

eIACUC ELECTRONIC FORMS

The following is a detailed guide for creating protocols in the eIACUC platform.

INTRODUCTION

The eIACUC underlying coding structure **requires** the definition/description of “Research Teams,” “Substances,” “Procedures” and “Experiments,” **in that order**. Substances and Procedures are fundamental components (building blocks) for the subsequent completion of the eIACUC section entitled “Experiments.”

Definitions:

- I) The term “Research Team” refers to the group of persons participating in the study.
- II) The term “Substance” in eIACUC encompasses the wide range of compounds or biologic materials that may be *administered* to or *injected* into animals during the course of a study (see Note below for more examples)
- III) The term “Procedure” refers to techniques, methods, and tests applied to experimental animals.
- IV) The term “Experiment” is defined as “a set of procedures, methods and techniques performed to test specific hypotheses.”

It is important to keep in mind that “Procedures” and “Experiments” are distinct entities in eIACUC. Thus, simply describing procedures in the Experiments, or in the Study Design sections of the forms would not capture all the relevant information about a study. This lack of information would require amendments of the forms and approval delays. Furthermore, not keeping this distinction may result in overestimations of the numbers of animal needed for a study, in clear violation of the 3Rs regulatory principle (Reduce, Refine, Replace).

Note: Examples of “Substances” administered to animals are: chemical compounds, drugs, carcinogens, organ-toxic agents, bone marrow cells, cell lines, tumor cells, tumor tissue fragments, viruses, infectious agents, nanoparticles, recombinant DNA, therapeutics agents, food or water additives, biologics, normal cells, etc.

SECTION 1. SUBSTANCES

PLEASE REVIEW THIS GUIDE IF THIS IS THE FIRST TIME THAT YOU ARE SUBMITTING A PROTOCOL IN eIACUC.

IF THE STUDY DOES NOT INVOLVE ADMINISTERING SUBSTANCES TO ANIMALS, SKIP TO SECTION 2: Examples: protocols involving breeding only, observational studies only.

Note: A set of standard IACUC-approved procedures to administer commonly used pharmaceutical-grade drugs (e.g. anesthetics, analgesics) has already been pre-loaded into eIACUC, and can be easily added to the protocol.

Each PI (or proxy) has a **team page** that looks like this:

Submissions Standard Library Concerns Inspections Meetings Reports Help Center

Active

Next Steps

Edit Research Team

Create Protocol

Create Procedure

Create Substance

(IACUC - Research Team)

TEAM00000005

Team for [PI Name]

Principal investigator: [PI Name]
[PI Name] (O: 0) 5-1-2500
[PI Name] [PI Name]

Submissions Procedures Substances History Research Team Contacts Archived Procedures Archived Substances ...

Filter by ID Enter text to search for + Add Filter X Clear All

ID	Name	Date Modified	State	Submission Type
PROTO201900124	cell cycle inhibition in cancer	4/6/2020 12:01 PM	Approved	New Protocol Application
PROTO201900122	IACUC-2016-0054	3/27/2020 9:23 AM	Approved	New Protocol Application
PROTO201900121	LA10-00136	12/13/2019 12:00 AM	Approved	New Protocol Application
PROTO201900118	LA10-00368	11/21/2019 1:26 PM	Approved	New Protocol Application

Click on **“create substance,”** which will take you to the following screen:

Creating New Substance

Substance Information

1. * Name:

2. * Substance types: (select all that apply)

- Analgesic
- Anesthetic
- Antibiotic
- Antitumor Agent
- Bacteria
- Biological Hazard
- Carcinogen
- Cell Line
- Chemical Agent
- Chemical Hazard
- Controlled Substance
- Feed Additive
- Infectious Agent
- Parasitic Agent
- Parasite
- Pesticide
- Radioactive Agent
- Radiopharm
- Toxicant
- Toxin
- Virus
- Other
- Select agents
- Investigational Drugs
- Recombinant DNA
- Tumor Cells
- Animal Cells
- Neurotoxic
- Nanoparticles
- Sedative
- Antigenic
- Analgesic Patch
- Inhalant Inhaler
- Local Administration
- Anesthetic cocktail

3. * Is this a hazardous agent:

Yes No [Clear](#)

4. Supporting documents: +

Enter the following information:

I. Name of substance.

II. Substance type: If there is more than one, remember to independently select **all** types that pertain to the substance that you are planning to use.

