UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

Animal Study Protocol

PI: Matthew Gounis **Docket # A-2244-10**

Instructions for IACUC Animal Study Protocol application:

1. Complete the **Animal Study Protocol** application form if you are applying for a **new, 3-year renewal or *major amendment.**
   Note: Complete a separate **Breeding protocol** if you intend to share animals with other UMMS investigators or outside collaborators (please contact IACUC Office).
2. Save your file as [Your last name-IACUC] and e-mail the completed document as an attachment to: Angela.Muise@umassmed.edu
3. Print a copy and collect signatures where appropriate; send the hard copy to Angela. Muise, Office of Research, S1-859
4. Keep a copy of the document for your files
5. Call the IACUC Office for any questions to:
   Angela Muise - IACUC Coordinator at 508-856-5384 or
   Samuel Varghese, Ph.D., - IACUC Director at 508-856-5416

All Principal Investigators are required to fill out the application face page (next page) and the sections I through X of the Animal Study Protocol. In addition, please complete appropriate forms and check the boxes below. Attach the filled out forms with your application.

Forms:		
A	☒	If animals are going to be used outside of animal facilities
B	☐	If animals are going to bred just for the use in this protocol
C	☒	Using anesthesia
D	☐	Doing survival surgery
E	☐	Administering substances other than anesthetics (therapeutic agents, toxins, cells, cell lines, cell/tissue extracts, viruses and other infectious agents, purified biological products, etc.)
F	☐	Food or water restriction, prolonged physical restraint or animal care done by lab staff.
G	☐	If using radioactive agents, toxic chemicals, recombinant DNA, infectious agents, biotoxins, human or non-human primate materials
H	☐	To indicate adverse effects of procedures and experiments/monitoring and managements
I	☐	If using any of the UMMS Core Facilities
J	☐	If using sites or vendors outside UMMS
K	☐	If you are conducting a training course
Worksheet 1	☐	Animal number worksheet
Worksheet 2	☐	Breeding worksheet

Visit IACUC Website for IACUC policies, forms, instructions and guidelines

http://inside.umassmed.edu/subjects/iacuc/index.aspx

***Major amendment**: Any change that could affect the well being of animals (addition of surgical procedures, use of hazardous agents as infectious agents or radioisotopes), change of animal species.
Please send a cover letter indicating what part of the protocol you are changing, and justify the reason for requesting the change. In the protocol-form use a ***different font*** or different color for the section that you wish to amend or to change.

Docket No. A-2244-10

APPLICATION TO USE VERTEBRATE ANIMALS IN RESEARCH OR INSTRUCTION

UMMS Institutional Animal Care and Use Committee

Principal Investigator	**Name and Highest Academic Degree(s)**	Matthew Gounis, PhD
	Faculty Title	Asst Professor
	Department \ Division or Company Name	Radiology
	Mailing Address or UMMS Building	SA107R
	E-mail Address	Matthew.Gounis@umassmed.edu
	Contact Phone Numbers	Pager #: 508-722-1297 Office: 61884 Home:786-423-1382
Faculty Sponsor (if required) or co-investigator	**Name and Degree**	Shaokuan Zheng, PhD
	Faculty Title	Instructor
	Department/Division	Radiology
Primary Contact Person	**Name**	Jaime O'Callaghan, CVT
	Telephone No.	**Office 508-856-6964** **Home 508-722-3000**
	Mailing Address Building	SA107Q
Project Title	Advanced MRI Center General Protocol	

New **3-Year Renewal** **Major Amendment X** **(state changes in a cover letter)**

USE OF THIS APPLICATION FORM

- **DO NOT change formatting of this document. Type in non-shaded areas only. Forms submitted to IACUC MUST include shading. If attachments are used, they should be minimum and not replace answers to any section.**
- **If you have questions regarding the completion of this form, please contact the IACUC office (508.856.5384).**
- **Please note that upon request the University may be required by law to release a copy of this application to the public**

Signature of Department Chair **Date**	**Name (Please Print or Type)** Joseph T. Ferrucci

For IACUC USE ONLY:

Approved: **Yes** **No**

Approved with conditions: **Yes** **No**

Date **Chair/Vice Chair, IACUC**

Section I. OBJECTIVES OF PROPOSED RESEARCH OR INSTRUCTION

a. Check the box below that describes the type of animal use being proposed.

Basic Research	**x Service (Cores, Sentinels, etc.)**	**Instruction or Training**
Field Research	**Testing (Biologicals, Toxicity, etc.)**	**Applied Research**
Other_____		

b. Lay Summary: In clear, concise, *non-technical,* language (i.e., that could be understood by someone at a high school level), summarize the background and objectives of your studies involving animals.

This protocol describes the Advanced MRI Center's procedures for rats and mice when imaging as a service for users. MRI allows for a non-invasive view of the anatomical and physiological aspects of normal and diseased rodents. We provide users with imaging data to support their experimentation and hypotheses.

c. Scientific Summary: Include an abstract of the study briefly describing the specific aims and scientific approaches to achieve these specific aims. This should serve as a scientific summary of the proposed study. Please note that the detailed procedures need not be included here.

The specific aim of this protocol is to non-invasively acquire imaging data for users of the Advanced MRI Center to support their individual research. We use magnetic resonance imaging (MRI) to make detailed images of rodents which can provide quantitative characterization of anatomy and physiology. MRI uses magnetic fields and radio frequency waves to acquire images. The magnetic fields and RF waves are harmless to living organisms and thus can be used safely to investigate animal anatomy and physiology.

d. Briefly explain the relevance of the proposed research or instruction to human or animal health and/or to the advancement of scientific knowledge.

