specific care is required, and more.

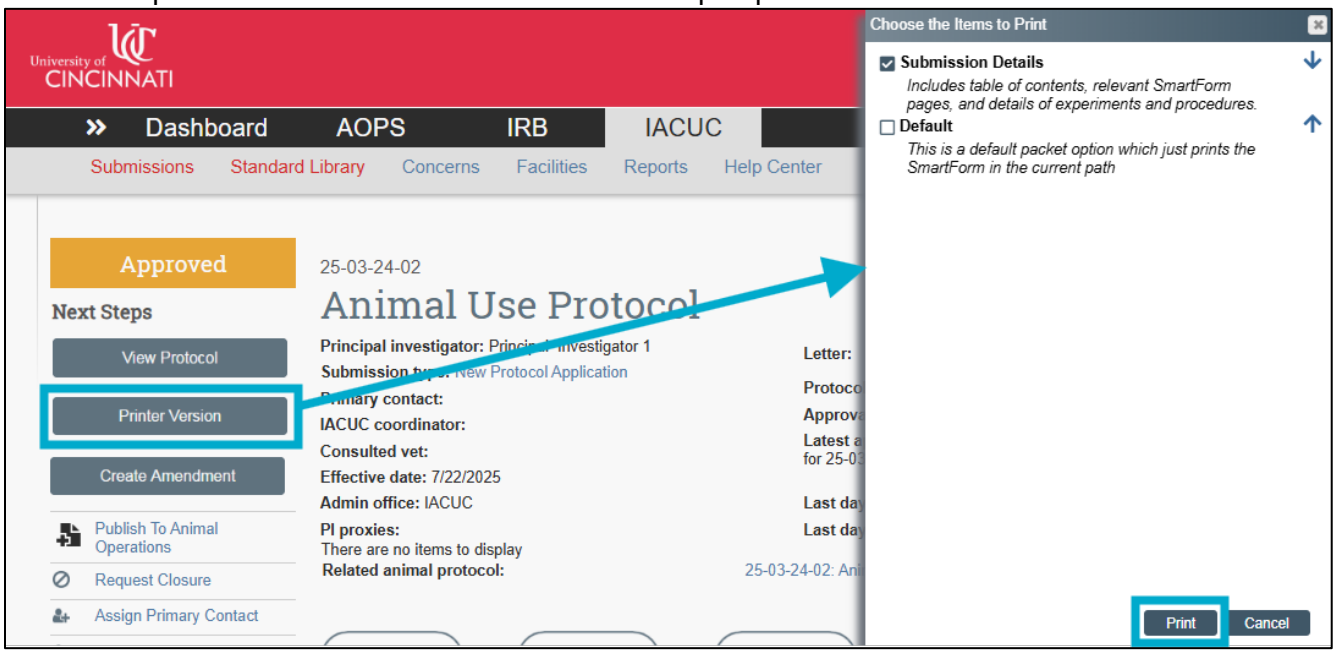


3. Substance Administration procedures describe details in the Administration of Substances section of the procedure form:
    a. Question 1: substance name, administration route, dosing and frequency, volume, how and why the substance is used, and substance grade (pharmaceutical grade or not)
    b. Question 2: detailed description of the administration procedure




## Reviewing your Protocol Using the Printer Version Button

1. On the protocol page, click the “Printer Version” button, then select the Submission Details option on the slide-in panel and click the Print button. This will open protocol details in a new window.

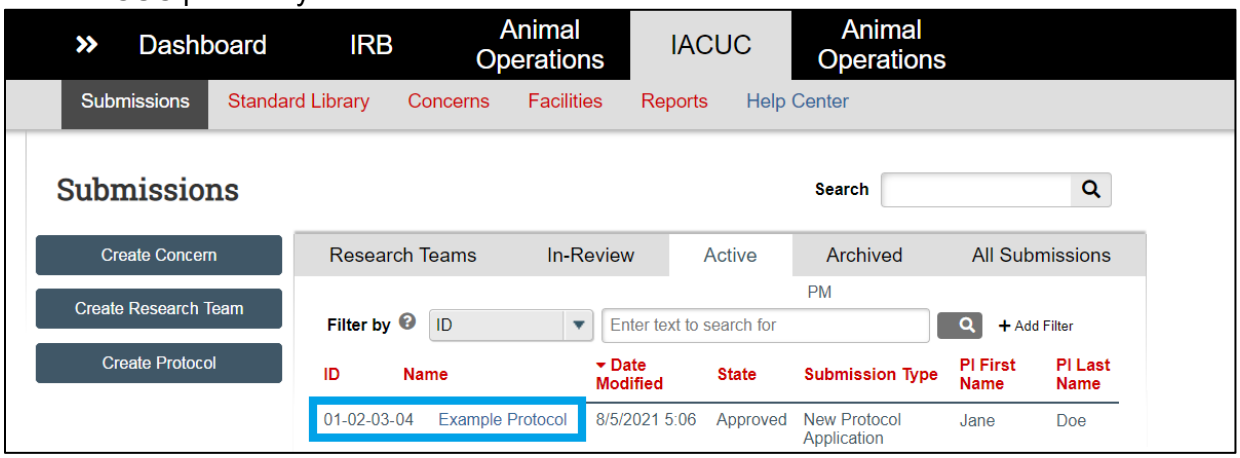



| Benefits | Drawbacks |
|---|---|
| • You can scroll through the entire protocol.<br>• Experiments are fully expanded to show all details<br>• Procedures are fully expanded to show all details<br>• Use Ctrl-F to find keywords. | • A lot of extra language and duplication of unnecessary information.<br>• Not actually printable. **Do NOT print in this form as each section prints on a different page**. Contact the IACUC Office for a printable version in Word. |

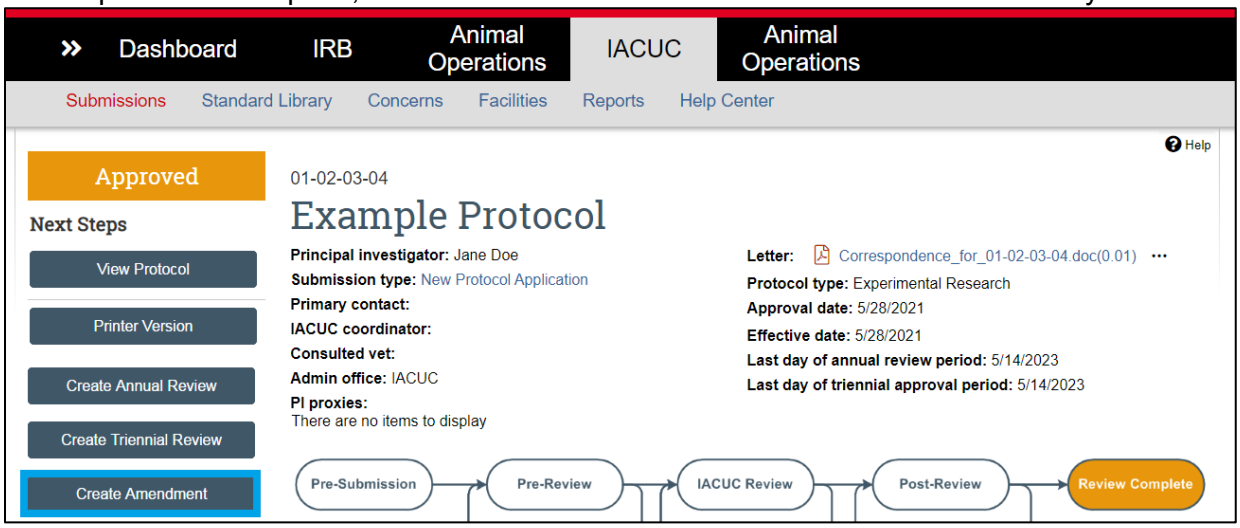
## Create and Submit an Amendment

To make changes to your approved IACUC protocol, you must create and submit an amendment, which is subject to review and approval by the IACUC.

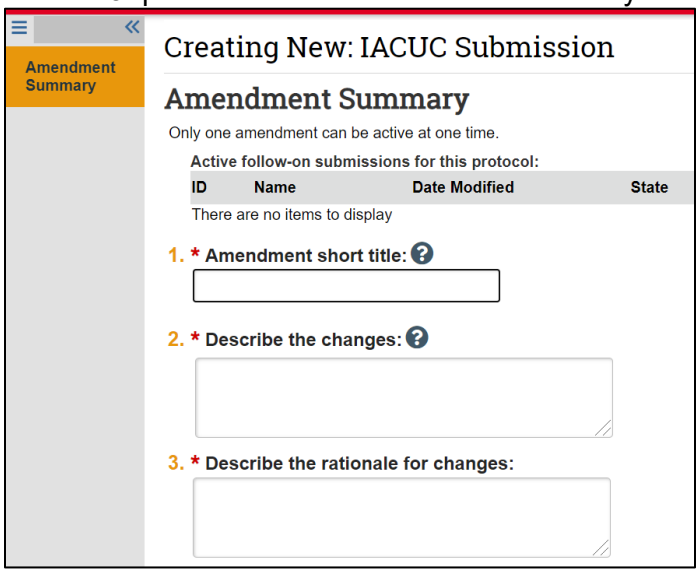
1. Select the “IACUC” tab, then select the “Active” tab on your main workspace. Click on the ID or Name of the IACUC protocol you want to edit.




2. On the protocol workspace, select the Create Amendment button on the left side of your screen.




3. Answer 3 questions in the Amendment Summary section, then press the Continue button to advance.




- **Amendment short title:** change title to reflect a summary of the amendment.
- **Describe the changes:** provide a brief description of your change request.
- **Describe the rationale for the changes:** provide a reason for your change request.