An example of a substance that has more than one type is an investigational drug that is administered orally in an animal's feed. "Feed additive" and "investigational drug" would be selected in this section. Another example is a tumor cell line that has been genetically modified to express a reporter gene. "Biological hazard," "cell line" and "recombinant DNA" would be selected in this section.

III. Answer "yes" or "no" as to whether each substance is a hazardous agent. Note that if the substance is a hazardous agent, requisite safety reviews (e.g. by the IBC, Chemical Safety, etc.) must be performed prior to the final approval of the protocol.

IV. Upload any supporting documents, such as safety data sheets (SDSs), standard operating procedures (SOPs), tumor cell IMPACT test results, or signed IBC approval letters.

V. **Click finish**. Your substance has now been successfully created in eIACUC and will always be available to you and members of your team for use in future protocols.

Repeat these steps for **all** of the substances that you are planning to use.

2. CREATE TEAM PROCEDURES

Now that you have successfully entered "Substances," you can create procedures for their use by selecting from the list below in the category of Substance Administration. **Each** "Substance" should be associated with **its own** administration procedure.

Please note that the guidelines in this section also apply to creating team procedures that **do not** involve administration of a "Substance."

The following are considered procedures within eIACUC:

- Antibody Production
- Behavioral Studies
- Euthanasia
- Food or Fluid Restriction
- Imaging
- Non-survival Surgery
- Physical Restraint
- Substance administration
- Survival Surgery

- Tissue/Blood Collection
- Special Diet/Water

Go to your team page and click on **create procedure**:

Submissions Standard Library Concerns Inspections Meetings Reports Help Center

Active TEAM00000005
Team for
 Principal investigator:

Next Steps

- Edit Research Team
- Create Protocol
- Create Procedure**
- Create Substance

Submissions Procedures Substances History Research Team Contacts Archived Procedures Archived Substances ...

Filter by ID Enter text to search for + Add Filter X Clear All

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PROTO201900119	LA10-00368	11/21/2019 4:26 PM	Approved	New Protocol Application

4 items page 1 of 1 25 / page

You will then be taken to the following page:

Creating New Procedure

Procedure Identification

1. * Name of the procedure or surgery:

2. * Select procedure type:

- Antibody Production
- Behavioral
- Euthanasia
- Food or Fluid Restriction
- Imaging
- Non-Surgical Surgery
- Physical Restraint
- Substance Administration
- Surgical Surgery
- Tissue/Blood Collection
- Irradiation
- Special Diet/Water

3. * Species:

4. * Would conducting this procedure cause any more than momentary pain and distress?

If yes:

i. Identify expected symptoms from administering this procedure:

ii. Identify criteria under which animals will be removed from research:

Exit Save

Enter the following information:

I. Name of the procedure.

II. Select the most appropriate procedure type for your study.

III. Species (should be pre-populated if using only one species).

IV. Answer “yes” or “no” to whether conducting this procedure will cause more than momentary pain and distress, and if **yes**, complete the requisite fields.

Click continue.

You will now be directed to a new screen(s) that is unique to each type of procedure in eIACUC. These screens will differ depending on procedure type. It is critical that you complete all of the required sections as they capture details that are specific to the procedures related to your study.

Examples of such information include but are not limited to:

- i) Justification for using non-pharmaceutical grade substances and details regarding their preparation (e.g. sterility, vehicle,..),
- ii) Defining health monitoring plans, humane and experimental endpoints,
- iii) Describing post-surgical monitoring and analgesia.

IACUC reviewers, USDA inspectors and accreditation agencies (AAALAC) rely on this information for timely and efficient reviews of protocols.