MRI of small rodents provides information on normal physiology which can be useful to predict how similar functioning occurs in humans. Further, small animal models of disease allow researchers to ascertain the underlying physiological processes. MRI of these processes is non-invasive and thus can be used to get a true *in vivo* perspective of physiology.

Section II. RATIONALE FOR USING ANIMALS AND ALTERNATIVES TO THE USE OF ANIMALS

a. Briefly explain why animals are required for your studies.

The center images animals at the request of individual Advanced MRI Center users. Their need for animal studies varies widely, but most focus on understanding disease in a model organism that is well characterized. Human research has high variability due to individual differences whereas small animal models of disease can be repeated with low variability. Further, investigational treatment studies are conducted that use MRI as an endpoint to determine the efficacy of treatment.

b. Briefly explain why the species you propose to use is/are the most appropriate.

Users of the center will provide us with animals to image as a service. Their individual needs for rats or mice vary widely.

c. Describe the steps you have taken to reduce the usage of animals and to minimize the lethality of procedures in your experiments (e.g., using cell culture, computer simulations, or non-living models; doing pilot studies, using most specific assays possible).

We review all animal protocols before committing scanner resources to ensure that MRI studies are planned properly to ensure animal usage is kept to a minimum.

Section III. NUMBER OF ANIMALS REQUESTED: PAIN / DISTRESS LEVEL

a. List the number of animals you will use over the duration (to a maximum period of 3 years) of this protocol.

By NIH policy, you will still have to renew your protocol every 3 years. This requirement is independent of the need for the IACUC to initially review all animal activities described in your grant proposal, irrespective of the grant's time period.

All animals must be accounted for, including E-17+ embryos (rats and mice) and neonates. The total for each row should equal the sum of the values in that row.

Species	Number in Pain / Distress Level B	Number in Pain / Distress Level C	Number in Pain / Distress Level D	Number in Pain / Distress Level E	Total (should agree with numbers in worksheets I and II)
Sprauge Dawley Rats			200		200
Mice (Various Genetic Variants)			200		200

Pain / Distress level indicates <u>maximum</u> pain or distress level to be experienced by animal(s):

B = being bred but not used in testing, teaching or experiments
C = negligible;
D = pain / distress relieved by appropriate drug use;
E = pain / distress <u>not</u> relieved by appropriate drug use. <u>See the IACUC Instructions for definitions and examples</u>.

- **Induction of tumors is Category C if no distress is anticipated or if you monitor the status of animals and euthanize sick animals when detected..**
- ***Mice used for Ascites Production are <u>always</u> Category "E". CFA may only be used ONCE in an animal***

b. If you have animals in category E, use this space to provide a description of the procedures producing pain or distress, and list the reasons why pain-relieving drugs cannot or will not be used to relieve pain or distress. If pain/distress relief would interfere with test results, justify why that is true.

c. If there are federal guidelines or regulations that *<u>require</u>*** the use of laboratory animals then use this space to cite the agency, CFR title, number and specific section (e.g., Food and Drug Administration, 21:CFR1030.110).**

Section IV. JUSTIFICATION OF THE NUMBER OF ANIMALS REQUESTED

NIH rules require that animal use must be kept to the minimum consistent with a sound scientific outcome. Please use the space below to justify that the number of animals requested is appropriate for the goals of the experiments.

a. Write a brief description of experimental design. In a table below (for large number of animals, please attach an animal number worksheet in the appendix), show all of the experimental groups and the number of animals per group. Be sure that the totals in the table match the totals shown in section III (Number of Animals Requested). Provide a science-based justification for why you chose the number of animals needed per group or other division of your research.

The number of animals requested is an estimate of the total number of animals that users of the Advanced MRI center will image. The ultimate number of animals imaged will depend on the limits allowed for by each user. As mentioned above, 200 rats and 200 mice seems like a reasonable amount give past trends.

b. Describe, in general terms, the statistical tests required for the study.

Statistical justification for the specific number of animals will be determined by the Advanced MRI center users' protocols.

Section V. ANIMAL SPECIFICS

a. Describe the age/weight, sex, and source of each animal species/strain.

SPECIES / STRAIN	AGE / WEIGHT	SEX	*VENDOR
determined by user			

***Note that the UMass Transgenic Core should be listed as a vendor if animals are produced there for you.**

b. If any of your animals have special needs, use the space below to list needs for special handling or housing.

c. Specify what parameters you will assess to ensure that the animals are healthy before your experiments begin. Check all boxes that apply.

Activity	x	**Appearance**	x	**Appetite**		**Behavior**	
Excreta		**Respiratory Pattern**	x	**Temperature**		**Weight**	x
Laboratory tests or other observations (specify)							

Section VI. EXPERIMENTAL PROCEDURES: (*except* any survival surgery and procedures that may lead to a permanent physical or physiological handicap).

a. Basic chronology (please use a flow chart or a sequential list of activities)

1.) Animals will be delivered to the Advanced MRI Center at SA107 by individual users.
2.) Anesthesia will be induced in rodents through the use of 5% Isoflurane in room air
3.) Animals will be placed inside of an RF coil equipped with a tube delivering anesthesia to the animal
4.) Animals will be monitored for respiration, ECG, and temperature (High or low respiration or heart rate indicates an increase or decrease in anesthesia levels, respectively).
5.) Animals will be imaged according to the request of the users. Typical imaging sessions on small animals can range anywhere from 30min to 4hrs.
6.) Following imaging, the animals will recover or sacrificed as dictated by the users IACUC protocol. Animals which are allowed to recover while under the care of the core facility.

b. Detailed description of procedures (do not include details of in vitro procedures): Describe in narrative form all procedures to be carried out on living animals from initial contact to euthanasia.