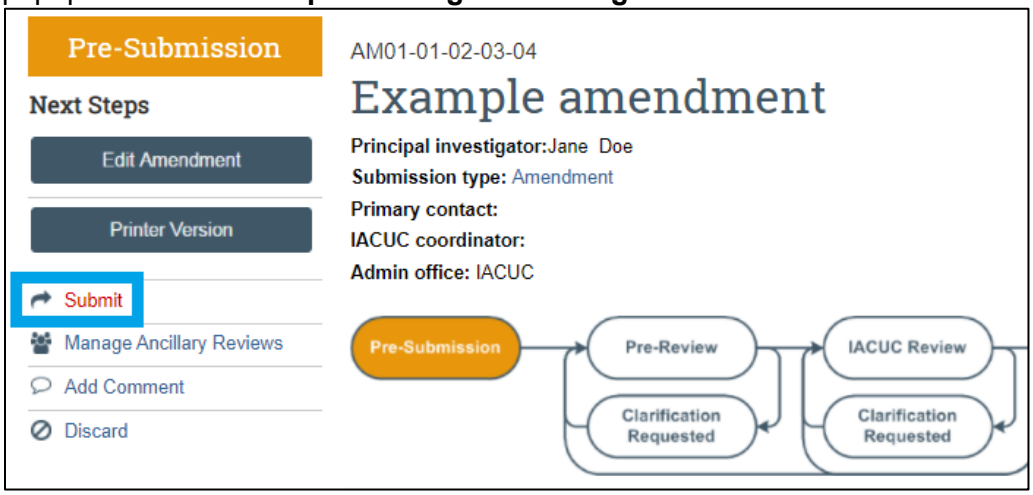
4. You now have the ability to edit each section of your IACUC protocol. After saving all changes, press the “Exit” or “Finish” button to close the form and return to the amendment workspace.

    - Refer to the Create a New or Triennial IACUC Protocol section of this manual for information on how to complete each section of the protocol form.
    - Refer to Appendix 1: Protocol Writing Examples and Appendix 2: Preferred Language and Definitions for helpful examples and resources.
    - Refer to Create a New Version of a Team Procedure to amend procedures.

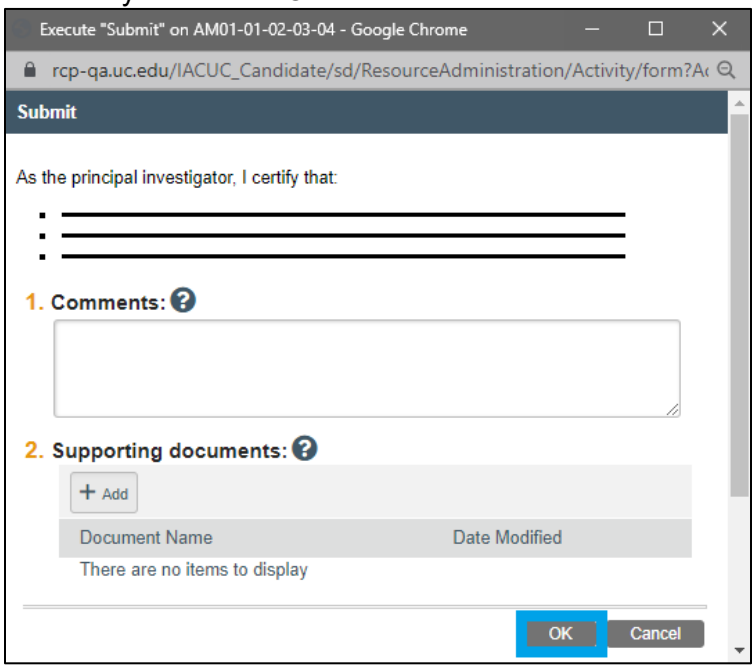
    We strongly recommend following these basic guidelines when editing an IACUC protocol:

    - Review the RAP Standard Library of substances and procedures before creating/copying a non-standard (team) substance and/or procedure (see Substances and Procedures).
    - All required form fields are denoted by a **red asterisk (*).**
    - **You must use the “Save”, “Continue”, or “Finish" buttons to save your changes. Switching sections without saving or pressing the “Exit” button will not save any changes.**

5. On the amendment workspace, select the “Submit” button on the left side of your screen to open a popup window. **IACUC processing cannot begin until the amendment is submitted.**




6. Carefully review each confirmation statement and provide comments or supporting documents if necessary. Press the OK button to submit the amendment and close the popup window.

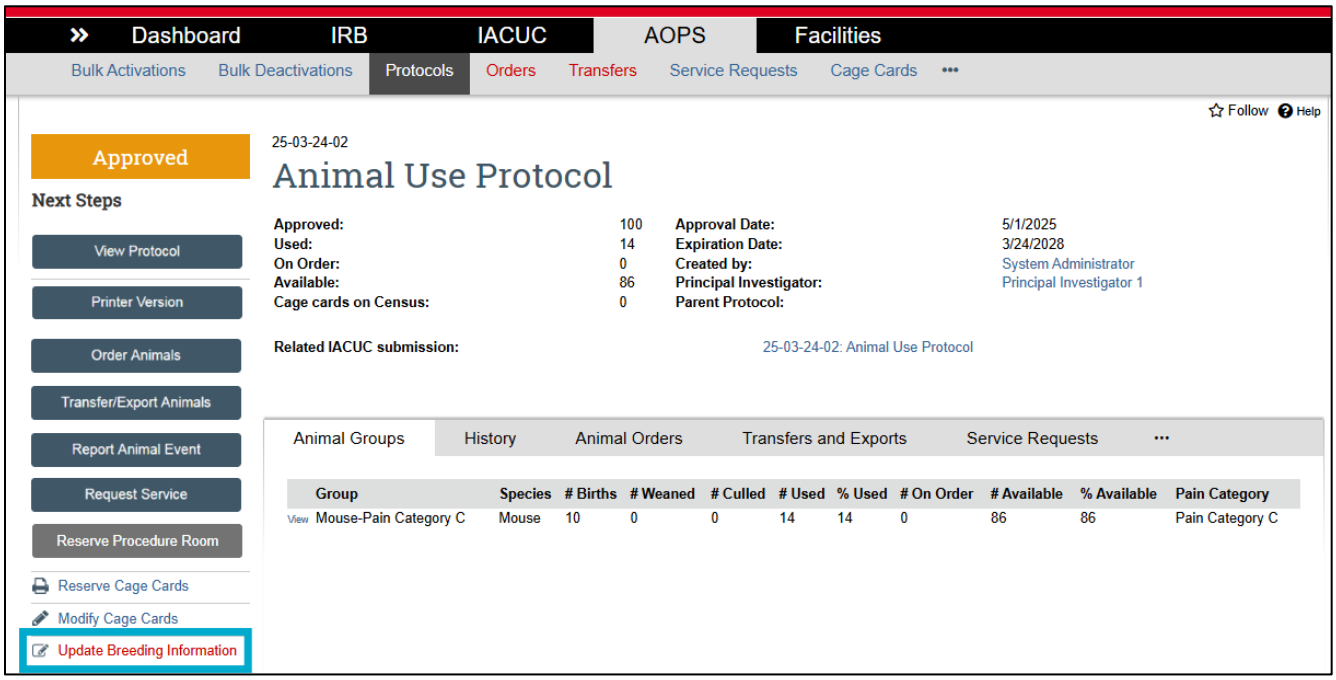


## Jumping Between IACUC and AOPS

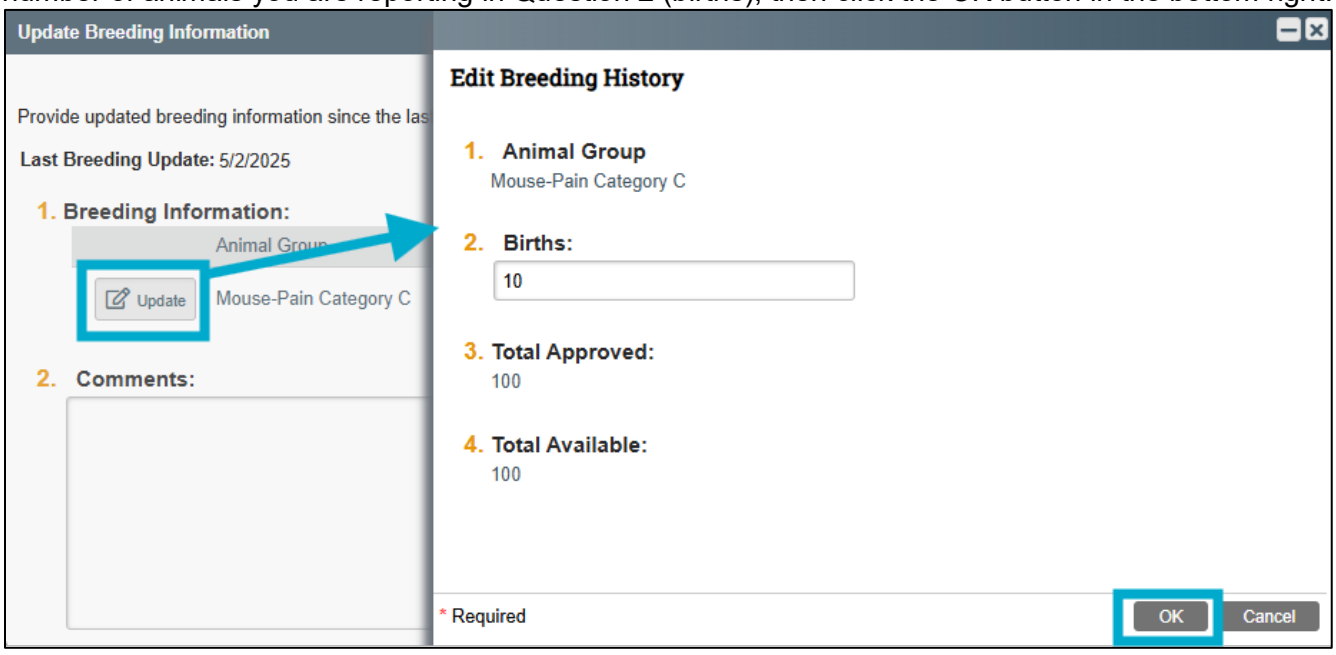
1. There are 2 areas of the RAP website that each have unique functions:
    a. IACUC RAP - protocol and personnel management
    b. AOPS RAP - animal census and LAMS services
2. On the IACUC protocol page, there is a link to the related animal (AOPS) protocol. This facilitates a seamless connection between the two areas of RAP (may require login again).