Once all of the information has been entered into eIACUC, **click finish**. Your Team Procedure has now been successfully created in eIACUC and will always be accessible to you and members of your team for use in future protocols. Below are screen shots of a completed, team substance administration procedure:

Procedure Identification

1. * **Name of the procedure or surgery:**
Administration of Transferrin vivo 750 (pre-IVIS imaging)
2. * **Select procedure type:** Substance Administration
3. * **Species:**
Mouse
4. * **Would conducting this procedure cause any more than momentary pain and distress?**
 Yes No

If yes,

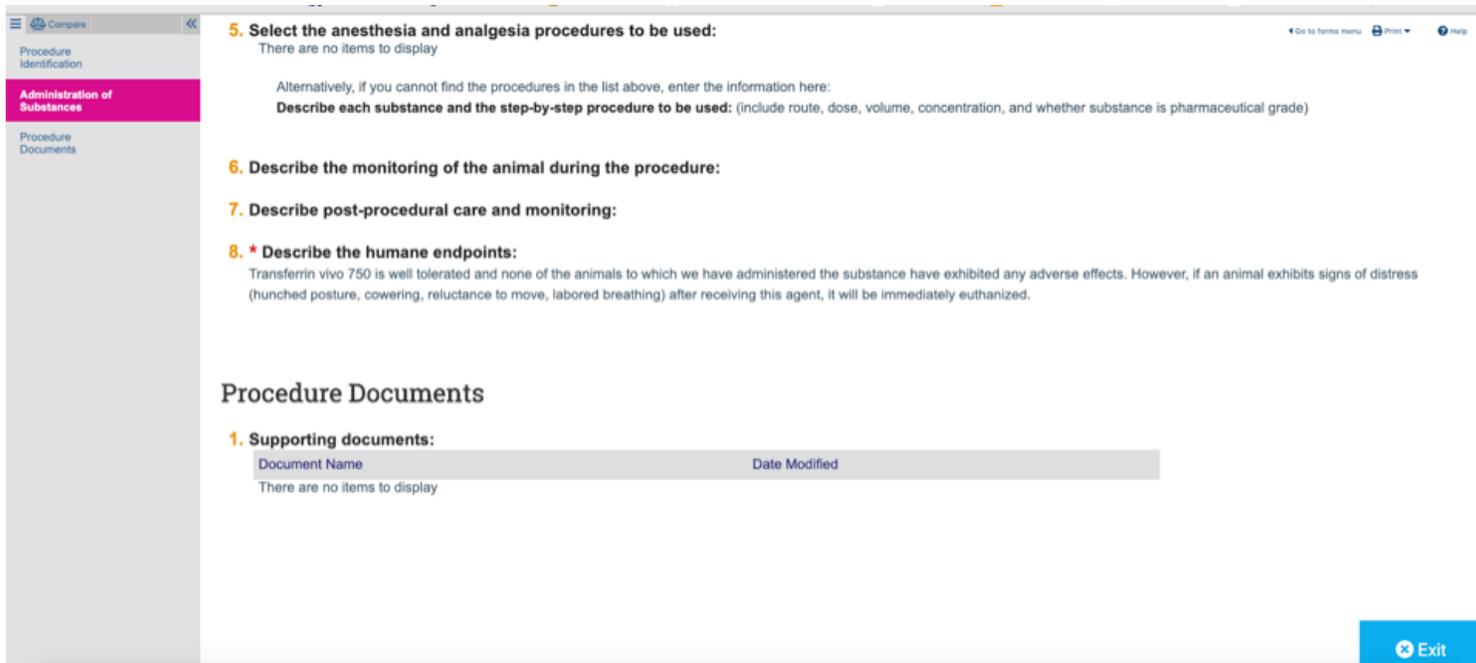
- i. Identify expected symptoms from administering this procedure:
- ii. Identify criteria under which animals will be removed from research:

Administration of Substances

1. * **Substances:**

Substance	Substance Scope	Route	Other Route	Dose	Dosage Frequency	Concentration	Volume	Complication Remediation	Substance Order for the Procedure
Transferrin vivo 750	Team	Intravenous		2 nmoles	once per week (1-4 times in total)		100ul		