This protocol is designed to lay out general procedures for animal handling as a service to users of the Advanced MRI Center. All animals imaged at the advanced MRI center must be processed through Animal Medicine as indicated by the user's protocol. Animal imaging will not be permitted by users whose animals have not originated from an University of Massachusetts Medical School Animal Medicine facility and who do not have UMMS IACUC approved protocols. Before imaging services are provided, users must submit an authorization form (attached) and prior to and following each experiments, users are required to report the condition of the animals using a reporting form (attached). Following delivery of animals by the users to the MRI facility, animals will be anesthetized using 5% isoflurane in room air. The depth of anesthesia will be judged by a reaction to a paw pinch. Once an acceptable depth of anesthesia is obtained, animals will be placed in the center of an Radio Frequency (RF) coil. Once in the RF coil, the animal will be administered anesthesia through a nose cone using between 1-3% isoflurane in oxygen. The isoflurane level will be determined by the animals physiological response (High or low respiration or heart rate indicates an increase or decrease in anesthesia levels, respectively). The exact position of the animal will depend on the organ to be imaged. Next, ECG pin electrodes (2cm length) will be inserted in the subQ space on the dorsum of the both the left hindfoot and right forefoot. An air bellows will be placed around the animals' abdomen for monitoring respiration. A temperature probe will be inserted in the rectum to determine appropriate animal temperature. Animals will be warmed using a hot air heating system or a heated water pad. The heating systems are under thermostatic feedback control such that they will power off if the animal's temperature rises above 37°C. The animals will then undergo imaging which can last from 30 minutes to 4 hours depending on the requirements of the user. During this time, anesthesia will be monitored and adjusted based on respiration and ECG derived heart rate. During imaging, the animal will not experience any pain or discomfort. Once imaging is complete, the physiological monitoring system will be removed and the animal will be transported out of the MRI system and into an adjacent area where animal recovery will be aided by the use of a heating lamp. Animals will be free to move around in their cages while recovering to avoid the full heat of the lamp. Once fully conscious, users will take procession of the animal or animal medicine will be called during regular working hours to retrieve the animals. Animals whom originated from the barrier facility will be returned to SA-487

c. Indicate how you will identify animals

Animals will be identified by temporary marking pen marks.

d. Will the studies result in adverse effects on animal health or well being?

☐ **Yes** ☒ **No If yes, please complete form H**

Guidelines Procedures Click Here

Section VII. TERMINATION OF STUDY / EUTHANASIA Guidelines Click Here

a. Is death used as an endpoint in this study? Death as an endpoint means that the animal is permitted to die as a result of experimental manipulation, i.e. exclusive of planned euthanasia. If yes, explain why an earlier end point is not acceptable. (Studies using death as an endpoint are Category E and require full IACUC review)	**Yes**	x **No**

b. What criteria will be used to perform euthanasia earlier than planned?

Euthanasia will be determined by the individual user's IACUC protocol. The advanced MRI center can provide space and certain equipment for euthanasia of animals. Only euthanasia approved by the user's IACUC protocol will be conducted in the Advanced MRI center. Further, users will be required to certify that they have euthanized their animals if euthanasia is required by the user's IACUC protocol following imaging. If euthanasia is approved as part of the IACUC protocol following imaging, it will be conducted in a manner consistent with AVMA guidelines as described in the users IACUC protocol. The investigator's method will be used whenever possible. However, in those cases where core personnel are not able to follow the investigator's protocol, the core will use an overdose of 5% isoflurane for 10 minutes followed by decapitation.

c. Other Use – Will animals be available for further use by other investigators?

This will be determined by the individual user's IACUC protocol

d. Describe the method(s) of euthanasia for each species or procedure. For injectable drugs, give name, dose and route. Must comply with 2000 Report of the American Veterinary Medical Association (AVMA) Panel on Euthanasia. Reference: Animal Welfare Act, 9 CFR, 2.31; PHS Policy – Section B-2-3; AVMA Panel on Euthanasia

Species	Method/Drug	Dose (mg/kg body wt.)	Route

e. Current rules require that after euthanasia, death be confirmed by using a second method. For example bilateral pneumothorax is done after euthanasia using CO2. Indicate below how you will double kill your animals.