## Offspring Reporting

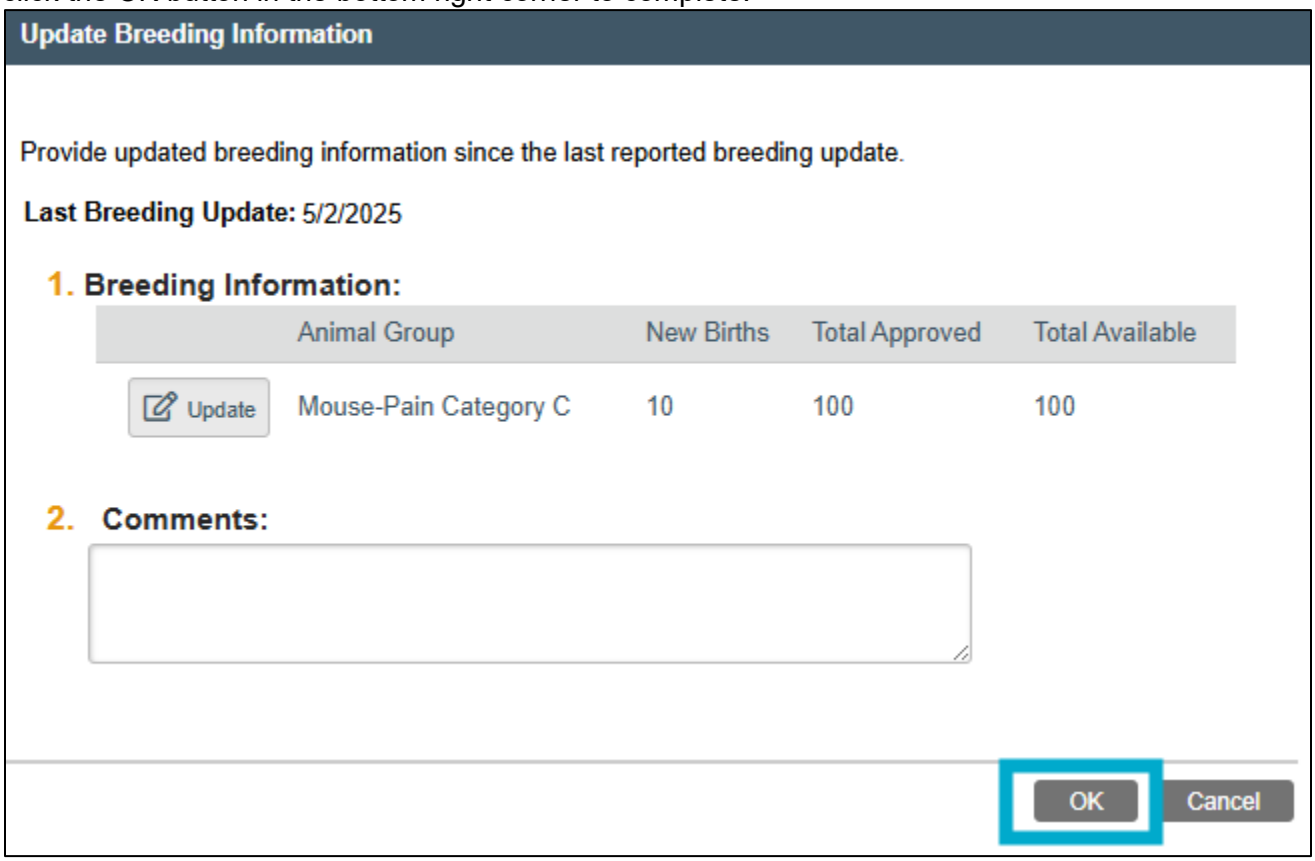
1. Must be submitted through AOPS RAP monthly and notify the IACUC Office to let us know that you will be reporting offspring in this manner per Rodent Colony Management Guidelines.
2. On your AOPS protocol page, click the Update Breeding Information link in the left navigation to open the Update Breeding Information form in a popup window.



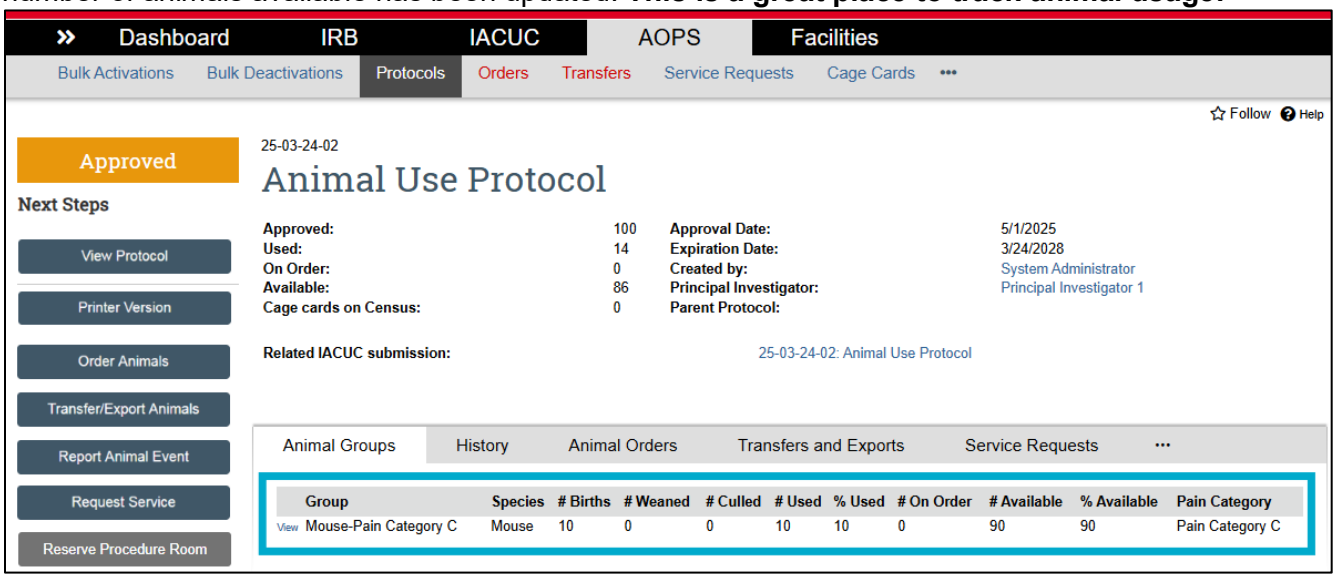
3. In the Update Breeding Information form, Question 1 (breeding information) displays the species and number of animals currently approved on your protocol. Click the Update button in Question 1 next to the species for which you want to report offspring. In the Edit Breeding History slide-in panel, enter the number of animals you are reporting in Question 2 (births), then click the OK button in the bottom right.




4. In the Update Breeding Information form, add any comments that you may have to Question 2, then click the OK button in the bottom right corner to complete.



5. The reported births are now documented on the AOPS protocol in the Animal Groups tab, and the number of animals available has been updated. **This is a great place to track animal usage!**




## LAMS Services

1. Veterinary Services: In addition to providing veterinary care and oversight of your animals, LAMS veterinary staff also provide the following services:
    - Anesthesia machine rental
    - Surgical supplies (e.g. clippers, scales, warm water blankets)
    - Surgical packs
    - Review of expected clinical symptoms (ECS) and related treatment plans
    - Handling and techniques training

2. Husbandry Services: In addition to providing animal husbandry and LAMS facility oversight, LAMS husbandry staff also provide and/or work with research staff to implement or delegate the following services:
    - Animal ordering
    - Using hazards in LAMS
    - Transportation
    - Import/Export Quarantine
    - Special requests:
        - Special caging or bedding requests
        - Special diet/water requests
        - Alternate light cycle/do not enter room requests

## *RAP Navigation Tips*

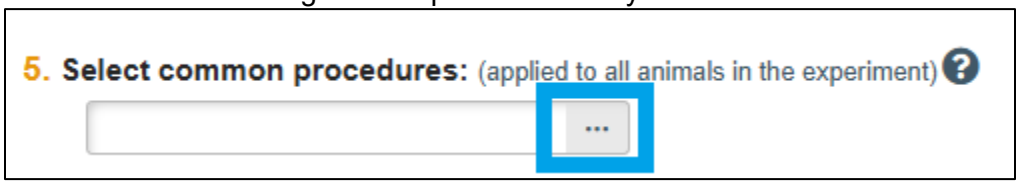
Clickable Contents

In this system, anything with red or blue lettering is clickable.