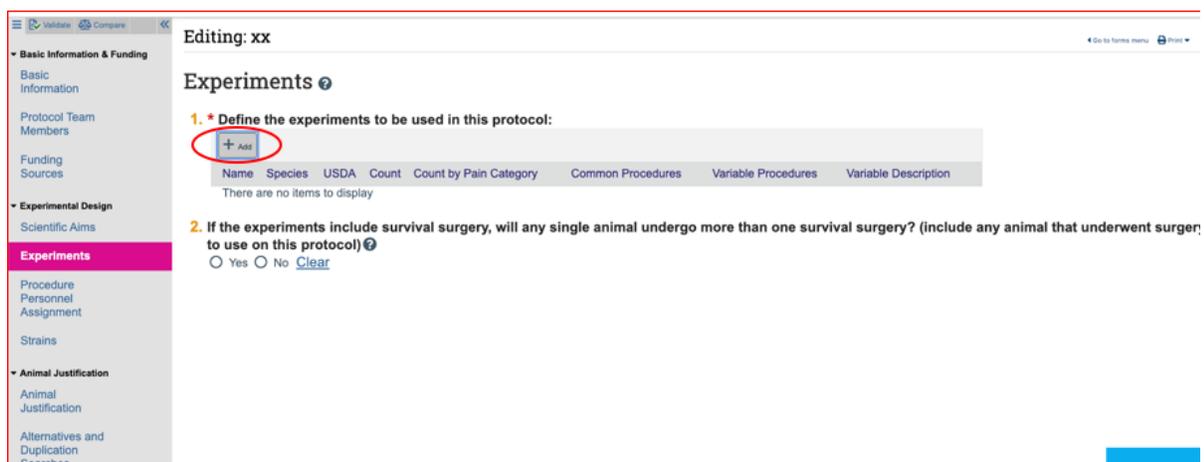
2. * **Describe step-by-step the procedure for administering the substance:**
Mice will be injected with Transferrin vivo 750 18-24 hours prior to undergoing IVIS imaging
3. **Describe any anticipated adverse reactions to administering the substances:**
4. * **Are all substances being administered in this procedure of pharmaceutical grade?**
 Yes No
 - a. * For each non-pharmaceutical grade substance, provide justification for not using the pharmaceutical grade:
This reagent is not available as a pharmaceutical grade substance. However, it is in vivo grade, which is one of the purest non-pharmaceutical grade that is available for administration to animals.
 - 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:
The stock bottle of reagent is sterile. Dilutions will be made using sterile water. All material is handled in a biosafety cabinet.
 - c. For each non-pharmaceutical grade substance, describe the storage method, if any:



3. APPLYING PROCEDURES TO EXPERIMENTS

Now that you've created substances and/or procedures for your team, you can apply them to your experiments. Applying team procedures to experiments is done in the same way as that used to apply preloaded IACUC-approved standard procedures for the administration of pharmaceutical-grade analgesics, anesthetics and euthanasia.

The following screen is what you will see when you go to the "experiments" section of the protocol.



Click add to create an experiment, and if your protocol includes survival surgery, remember to answer "yes" or "no" if animals will undergo multiple survival surgeries. You will then be

directed to a page where you:

- I. Provide details of the experiment;
- II. Add the procedures to which animals will be subjected as part of the experiment;
- III. Provide the number of animals used in the experiment as a whole.

Remember, procedures and experiments are **not** identical in eIACUC and proper use of these building blocks not only facilitates review, but also permits accurate calculation of animal numbers so that we adhere to the “3Rs” (Reduce, Refine, Replace).

You will be asked to enter information into twelve fields. Although not all are mandatory in eIACUC’s coding, providing concise and relevant information in all fields facilitates the IACUC review process. Screen shots of what you will see when you write experiment in eIACUC and an example of how it looks when procedures are incorporated into an experiment are provided immediately below:

- I. Enter the name of the experiment.
- II. Species (should be pre-populated if using only one species).
- III. Describe the experiment: this section is the equivalent of a general outline of how the experiment will be performed, along with other details such as strains, sex, age, etc. The description provided here essentially outlines the procedures used in the experiment and how they will be employed to accomplish the aim of that particular Experiment.
- IV. Justify the purpose of the experiment. What goal(s) will it accomplish?
- V. Select common procedures: these are procedures which will be conducted on **all** animals in the experiment. These can be team (generated by you) or standard procedures.
- VI. A. Define and enter variable procedures: these are procedures, which would be conducted only on **some** animals in the experiment. These can be team (generated by you) or standard procedures.
B. Define the variables of the experiment: this typically refers to the control and experimental groups to which animals are assigned, but is not restricted to only this variable.
- VII. This question refers to changes that might be needed in the pre-loaded IACUC-approved procedures for the administration of pharmaceuticals. Please enter information about changes here.
- VII. Procedure timing: although not required by eIACUC’s coding, this section is extremely helpful to IACUC reviewers for understanding the timing of the experiment as a whole. **The IACUC encourages all PIs to complete this field.**

IX. Enter the total number of animals used in the experiment. (See section 4 for additional information).

X. Assign animals to the correct pain category or categories. For example, a mouse that is used only as a source of bone marrow should be assigned to a different pain category than a mouse that will undergo a bone marrow transplant.