Section VIII. DATABASE SEARCHES

In the space below, document that you have searched databases

1. **To determine that you are not unnecessarily duplicating previous experiments,**
2. **To determine that alternatives to animal use are either not available or not appropriate,**
3. **To determine that procedures involving animals will avoid or minimize discomfort, distress and pain, AND**
4. **To determine that alternatives to procedures that may cause more than momentary or slight pain or distress to the animals have been considered**

Sources of information regarding possible duplication and alternatives include:

- **Medline**
- **Animal Welfare Information Center (Tel 301.504.6212)**
- **UMMS veterinarians (508.856.3151)**
- **National Agricultural Library (Tel 301.504.5755)**
- **WWW Virtual Library of Biosciences (**http://golgi.harvard.edu/biopages.html**),**
- **WWW Virtual Library of Veterinary Medicine (http://netvet.wustl.edu/vetmed.htm)**
- **National Library of Medicine**
- **Altweb - http://www.jhsph.edu/~altweb/**

a. Dates of Searches:

07/24/10-03/21/11

b. Name of the database(s) you searched:

Pubmed, Google Scholar

c. Years Covered by Searches

2000-present

d. Keywords Searched:

MRI Anesthesia, Small Animal MRI, MRI Physiology Monitoring, MRI Animal Warming

e. Other Sources of Information:

Discussions with users, personal experience

Section IX. PARTICIPATING PERSONNEL (including PI)

a. Identify all personnel expected to be manipulating and/or euthanizing animals at the time of this application. All individuals who are new to UMMS or those who never worked with animals should complete all the New Personnel Training and Occupational Health and Safety Requirements before included in an IACUC protocol. For details, please follow instructions in the New Animal User Checklist: Checklist for New Animal Users Click Here

Name	UMMS Phone	Emergency Phone	What are this person's responsibilities with animals on this study?	Years of experience with the technique to be used	Years of experience with the technique in species to be used	Received Health Clearance from Employee Health Service (EHS) and other Occupational Health and Safety Training
Matthew Gounis, PhD	6-1884	508-722-1297	Directing MRI Center	15	15	XYes No
Zheng, Shaokuan	508-856-5122		Conducting day to day operations of scanning, animal handling	2	2	XYes No
Jaime O'Callaghan	6-6964	508-722-3000	Animal handling and scanning	15	15	XYes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No

b. Briefly describe how the individuals with less than one year of experience with the technique(s) in species will be trained and/or supervised. Indentify the individual(s) who would be responsible for training and/or supervising new or inexperienced personnel. Note that hands-on training can be given by an experienced personnel, designated Department of Animal Medicine staff (contact Van Gould at ext'n: 66811), or Animal Medicine Course. Those who never performed survival surgery must receive Surgery Training from the Department of Animal Medicine and submit documentation to the IACUC Office before performing surgery. Please contact Van Gould (extension 66811) or Suzanne Wheeler (extension 62363) the training

c. Signatures of all personnel listed above (including PI and Co-Investigator)

I have read this proposed research study and understand my responsibilities with regard to the care of animals involved.

Signature: _____ **Name (please type): Matthew Gounis**

Signature: _____ **Name (please type): Shaokuan Zheng**

Signature: _____ **Name (please type): Jaime O'Callaghan**

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

ADDITIONAL NOTES ON PARTICIPATING PERSONNEL:

- **Before other new personnel perform any procedures, a written minor amendment request must be submitted to and approved by the IACUC. All personnel new to UMMS or those who never worked with animals will have to complete all the Training and Occupational Health and Safety Requirements before added on an IACUC protocol.**
- **If new personnel are going to be at UMMS for a training course that involves working with animals on a short term basis, they will be able to substitute the Health Clearance with signing a "Heath Risk and Animal Research-Informed Consent Form": Informed consent form for trainees**

Section IX. PARTICIPATING PERSONNEL (CONTINUATION SHEET)
Use this sheet or additional copies, if there are more participating personnel.

a. Identify all personnel expected to be manipulating and/or euthanizing animals at the time of this application. All individuals who are new to UMMS or those who never worked with animals should complete all the New Personnel Training and Occupational Health and Safety Requirements before included in an IACUC protocol. For details, please follow instructions in the New Animal User Checklist: Checklist for New Animal Users Click Here

Name	UMMS Phone	Emer-gency Phone	What are this person's responsibilities with animals on this study?	Years of experience with the technique to be used	Years of experience with the technique in species to be used	Received Health Clearance from Employee Health Service (EHS) and other Occupational Health and Safety Training
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No
						Yes No

d. Signatures of all personnel listed above (including PI and Co-Investigator)

I have read this proposed research study and understand my responsibilities with regard to the care of animals involved.

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Signature: _____ **Name (please type):** _____

Section X. APPLICANT'S CERTIFICATION

IACUC is charged with carrying out the rules and regulations of the Federal Government's Animal Welfare Act governing the care and use of animals in research and instruction. The Act stipulates that (a) Principal Investigators must give written assurance that the activities do not unnecessarily duplicate previous experiments; (b) procedures involving animals must avoid or minimize discomfort, distress, and pain to the animals; (c) Principal Investigators must consider alternatives to procedures that cause more than momentary or slight pain or distress to the animals and give a written description of methods used to determine that alternatives are not available; and (d) paralytic agents cannot be used in unanesthetized animals. Accordingly, the Applicant, who must be a member of the faculty holding Principal Investigator status, is required to read and sign the following certification:

BY SIGNING BELOW, I CERTIFY THE FOLLOWING:

1. **I am thoroughly familiar with the literature in the field of research proposed in this application, and I have determined that the research does not unnecessarily duplicate experiments, that appropriate non-animal models are not available, and that the research must be conducted on living animals.**
2. **I will abide by all UMMS policies and procedures regulating use of animals in instruction and research, by the provisions of the PHS/NIH Guide for the Care and Use of Laboratory Animals, and by all other applicable laws, policies, and regulations governing the use of animals in instruction and research.**
3. **I will supervise all experiments involving live animals. Furthermore, I will ensure that all listed participants are qualified or will be trained in proper procedures, including animal handling, anesthesia, surgery, post-procedural management, and euthanasia. Also, I will ensure that individuals not listed in the application will not have responsibility in experiments involving animals.**
4. **All listed personnel will read the IACUC-approved Application to Use Vertebrate Animals in Research or Instruction before undertaking any procedures on laboratory animals.**
5. **Survival surgery will be performed using standard aseptic procedures.**
6. **Animal Medicine clinical veterinary staff will be consulted as needed to ensure satisfactory veterinary care.**
7. **If I cannot be contacted, and animals in this project show evidence of illness or pain, emergency care, including euthanasia, may be administered at the discretion of the Animal Medicine veterinary staff.**
8. **This application meets all animal use and care requirements of the funding agencies that have been asked to support the research.**
9. **By signing below, I certify that all animal studies described in grant proposals using this protocol are described in this animal use application.**

PI's Signature: **Date:**

GRANTS ASSOCIATED WITH THIS ANIMAL PROTOCOL
To filled out based on information provided by the UMMS Funding Office

Sponsor	Funding period	Grant ID #	Initial

FORM A USE OF ANIMALS OUTSIDE OF ANIMAL FACILITIES		
A1. Will animals be used in areas, e.g., laboratories, outside one of the general animal facilities? (A Level, BioTech II, Shriver main facility, MBL main facility, BNRI 1st floor, LRB 1st floor, Rose Gordon Facility)	**x Yes**	**No**
If "yes", list the building and room number(s) where animals will be housed or used outside the animal facility.	SA107	
A2. Indicate which of the following procedures will be used outside of the animal facility:		
___ Breeding ___ Fluid Collection __x_ Non-Surgical Procedure ___ Non-Survival Surgery ___ Survival Surgery **___ Tissue Harvesting ___ Other:**		
A3. Will animals be held, housed, and/or used in study areas outside of the animal facility for <u>more than 12 hours?</u> **If "Yes", in the space below list the building and room number(s), and justify scientifically the need to hold animals for over 12 hours.**	**Yes**	**x No**
A4. Use this space to describe how you will transport animals between the animal facility and the study area		
The animals will be transported by the users in whatever method is determined in their IACUC protocols.		
A5. Is a patient procedural area to be used for animal studies? **If "Yes", use the space below to provide room number and/or location of patient area.**	**x Yes**	**No**
SA107 MRI suite		
A6. If "Yes", describe any special animal transport or facility procedures that will be followed to assure health and safety of both animals and patients.		
Animal and human equipment are completely separated. No equipment is shared between patients and animals. After every experiment (animal and human) the MRI is cleaned with disinfectant to ensure no contamination. The disinfectant used will be both a disinfectant scrubbing solution and 70% ethanol.		

FORM B
BREEDING

Use this section if you are breeding animals exclusively for this project. If you are going to be breeding animals to be used in multiple protocols, including this one, or sharing animals other investigators, please use a separate breeding protocol.

B1. Describe the species, strain, and source of each animal that you plan to breed

SPECIES / STRAIN	AGE	WEIGHT	VENDOR

B2. Specify what parameters you will assess to ensure that the animals are healthy. Check all boxes that apply.

Activity		**Appearance**		**Appetite**	
Excreta		**Respiratory Pattern**		**Temperature**	
Laboratory tests or other observations (specify)					

B3. In this space describe how many animals you anticipate breeding over the next 3 years. The total should include all animals bred for use in experiments listed in categories C, D, and E in section IIIa plus all animals discarded due to the wrong genotype and/or sex, which should be listed under Category B in IIIa. Mouse fetuses ≥E17.5 should be included. The totals here should match what is requested in IIIa. Briefly explain your calculations below.

B4. Anticipated health problems in the animals being bred. If there are known health or well being issues associated with the animals you are proposing to breed, or their offspring, please describe them in detail.

B5. Male:Female Ratio

☐ **A ratio of 1:1 will be used.**

☐ **A ratio of 1:2 or 1:3 will be used (harem breeding). Please see below**

☐ **I have read the IACUC Breeding Policy that prohibits more than one litter per cage. I agree to separate pregnant females to other cages prior to their giving birth.**
http://inside.umassmed.edu/uploadedFiles/Mouse%20Breeding%20Policy.doc

B6. If your animals have special needs, use the space below to list needs for special handling or housing.

B7: Describe how you will identify your animals:

B8. Use this space to describe what will be the disposition of retired breeders or any excess animals.
B9. Will you require special caging? (If so it is your responsibility to provide it
B10. How often will each male and female be bred?
B11. If you will be using inbred or outbred animals, describe how you will ensure that they remain in- or outbred:
B12. Describe any special handling that you anticipate:
B13. Will males be removed from cages before birthing?
Yes No (if no, explain why not)
B14. What nesting materials will you use? **(For rodents, consider Nestlets or similar material)**
B15. At what age will the young be weaned?

FORM C
ANESTHESIA

Guidelines Procedures Click Here

C1. PRE-ANESTHETIC AGENTS (e.g., tranquilizers, narcotics) and ANESTHETIC AGENTS: Describe how these agents will be used in your studies. If none will be used, enter "none" in the "Agents" column.

Frequency of administration	Species	Pre-anesthetic Agents & Anesthetic Agents	Dose	Route/Volume
Continuous	Rat/Mice	Isoflurane	5% for induction 1-3% for maintenance	Inhalation

C2. MONITORING OF ANESTHESIA: In this space, describe (a) what will be monitored (e.g., corneal reflex, heart rate, respiration, response to noxious stimulus) and (b) how frequently each of these variables will be monitored.