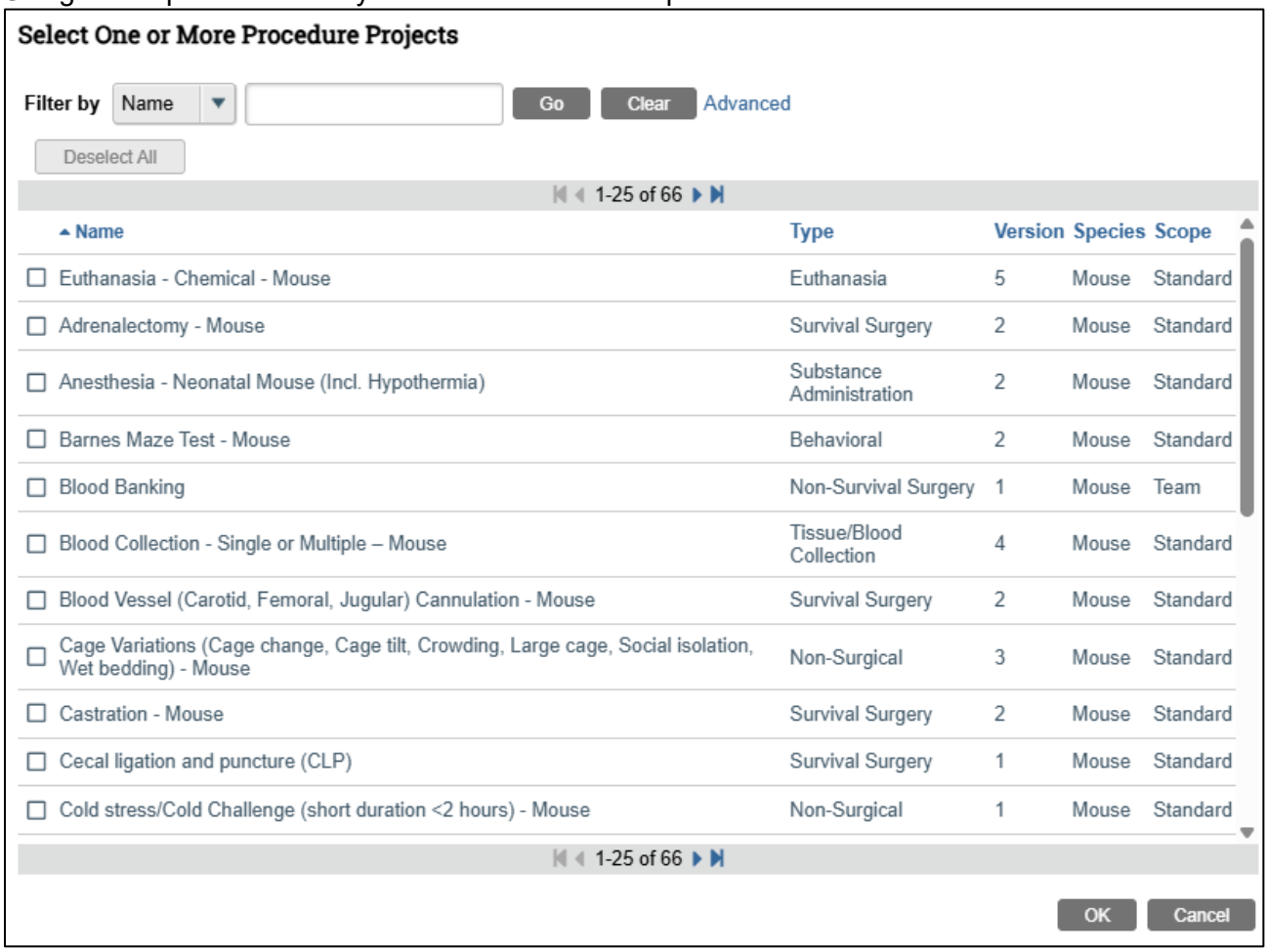
- Click a column header to sort the contents ascending or descending.
- Clicking the name of a protocol, procedure, or substance will open its contents for viewing.

Viewing and Scrolling Lists Using Ellipses (…)

1. Several locations throughout the protocol forms you will find a search box with an ellipses button.

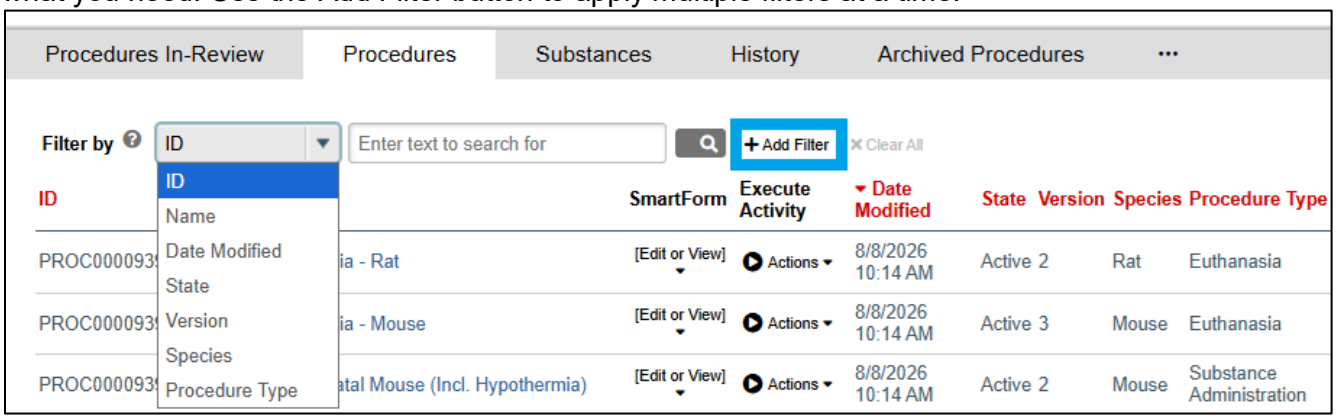


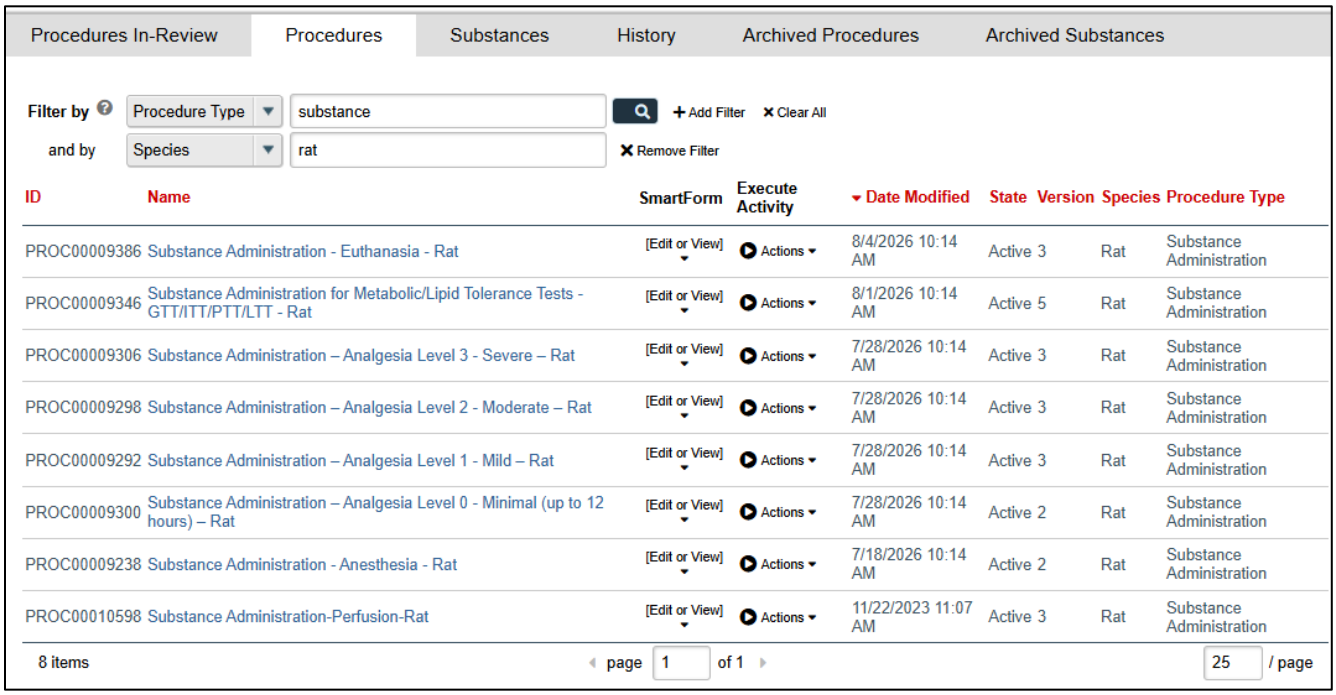

2. Using the ellipses will allow you to view a full list of options to choose from.



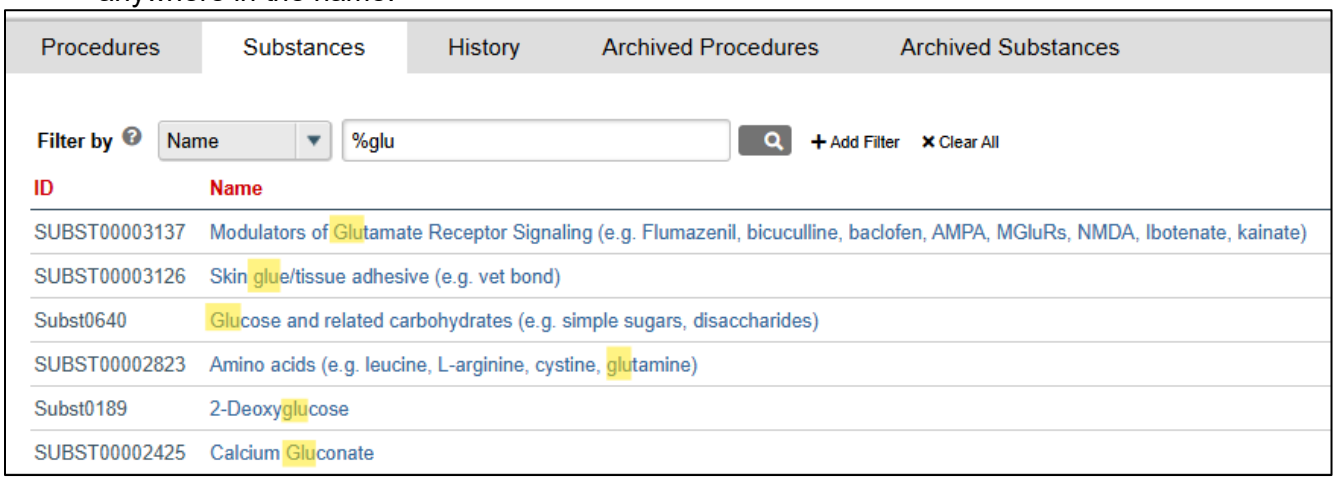
## Easy Filtering and Searching

1. Use the filter dropdown menu to sift through a large amount of information to find and focus on only what you need. Use the Add Filter button to apply multiple filters at a time.