XI. Identify any exceptions to CCMS husbandry practices.

XII. Upload any supporting documents, if any, which are relevant to the procedure.

Screen shots showing an example of how these 12 fields can be completed are provided below. This is an experiment that has been adapted and modified from a tumor protocol. The PI generated 8 procedures that involved administration of substances, imaging, surgery, use of a special diet and euthanasia. Those procedures were outlined in the description of the experiment and applied as common or variable procedures where applicable.

1. * Experiment name:
Efficacy studies

2. * Species: ?
Mouse

3. Describe the experiment: (including animal characteristics such as age, weight, and sex)
We will determine the efficacy of compound X against solid tumors with RAS mutations. Selection of these models is based on the high frequency of RAS mutations (greater than 90%) in these types of human tumors. Two types of xenografts will be used: 1. Heterotopic xenografts derived from HCT-116 (colon) and A549 (lung) cell lines. These will be subcutaneously implanted into nu/nu mice. 2. Patient-derived xenografts (PDX) derived from lung and colorectal tumors will be implanted into NSG mice.

Mice will be monitored twice weekly until tumors reach a size of 50-100mm³. Mice will then be assigned to 2 treatment groups: vehicle and compound X. Mice assigned to the vehicle-treated group will be fed LabDiet 5053 while compound X-treated mice will be fed a custom chow (LabDiet 5053 containing 1725ppm compound X). Animals will be monitored three times per week for a period of 21-28 days and tumor volumes, body weight and body condition score will be recorded. In addition to manual tumor measurement using Vernier calipers, we will also perform IVIS imaging (once at the beginning and once at the end of the study) to confirm tumor burden. At the end of the study, mice will be euthanized and the tumor (or site of inoculation) will be harvested for further analysis.

4. Justify the purpose of this experiment:
To determine the efficacy of compound X in tumors that have a high frequency of mutations in the RAS pathway.

5. Select common procedures: (applied to all animals in the experiment) ?

Name	Type	Version	Scope
Euthanasia	Euthanasia	1	Team
IVIS imaging	Imaging	1	Team
Administration of Transferrin vivo 750 (pre-IVIS imaging)	Substance Administration	1	Team
Efficacy studies and tumor monitoring-	Substance Administration	1	Team

← Team procedure shown in section 2.

6. Define variable procedures: (applied to some animals or differently across animals in the experiment)

a. Select the variable procedures: ?

Name	Type	Version	Scope
Use of special diet-	Special Diet/Water	1	Team
Efficacy studies and tumor monitoring-	Substance Administration	1	Team
Generation of sub-cutaneous xenografts (cell lines)	Substance Administration	1	Team
Generation of sub-cutaneous xenografts (PDX)	Survival Surgery	1	Team

b. Describe the variables of the experiment: ?

Non-experimental variables pertain to the strain of mouse and tumor type. Cell lines are transplanted into nu/nu mice while PDX fragments are transplanted into NSG mice. The variables of each individual experiment (regardless of tumor type and mouse strain) are the treatment groups to which the animals are assigned (vehicle or compound X).

7. Describe any variations to the selected standard procedures: ?

8. Procedure timing: ?

1. Inoculate tumor cells (cell lines) or tumor fragment (PDX). 2. Monitor tumor growth until tumors reach 50-100mm³. (The time that it takes tumors to reach this volume vary depending on the cell line and tumor fragment). 3. Perform baseline IVIS imaging 3. Initiate efficacy studies and monitor tumor burden for 21-28 days (or sooner if a mouse reaches a humane endpoint. 4. Perform terminal IVIS imaging. 5. Euthanize and collect tissues.