Animals will be monitored for heart rate, respiration, and temperature. Anesthesia will be adjusted accordingly. Low respiration (<30 for rats, <60 for mice) will indicate the need to decrease isoflurane levels. Low heart rate (<200 for rats, <300 mice) will indicate the need for intervention. Temperature will be monitored to allow for adjusting the heating system. High heart rate will indicate the need for an increase in the isoflurane delivery levels (i.e. increase anesthesia by .5-1% To high of respiration (>100 rats, >150 mice) or hear rate (>400 rats, >600 mice) will indicated the need to raise anesthesia by .5-1%. Post anesthesia, animals will be monitored by staff every 15 minutes until the animal has fully recovered or the animals are claimed by the user.

C3. Use of Isofluorane: It is IACUC policy to ensure that animals do not contact liquid isofluorane. Please see the IACUC policy on isofluorane use and describe the measures you will take below.

Animals will not be exposed to liquid isoflurane for any purpose. The vaporizer is located a distance from the MRI such that no contact is possible.

C4. Describe the anesthetic gas scavenging system you will use to eliminate waste anesthetic gas. Please see the IACUC scavenging policy.

Active scavenging system is used.

FORM D

SURVIVAL SURGERY INCLUDING LAPAROSCOPY, ENDOSCOPY, and any procedure that has a *reasonable* potential of causing a permanent physical or physiological handicap (see instructions for examples). Guidelines Procedures Click Here

Complete this section if any animals will recover from local or general anesthesia after a surgical or other major operative procedure.

D1. In the space below, explain why it is necessary for the animals to recover from surgery/anesthesia.

D2. In the space below, describe pre-operative care (including physical examinations, lab tests, and any preconditioning apparatus). All anesthetic agents and pre-operative medications should be listed in Section I (above).

D3. Use the space below to describe in detail the surgical procedure(s)/other major procedure to be used.

Animal pre-surgical preparation:

Instrument pre-surgical preparation:

Surgeon's pre-surgical preparation:

Details of Techniques:

D4. List all participating surgeons, technicians, and students, and indicate the number of years of experience with the particular species and surgical or other major operative procedures to be used. **Those who never performed survival surgery must receive Surgery Training from the Department of Animal Medicine and submit documentation to the IACUC Office before including the name below for survival surgery. Please contact Van Gould (extension 66811) or Suzanne Wheeler (extension 62363) the training.**

Name	Role in surgery	Are you performing survival surgery?	Years of experience with the role

D5. Describe immediate postoperative care, and provide dosage, route, and frequency of administration of specified analgesics (pain relieving drugs) <u>for the first 48 hours</u>.

Note that **"As needed**" or **"PRN**" do not constitute an acceptable schedule for analgesia**.**

Species	Analgesic Agents	Dose	Route/Volume	Frequency of Administration

Describe the immediate postoperative care for the animal until it is able to maintain a sternal position (e.g., maintaining body temperature, fluid administration, bandaging, vital signs monitoring and monitoring frequency).	

D6. List the names of individual(s) who will check animals during recovery.

NAME **AREA CODE/TELEPHONE#**

a. _____ _____

b. _____ _____

c. _____ _____

d. _____ _____

e. _____ _____

D7. In the space below describe any expected or potential postoperative complications and describe how you will handle them.

D8. Where will surgery/procedure be performed?	**Rm**
D9. Where will animals be housed during recovery?	**Rm**
D10. Where will animals be housed after recovery?	**Rm**

D11. ARE MULTIPLE SURVIVAL SURGERIES PERFORMED ON THE SAME ANIMAL?

Yes No

D11a: Justify the need for multiple survival surgeries

D11b: Give the species and number of animals that will have multiple survival surgeries.

D11c: Specify the time intervals between the surgical procedures

FORM E
ADMINISTRATION OF SUBSTANCES OTHER THAN ANESTHETICS

Guidelines Procedures Click Here

List all 1) Therapeutic , 2) Cell lines or Cell/Tissue extracts and 3) Other Experimental/Study non-anesthetic agents that will be administered to the animals, including but not limited to: 1) drugs such as antibiotics, analgesics or local anesthetics used to minimize post-procedural pain, distress, or discomfort, 2) isolated cells, cell lines, cell or tissue/cell extracts and 3) drugs, infectious agents such as viruses or other substances under study. For drugs under study in the experimental component of your protocol, drug type or group (e.g., non-steroidal anti-inflammatory agents, α-adrenergic receptor blockers) will suffice; however specific drugs should be indicated if known.

E1. Therapeutic agents:

Species	Agent	Dose	Route	Volume	Frequency & Total Duration

E2. Cells or Cell/Tissue Extracts (do not include purified cell products here) Rodent cell lines and cell/tissue products can only be used in animals after confirming the absence of rodent infectious agents by MAP or PCR testing.