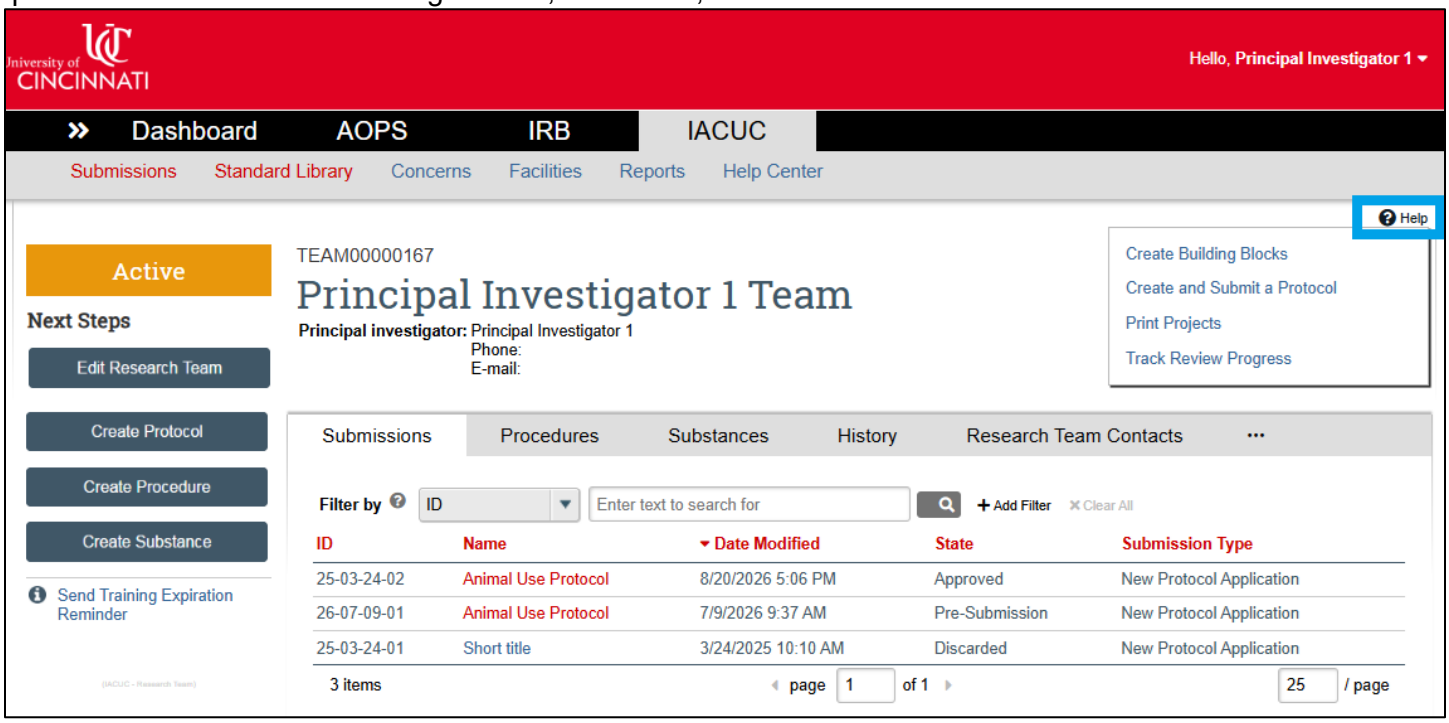



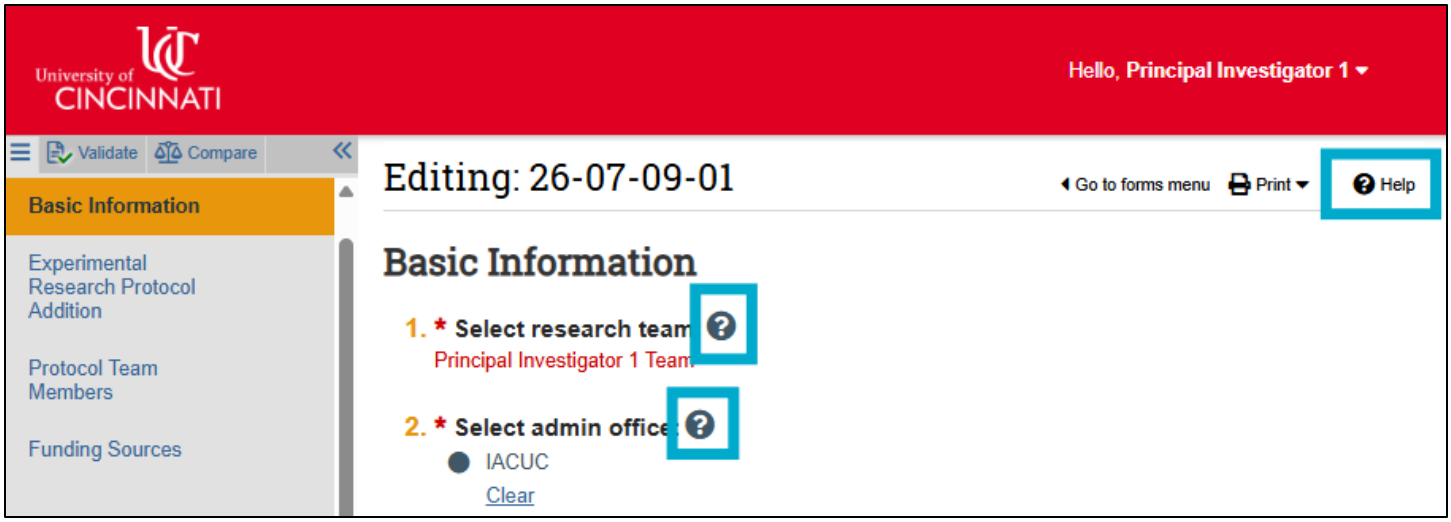

2. You can perform a partial search of data using the wildcard symbol (%).
   a. Example: searching for %glu on the substances tab will result in a list of results with “glu” anywhere in the name.



## ? Help

As you navigate through the RAP system you will see a Help button located throughout. Click on the question mark to view additional guidance, definitions, and short instructional videos.