9. * Total number of animals used in this experiment: (including all the animals to be produced/bred)

120

10. Number of animals by pain category: (include each animal only once in the highest pain category) ?

B: 0

C: 0

D: 120

E: 0

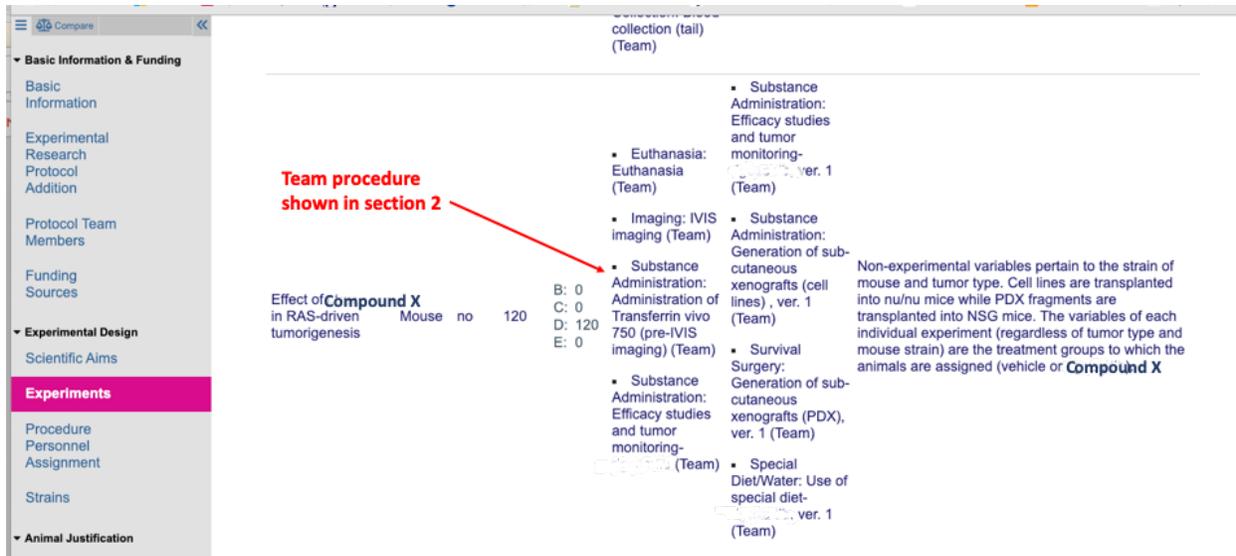
11. Identify husbandry exceptions:

Exception Type	Description and Justification
Special Diet	Compound X will be delivered via a custom formulated chow made by Envigo. Food will be provided by a member of the research team. Cages will be marked accordingly with CCMS-supplied cards ("special diet" and "do not change")

12. Supporting documents: ?

Document Name	Date Modified
There are no items to display	

If you did everything correctly and exit the above page, you will see a page similar to this when all of the procedures have been applied to the experiment and the information saved in eIACUC:



All of the blue text in the above screen shot are actually links to either the full experiment, common or variable procedures.

This process should be repeated for all of the experiments in your protocol. Remember, the same procedure can be applied to multiple experiments (and protocols) so there is no need to re-create the same team procedure for another experiment. You only need to create new substances and procedures if they do not already exist in eIACUC.

4. A NOTE ON ANIMAL NUMBERS AS THEY RELATE TO EXPERIMENTS:

The number of animals must be calculated based on what is required to meet the needs of an experiment, **not** a procedure. It is not the number of procedures to which an animal is subjected that dictate animal numbers, it is the **experiments** in which they are used. This is an important distinction.

Example 1): 20 animals undergo surgery to implant tumor fragments, and baseline tumor burdens are recorded via imaging. Mice are then randomly assigned to 2 treatment groups: vehicle- or drug-treated (n=10 per group). The total number of animals used in this study is still 20, even though not all animals receive the same treatment.

Example 2): 100 mice are subjected to a paradigm that induces a depressive state. Subsequently, these mice undergo additional behavioral studies when treated with placebo or anti-depressants. The number of mice needed for that experiment is still 100, even though the mice are subjected to 3 different procedures.

SECTION 5. GENERAL GUIDELINES FOR COMPLETING OTHER SECTIONS OF THE eIACUC APPLICATION

- I) **Lay Summary:** Please use *lay terminology* when completing this section. The summary should be understandable to the non-scientist and the lay members of the IACUC.

- II) **Scientific Aims:** in completing this section, please *do not* copy and paste complex, technical text directly from extramural applications. Please be mindful that the text should be understandable to fellow scientists, who are not specialists in your field. The narrative should be focused on aims, and concise descriptions of the experimental approach for achieving the aims of the study.