Species	Cells or Cell/Tissue extracts	Dose	Route	Volume	Frequency and Total Duration

E3. Experimental / Study Agents

Species	Agent/Substance	Dose Range	Route	Volume	Frequency & Total Duration
Rat/Mice	Magnevist (or other contrast agents as approved by user's IACUC protocol)	0.2mmol/kg-0.5mmol/kg	IV	0.1ml/kg	Once per imaging session

FORM F

PROLONGED PHYSICAL RESTRAINT OR STRESS OF CONSCIOUS ANIMALS FASTING, FOOD RESTRICTION, ANIMALS UNDER THE CARE OF THE INVESTIGATORS STAFF RATHER THAN ANIMAL MEDICINE PERSONNEL

Complete this section if any unanesthetized animals will be restrained, except when the restraint is for a brief examination, sample collection, or injection. Also complete if noxious stimuli will be administered, if food or water will be withheld, etc.

F1. Explain rationale for use of restraint or induction of stress:

F2. Describe device, dimensions, etc.:

F3. Duration and frequency animal will be confined to device:

F4. Observation intervals during confinement:

F5. Qualified faculty or staff making observations:
Name: **AREA CODE/TELEPHONE #:**

a. _____ _____

b. _____ _____

c. _____ _____

d. _____ _____

e. _____ _____

f. _____ _____

F6. Will pain or discomfort be induced? If yes, describe in detail using the space below.	☐ **Yes**	**No**
F7. Will stimulation, including light and sound, be used to modify animal behavior? If yes, describe in detail.	☐ **Yes**	**No**
F8. Will animals be fasted (food, approx. 24 hours and/or water, approx. 12 hours) or placed on a diet deficient in one or more nutrients? **If yes, provide the details below. How long animals will be restricted? How will the general well-being of the animal be determined How often will the animal be weighed?** ☐ **I have read the IACUC policy on fasting and agree to label all cages with start dates, stop dates, and telephone contacts.** http://inside.umassmed.edu/uploadedFiles/Policy%20on%20Food-Water%20Intake%20Restriction.doc	☐ **Yes**	☐ **No**

F9. Animal medicine staff will be restricted from caring for animals ☐ **I have read the IACUC policy on investigators caring for their animals and agree to label all cages with start dates, stop dates, and telephone contacts. http://inside.umassmed.edu/uploadedFiles/Policy%20on%20Food-Water%20Intake%20Restriction.doc** **Please explain why the restrictions are required below:**	☐ **Yes**	☐ **No**
F9. Will analgesics, sedatives, or tranquilizers be used to provide additional restraint? If yes, make sure that the agent(s) are listed in Section I (above).	☐ **Yes**	☐ **No**

FORM G
HAZARDOUS AGENT INFORMATION

The IACUC will take no action on your application until approval has been obtained from the appropriate committee(s).
If G1 to G4 checked "Yes", please contact the IBC coordinator, Joan Lynch (508-856-1572), to obtain the proper forms and to begin the process of approval for Biosafety issues.
If G5 is checked "Yes", please contact Marie Case at the Radiation Safety Office.(508-856-3209)
If ***G6*** is checked "Yes", please contact the EH&S office (508-856-3985)

G1. Will this project require the use of infectious biological agents? (pathogenic to man or animal) If Yes, an IBC form needs to be submitted	**Yes**	X	**No**
G2. Will this project require the use of recombinant DNA technology in live animals? If Yes, an IBC form needs to be submitted	**Yes**	**x**	**No**
G3. Will this project require the use of materials of human or non-human primate origin? If Yes, an IBC form needs to be submitted.	**Yes**	**x**	**No**
G4. Will this project require the use of non-exempt biotoxins (LD-50 of less than 100 ng/kg body weight)? If Yes, an IBC form needs to be submitted.	**Yes**	**x**	**No**
G5. Will this project require the use of ionizing radiation in live animals? If Yes, radiation safety approval is required	**Yes**	x	**No**
G6. Will this project require the use of cytotoxic or chemotherapeutic chemicals in live animals? If Yes, an Environmental Health & Safety form needs to be submitted	**Yes**	x	**No**

G7. If you will be using any of the above agents, use this space to describe briefly what you will be doing. Please indicate if you already have approval from IBC, Radiation Safety and Environmental Health and Safety (EH&S) for these studies. Please provide the IBC Docket #, if you have the IBC approval.

FORM H

ADVERSE EFFECTS OF PROCEDURES AND EXPERIMENTS/MONITORING AND MANAGEMENT Guidelines Procedures Click Here

H1. What will be monitored to assess the presence of pain, discomfort, or other potential adverse effects caused by your studies? NOTE: This period includes the time from initiation of experiments until the animals are removed from the study; for surgically operated animals, this includes the time after anesthesia recovery (Section J) until animals are removed from the study. Check all that apply.

Activity		**Appearance**		**Appetite**		**Behavior**	
Excreta		**Grooming**		**Guarding**		**Heart rate**	X
Licking, biting		**Posture**		**Respiratory rate**	X	**Temperature**	x
Vocalizing		**Weight loss**		**Wound site**		**Other**	
Laboratory tests or other evaluation (specify)							

H2. Indicate the frequency with which you will monitor your animals during and after all procedures. Please indicate both monitoring interval and total length of time.

Animals will be monitored continuously via our small animal monitoring system (SAI). The system can be programmed with alarms to indicate that an animal's heart rate or respiratory rate is outside of normal parameters. If so, anesthesia will be monitored accordingly (High or low respiration or heart rate indicates an increase or decrease in anesthesia levels, respectively). If a slow heart rate is not resolved with lower anesthesia, the vaporizer will be bypassed and pure oxygen will be administered until the animals physiological signs stabilize. Low heart rate (<200 for rats, <300 mice) will indicate the need for intervention. Temperature will be monitored to allow for adjusting the heating system. High heart rate will indicate the need for an increase in the isoflurane delivery levels (i.e. increase anesthesia by .5-1% To high of respiration (>100 rats, >150 mice) or hear rate (>400 rats, >600 mice) will indicated the need to raise anesthesia by .5-1%.Post anesthesia, animals will be monitored by staff every 15 minutes until the animal has fully recovered or the animals are claimed by the user.