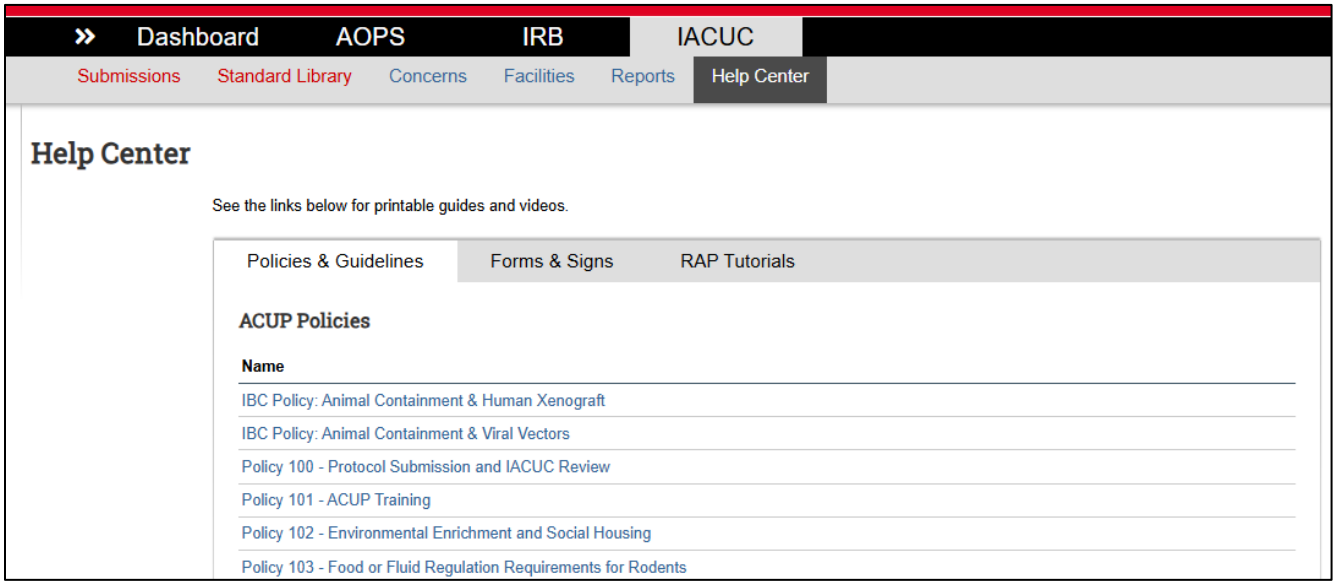



## *Where to Get Help*

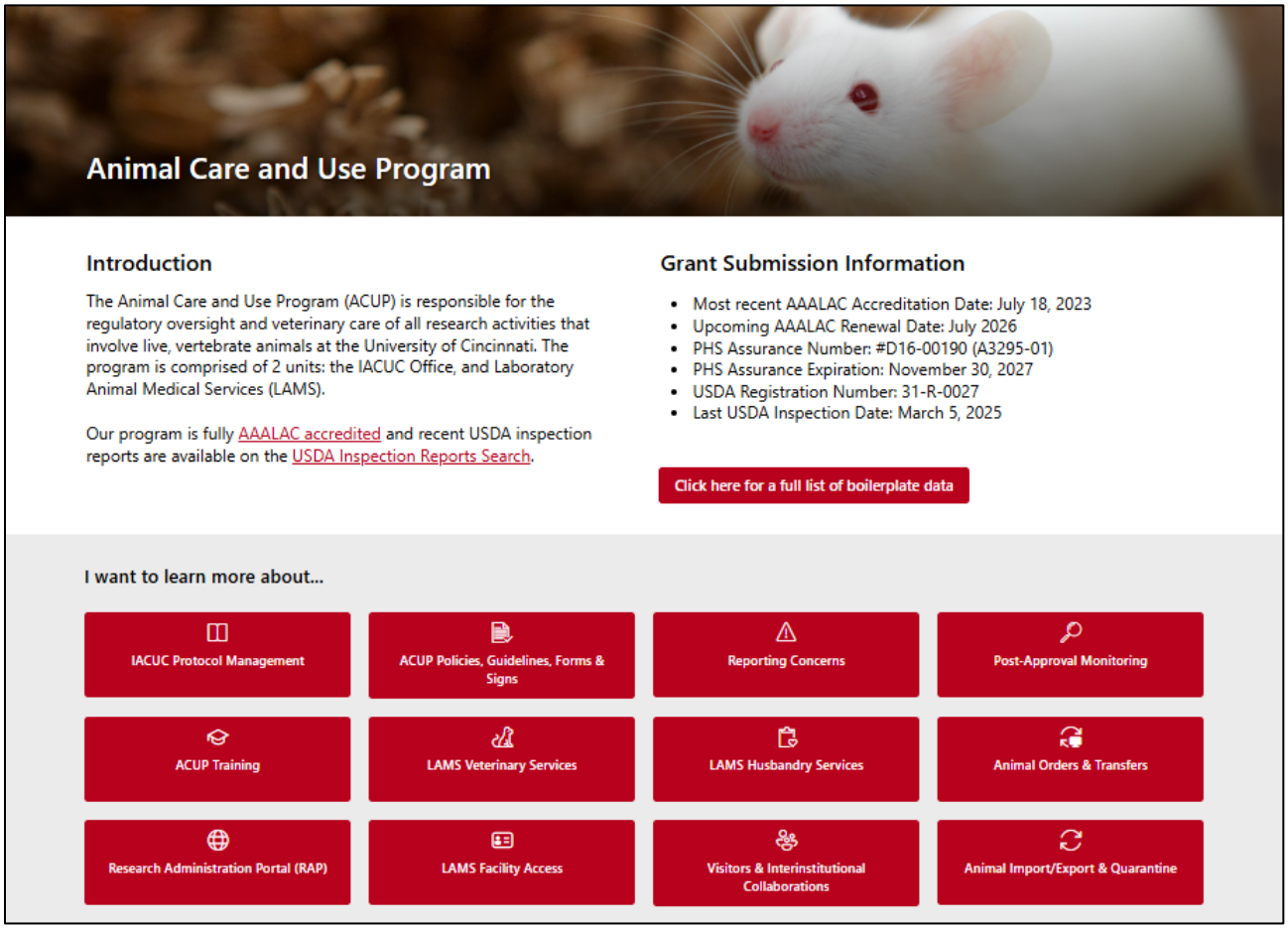
Animal Care and Use Program (ACUP) policies, guidelines, forms, signs, and IACUC/AOPS RAP tutorials are available in many convenient locations. Bookmark these pages for quick access!

1. **IACUC RAP Help Center**

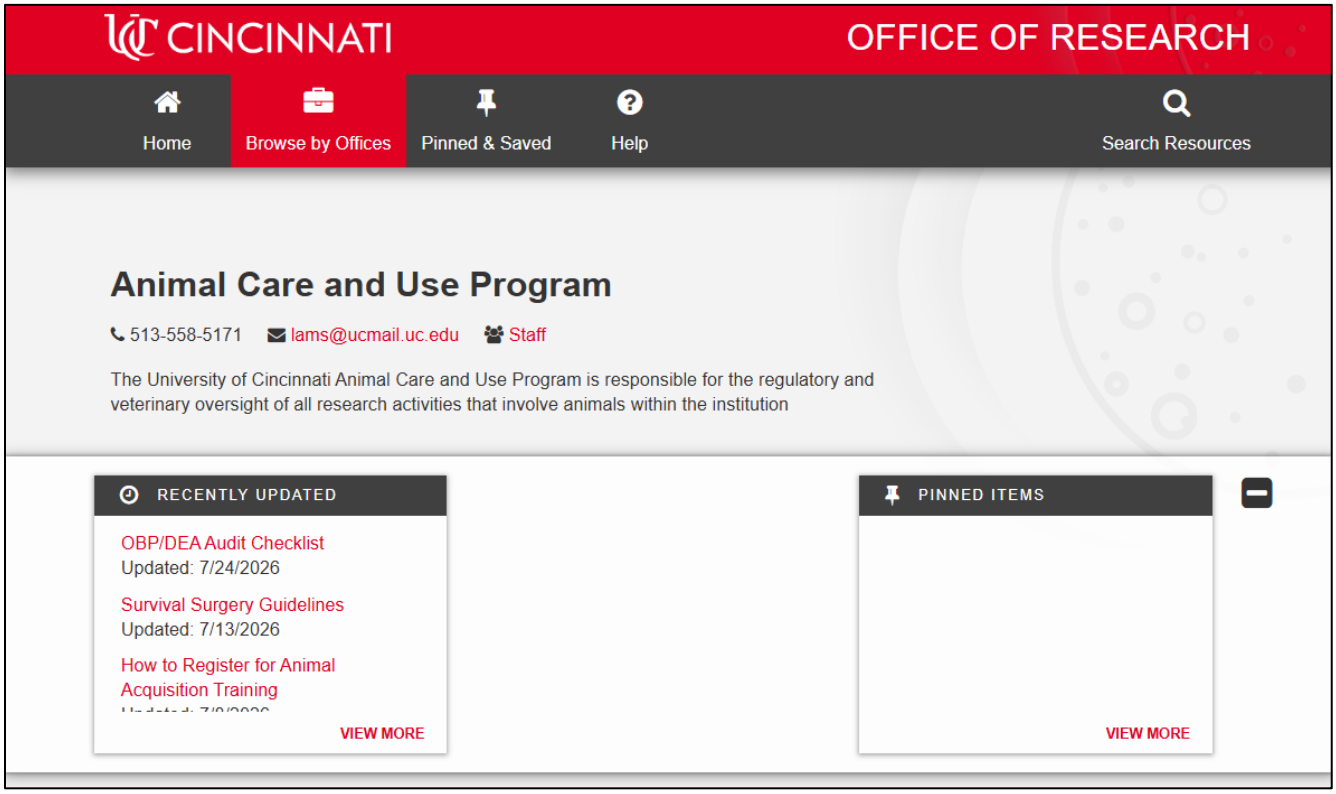
   Click the Help Center link in the top navigation of IACUC RAP.




2. **Bearcats Landing** (requires VPN)



3. **Research How 2**
   In the top navigation, you can browse by office (Animal Care and Use Program) or search resources using keywords.




4. **Contacts**

**Animal Regulatory Compliance (IACUC Office)**

| | |
|---|---|
| • General inquiries | IACUC@uc.edu |
| • IACUC RAP navigation<br>• Protocol writing & review | Nathalie Conway-James - 513-558-5106, conwayne@ucmail.uc.edu |
| • Onboarding training | Abbie Thompson - 513-936-7173, animaltraining@ucmail.uc.edu |
| • Post-approval monitoring<br>• Offspring reporting | Shandra Wombles - 513-558-5713, bohlansk@ucmail.uc.edu |
| • Compliance issues | Jenn White - 513-558-5103, brombejr@ucmail.uc.edu |

**Laboratory Animal Medical Services (LAMS)**

| | |
|---|---|
| • Urgent veterinary issues | 513-558-5518 & 513-558-6213 |
| • General inquiries<br>• AOPS navigation<br>• Service requests | LAMS@uc.edu, 513-558-5171 |
| • Caging, supplies<br>• Technical services<br>• Husbandry questions | LAMS-Husbandry@uc.edu |
| • Procedure & surgery<br>• Animal health & care | LAMS-Veterinary@uc.edu |

**Health and Safety Offices**

| | |
|---|---|
| • Biosafety | inbiocom@ucmail.uc.edu, 513-558-6182 |
| • Chemical Advisories | 513-556-8488 |
| • Radiation Safety | RadiationSafety@uc.edu, 513-558-4110 |
| • Environmental Health and Safety (EH&S) | joslinsm@ucmail.uc.edu, lamberjp@ucmail.uc.edu, 513-556-4968<br>Environmental Health and Safety website |
| • UC Health | 513-585-6600 |

**Miscellaneous**

| | |
|---|---|
| • Controlled substances | integrity@uc.edu, Controlled Substance website |
| • Human Research Protection Program | irb@ucmail.uc.edu, 513-558-5259 |
| • Sponsored Research Services (SRS-grants) | ospaward@uc.edu, 513-558-5969 |

## *Appendix 1: Protocol Writing Examples*

Example 1: Simple Experiment

Toxicological assessment of XYZ in Rats. This study will evaluate an equal number of male and female Sprague Dawley rats in up to 4 experimental doses of XYZ up to 100 mg/day for up to 28 days. Animals will be weighed and have blood and urine collected prior to study onset, and weekly thereafter. At the end of the 28 days, animals will be euthanized and tissues collected for pathology and histology.

10 animals per group (N) X 2 sexes (male/female) X 4 doses X 5 timepoints = 400 total animals

Example 2: Complex Experiment

These studies are designed to characterize the effect of chronic, early life exposure to XYZ therapies on brain function and behavior.
Using a combination of in vivo modeling, pharmacology, electrophysiology, immunohistochemistry, transcriptomics, and behavioral testing, we will test whether early intervention with low-dose XYZ activation in mouse model of early disease reduces neuroinflammation, resulting in improved outcomes. Electrophysiology, immunohistochemistry, and transcriptomics experiments will be performed at an early and late timepoint, while behavior experiments will be performed only at the late timepoint.

Experiments will involve a genetic strain of mice that develops early markers of neuropathology that are consistent with ABC disease. Experiments will use both the wild-type and the transgenic mouse, both males and females. Some mice may be fed a high fat diet (HF= 60% calories from fat) for up to 12 weeks. Beginning at 30 days of age, animals will be treated with the incretin (or saline) daily or every other day. For some animals, experiments will end at day 60 (euthanized, brains removed for experiments). For other animals, behavioral testing will begin at 3-4 months of age, and at the end of behavioral testing, animals will be euthanized, and brains will be removed for experiments. These experiments will include immunohistochemical analysis of proteins to analyze neuropathological changes related to ABC disease as well as transcriptional profiling of RNA in specific regions of the brain. Behavioral tests will include open field and a variation (object recognition), followed one week later by the start of five choice serial reaction time task . Open field and variation will occur once. The five choice serial reaction time task involves daily testing for up to 5 months (dependent on how quickly an animal learns the task) throughout the workweek (M-F) testing (see procedure description for details). An additional control group of animals will be pair fed to reduce body weight without the XYZ therapy and tested in the same way as listed above. NMR imaging may be used to assess body composition (fat vs muscle) in select experimental groups. NMR would be done at most twice, at the start of treatment (p30) and at the end of treatment (p60 or ~p120).

1. We anticipate the maximum number of experiments for this project in a 3-year period to be 2 (these experiments reflect various drugs to test interventions and mechanisms and routes of administration or diets, different behavioral tasks, different brain measures, etc.). Maximum duration of study is 9 months.
2. Up to 4 doses will be tested for each compound, as dose response studies are required in this field.
3. All behavior testing may be recorded with a video/ software system or small recording device.
Euthanasia methods: (1) At P30 and P60 some animals will perfused under anesthesia, (2) to rapidly extract brains for transcriptional profiling experiments, at p30 and p60 some animals will undergo cervical dislocation without anesthesia and then physical decapitation without anesthesia, and (3) euthanasia-chemical ($CO_2$ inhalation) will be used for any animal removed from the study for health reasons (e.g., weight loss >20%).

3 groups (wild type vs transgenic vs pair fed controls) x 2 sexes x 16 interventions (4 drugs x 4 doses) x 16 animals per group x 2 timepoints= 3072 animals

Example 3: Breeding Experiment

This experiment aims to produce animals for future experiments.
It is estimated that half the total experimental number of mice used will be transgenic.
9952 total mice / 2 = 4976 transgenic mice to be bred.
The total number of experimental mice of 4975 transgenic mice will be produced through in-house breeding.

Breeding pairs consist of one male and one female aged over 8 weeks old. We estimate litter sizes of 5 (some of our lines do not breed well). For the crosses we use to produce mice for experiments, all currently have breeding schemes in which two parent strains are crossed and produce litters in which all the mice born can be used for experiments. With an average litter size of 5, producing 4976 mice requires an additional 2* 4976/5/4 = 249 mice as production breeders, assuming each breeding pair is used 4 times. Additional mouse use comes from the breeding used to maintain the parent strains that are crossed to produce the mice used for experiments. We estimate having 8 such lines at any given time, with a minimum of 2 breeding pairs used to ensure survival of the line. With breeding every 4 months this is 2 pairs/line x 8 lines x 2 parents x 9 intervals per 3-year period = 288 mice used over the course of the protocol to maintain the parent lines. Pairs used to maintain the parent lines generally produce more mice than are needed to set up the next set of breeding pairs, so in addition to producing the 288 mice needed for the next round of breeding, these mice will produce an additional 288*5/2 = 720 mice that cannot be used and will be culled.

249+288+720=1257 culled, used as replacement breeders, or transferred to other protocols.

## *Appendix 2: Preferred Language and Definitions for Procedures*

Food and Fluid Restriction

Separate procedure is required for 16 or more hours of food restriction and 8 or more hours of water restriction. Otherwise, the restriction must be described in its associated procedure and/or experiment.

Prolonged Physical Restraint

Separate procedure is required for physical restraint greater than 10 minutes. Otherwise, the restraint must be described in its associated procedure and/or experiment.

Imaging

Separate procedure is only required if you will be performing the imaging or irradiation. Separate procedure is not required if the procedure is performed via temporary transfer.

**Question 4 (Purpose):** Include a description of the imaging or irradiation procedure and the reason the procedure is needed.

**Question 6 (Describe post-procedural care and monitoring):** Animals will be returned to their home cage following the procedure.

Survival Surgery (Animals Recover/Wake Up from Anesthesia)

**Question 2 (Describe the surgical procedure):**
Specify preferred anesthesia/analgesia used for this surgery. E.g. animals will be anesthetized with Ket/xyl; animals will receive carprofen as standard analgesic.

Choose 1 of the following closure descriptions

- Incisions are closed in 2 layers - inner layer with absorbable suture, and skin with wound clips or non-absorbable suture.
- The skin incision is closed with wound clips (or non-absorbable suture).

**Question 3 (Describe how the animal, surgeon, & instruments will be prepared for aseptic surgery):**

- ACUP survival surgery guidelines will be followed.
- Animal Prep:
    - Hair removal followed by alternating scrubs of povidone iodine or chlorhexidine and 70% ethanol repeated 3 times.
    - After hair removal, the animal will be placed on a clean, absorbent surface, such as an absorbent pad, to minimize heat loss during surgery.
    - An ophthalmic ointment (e.g. Puralube®) is applied to both eyes to prevent corneal drying and trauma.
    - Animal is placed on a recirculating warm water blanket or self-regulating heating pad for the duration of anesthesia.
    - Animal is covered with a sterile drape to help minimize contamination of the surgical site.
- Surgeon Prep: clean lab coat, surgical scrubs or disposable gown; mask; sterile surgical gloves. Hair bonnet/cap is recommended.
- Instrument Prep: Instruments will be steam (e.g. autoclave) or chemical sterilized initially. Some items may come sterile from the manufacturer or may require chemical sterilization according to directions from the manufacturer.
- If batch surgeries are performed, instruments will be sterilized between animals via glass bead sterilization. A new surgical pack will be used following the 5th animal.

**Question 5 (Describe the anesthetic monitoring):**
Anesthesia monitoring details are in the Substance Administration Anesthesia form.

**Question 6 (Describe post-operative care and monitoring):** Include descriptions for immediate post-operative care and daily care thereafter.

- During and immediately following surgery, animals will receive supplemental heat (e.g. circulating warm water blanket or equivalent to prevent thermal injury) until they regain consciousness.
- Animals will be continuously monitored until they are ambulatory and able to access feed and water without causing injury to themselves.
- Wet chow or hydrogel may be provided post-operatively.
- Animals will be checked at least once daily for at least (1 day minimal, 2 days-minor, 3 days moderate, 5 days severe) following surgery to monitor (and document) the surgical site, behavior, and analgesic administration.
- The animal will receive analgesics as described in the Substance Administration-Analgesia form.
- Suture or wound clips will be removed in 10-14 days.
- LAMS Veterinary staff will be consulted if there are any clinical concerns or adverse events associated with this procedure.

Non-Survival Surgery (Animals Euthanized Prior to Anesthetic Recovery)

**Question 3 (Describe how the animal, surgeon, and instruments will be prepared for aseptic surgery):**

- Animal Prep: hair will be removed
- Surgeon Prep: clean lab coat and gloves.
- Instrument Prep: Instruments will be clean.

**Question 5 (Describe the anesthetic monitoring):** Anesthesia monitoring details are in the Substance Administration Anesthesia form.

**Question 6 (Describe post-operative care and monitoring):** N/A

Non-Surgical

Non-surgical procedures may have a behavioral component, but animal does not have a conscious choice to participate (e.g. forced exercise, Hargreaves, burn).

**Question 2 (Describe any apparatus you will use and provide details of sanitization between uses):** Apparatus may be cleaned with 70% ethanol (or equivalent) after each animal. At the end of the study, the apparatus is sanitized with a disinfectant (e.g. zepamine, peroxigard, clidox).

**Question 5 (Describe the anesthetic monitoring):** Anesthesia monitoring details are in the Substance Administration Anesthesia form.

**Question 6 (Describe post-procedural care and monitoring):** Animals will be returned to their home cage following the procedure.

Behavioral

Behavioral procedures are those in which animals have a conscious choice to participate (e.g. CPP, open field, running wheel without forced exercise.

**Question 2 (Describe any apparatus you will use and provide details of sanitization between uses):** Apparatus may be cleaned with 70% ethanol (or equivalent) after each animal. At the end of the study, the apparatus is sanitized with a disinfectant (e.g. zepamine, peroxigard, clidox).

**Question 3 (Indicate how animals will be monitored for stress during procedure, including criteria for prematurely ending the session):** This procedure may be used as part of a stress paradigm. However, the procedure does not result in distress to the animal.

**Question 6 (Describe post-procedural care and monitoring):** Animals will be returned to their home cage following the procedure.

## Substance Administration

**Question 2 (Describe the procedure for substance administration, including route if "Other"):**

- SQ/SC or IP: Animal is gently restrained, and injection is given.
- IV (tail vein): Animal will be manually or mechanically restrained, and the injection is given. Following injection, pressure is applied to the injection site with sterile gauze until bleeding stops.
- IV (retroorbital under anesthesia): Animal is anesthetized, and the injection is given. Following injection, pressure is applied to the injection site with sterile gauze until bleeding stops.
- Oral gavage: Animal is gently restrained, the oral gavage needle/tube is inserted, the substance is administered, and needle/tube removed.
- Food/Fluid: Animals are monitored at least weekly. Water bottles are replaced/sanitized at least weekly.
- Substance administered during a procedure: Substance administration description is provided in the associated surgical procedure.

**Question 4a: If you answered "No-other" above, please provide justification for not using pharmaceutical grade. Otherwise state "N/A"**

**Question 4b For each non-pharmaceutical grade substance, describe the procedures to be used to ensure the sterility, purity, stability and physiologic pH of the compound:**

Cells are received from: NOTE WHERE THE CELLS ARE RECEIVED FROM (E.G. ATCC)

All cell lines, stem cells, and biological products (serum) originating outside of UC animal facilities, including tissues from the ATTC (American Type Tissue Collection) must be confirmed the absence of contamination with rodent pathogens and mycoplasma by MAP or PCR testing. Biological products from a commercial manufacturer who certifies with testing or screening that the materials are not contaminated with excluded rodent viral pathogens are exempted from testing. Cells are maintained under sterile conditions in culture. Cell lines are prepared specifically to meet the needs of each experiment in the laboratory.

**Question 6 (Describe the monitoring of the animal during the procedure):**

Animal will be continuously monitored during the administration.
For food/water administration-animals are monitored weekly.
For surgical administration, animals will be monitored as per surgical smartform.
For administration under anesthesia, animals will be monitored as per anesthesia smartform.

**Question 7 (Describe post-procedural care and monitoring):**
Animals will be returned to their home cage following the procedure.
For food/water administration-animals are monitored weekly. (Note-see husbandry exception in associated experiment for details)
For surgical administration, animals will be monitored as per surgical smartform.
For administration under anesthesia, animals will be monitored as per anesthesia smartform.

## Euthanasia

**Question 3 (**Describe how death will be confirmed): A secondary physical method (listed below) will be performed:

- Bilateral thoracotomy
- Decapitation
- Removal of vital organ
- Cervical dislocation (mouse only)

Tissue/Blood Collection

Only required for survival procedures. Tissue/blood collection post-euthanasia does not require a separate procedure.

**Question 2 (Describe timing and frequency of collection and amount to be collected):**

- ACUP Blood and Fluid Guidelines will be followed.
- Provide maximum blood volume for each collection and maximum volume in a particular timeframe.
    - Example: Blood samples will be taken up to 6 times, with 15-minute intervals, 50 uL (not to exceed 7.7 mL/kg every 2 weeks)

**Question 4 (Describe the anesthetic monitoring):** Anesthesia monitoring details are in the Substance Administration Anesthesia form.

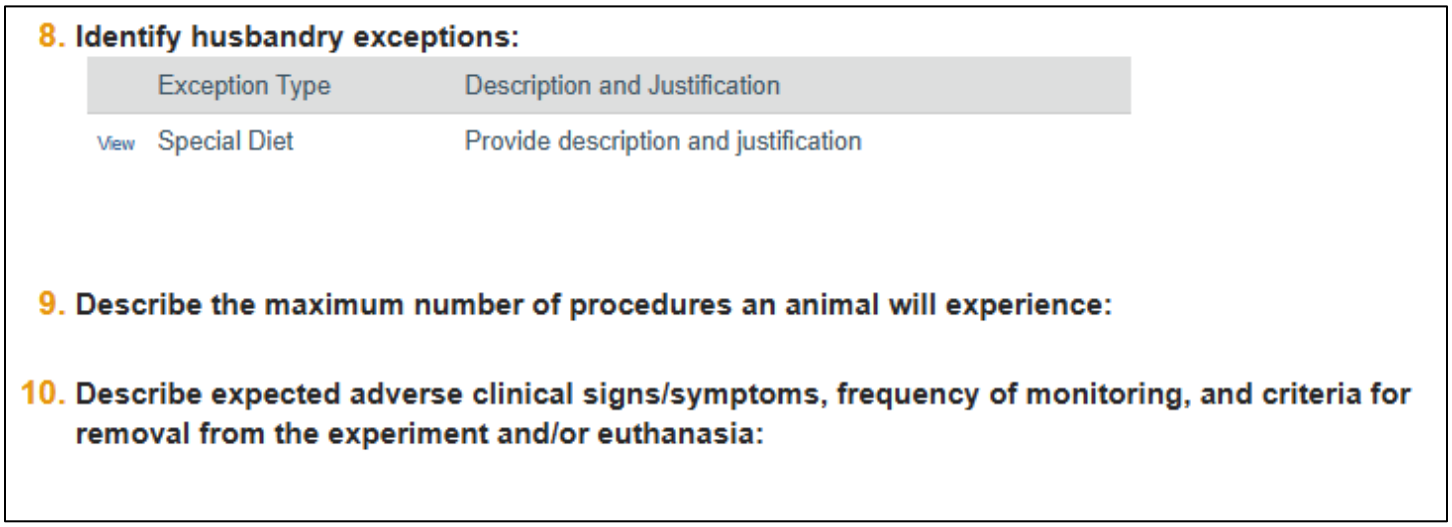
**Question 5 (Describe post-procedural care and monitoring):** Animals will be monitored to ensure that bleeding has stopped and will be returned to their home cage.

**Question 7 (Describe any potential complications from collection):**

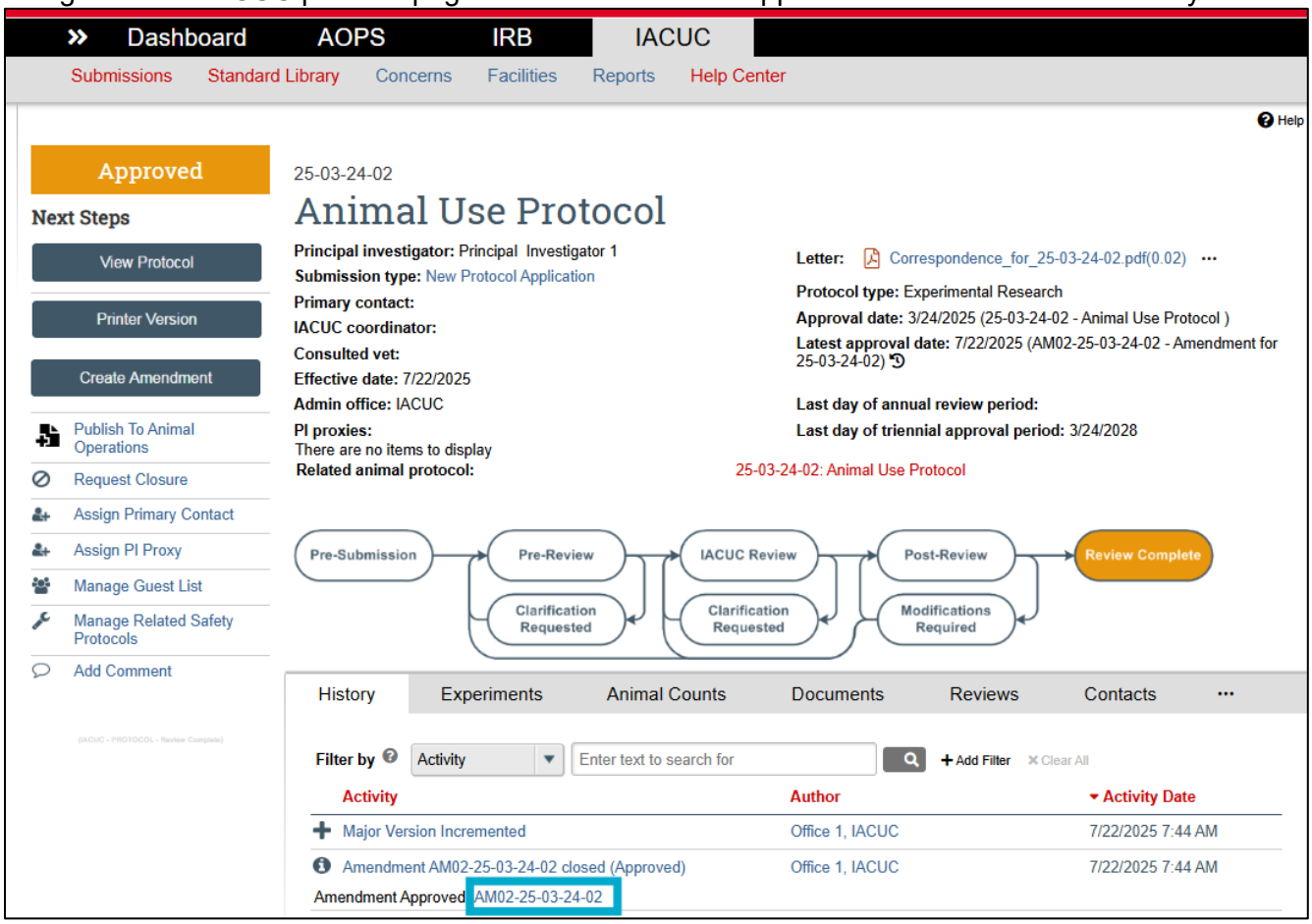
- Tail Vein: If tail becomes damaged/unsheathed, notify LAMS veterinary staff.
- If too much blood is taken/lost, subcutaneous or intraperitoneal injection of sterile 0.9% sodium chloride or lactated ringers (0.5-1 mL mouse/1-3 mL rat) depending on size of animal and amount of blood loss.

## *Appendix 3: View Missing Content for Experiment Questions 9 & 10*

If Question 9 and 10 appear blank on the View Experiment form, you will need to use the workaround described below to view this content.




1. Navigate to the IACUC protocol page and click on the last approved amendment in the History tab.



2. Click the View Amendment button in the left navigation.


3. In the Amendment Summary section, click the “here” link to open the full protocol in a separate window.


4. In the left navigation, click Experiments to jump to the section, then click the experiment name to open details in a slide-in form. Scroll down to questions 9 and 10 to view the related content.