H3. Describe the conditions and complications that would lead to removal of an animal from the study and how this will be accomplished (e.g., stopping treatment and/or euthanasia).

FORM I
PROCEDURES DONE IN THE UMMS CORE FACILITIES

Please note that if you are using one of the UMMS core facilities for this study, you need to get the approval for those animals used in the core facility under this protocol. However, you do not need approval for the specific procedures performed in the core facility if the procedures are carried out by the core facility personnel under the core facility protocol approved by the IACUC.

I1. List below the UMMS core facility services you will be using for this protocol.

Name of the core facility	Name of the PI of the core facility	Protocol # (Indicate procedure or SOP # if applicable)	Briefly describe the procedures/services provided by the core facility

I2. Is any of the procedure(s) performed by personnel other than the core facility personnel?	**Yes** ☐ **No** ☐
If the answer is "Yes" please name the individuals performing the procedures under this protocol in the core facility and identify the procedure(s) by core facility SOP# or by other means.	

I3. If any of the procedure(s) used in the core facility is different from the IACUC approved core facility protocol, please describe below the procedure deviations.

I4. Use this space to describe how you will transport animals between the animal facility and the study area

FORM J
ANIMAL WORK DONE OUTSIDE UMMS

Please fill out this form, if a UMMS investigator is going to perform animal studies in collaboration with a non-UMMS collaborator or commercial vendor. This includes production of antibodies by an outside company. According to Federal Regulations, UMMS, being the grantee institution, is responsible to verify that all animal work done outside UMMS has been reviewed and approved by a PHS assured institution, and approved by an IACUC.

J1. List below the details of animal work done outside UMMS

Name of institution or company	Name of the PI or contact (if a company), & contact information (phone # or email address)	IACUC Protocol number, if applicable	Animal Species used in the study

J2. Provide a brief description of the animal work done at the non-UMMS site below:

J3. List below the supporting documents provided with this application.

UMMS IACUC may require one or more of the following documents to attached to this application:

1. **Evidence of collaboration (letter from the collaborator or company indicating willingness for doing the animal work)**
2. **Copy of the IACUC approval from the non-UMMS institution to indicate that this work has been reviewed and approved by an IACUC. If this approval letter is in a foreign language, please provide an English translation along with a copy of the original Approval Letter.**
3. **Evidence for PHS Assurance of the non-UMMS institution (A copy of the Assurance Letter from NIH to the institution or company will be sufficient). This is not required if the Assurance number and period of validity is indicated in the IACUC Approval Letter)**
4. **A copy of the protocol (translation into English, if in another language), if the collaborating institution or company is from outside United States**

FORM K

IF ANIMALS ARE USED FOR TRAINING COURSES (TO TRAIN STUDENTS, RESIDENTS, FELLOWS AND OTHERS)

Please fill out this form, if this application is designed for training courses. The trainees should be under the supervision of a trained UMMS investigator during any contact with live animals. Please note that the trainees are not permitted to work independently with live animals; to do so, they have to be listed as personnel in the protocol (please see section IX). According to Federal Regulations, the IACUC is to ensure the occupational health and safety of personnel working with animals, and that all individuals working with animals receive appropriate training. Because the training participants are not known at the time of protocol submission, IACUC recommends the following options to meet the Occupational Health and Safety and Training requirements, and requests that a list of participants submitted to the IACUC Office before the training session(s).

K1. Occupational Health Evaluation of the trainees; please check all the choices that you are planning to recommend the training participants. Each participant has to full fill this requirement by full filling one the choices below.

a. Are the participants going to obtain health clearance from the UMMS Employee Health Service? This is required if the participant is a UMMS student, resident, staff or volunteer. Please submit an Initial Health Evaluation to the Employee Health Service for obtaining Health Clearance. This form is available in the IACUC website: http://inside.umassmed.edu/uploadedFiles/IACUC%20Initial%20Health%20Review%20Form.doc	☐ Yes ☐ No
b. Are the participants going to receive clearance for working with animals from a qualified physician? Health Clearance from a qualified physician is acceptable, if the participant is not affiliated with UMMS. The physician must review and accept the criteria established by the UMMS Occupational Health and Safety Policy. The UMMS Occupational Health and Safety Policy and Health Clearance Forms are available from the IACUC office.	☐ Yes ☐ No
c. Are the participants going to sign the "Informed Consent Form?" If the training participant is not affiliated with UMMS, the participant could sign the "Informed Consent Form" instead of obtaining a health clearance to work with animals and participate at his/her own risk. This option is only allowed if the trainees are only attending one or two training session(s). Please follow the link to the "Informed Consent Form" http://inside.umassmed.edu/uploadedFiles/Health%20risks%20and%20animal%20research-informed%20consent%20form.doc	☐ Yes ☐ No

K2. Training options: please check the option(s) below for participant training

a. Are you planning to provide an instructional lecture on working with animals? The PI or his designee can provide training in a lecture format (the lecture should include an overview of Federal Regulations, ethical guidelines for using animals, hazards and risks associated with the use of animals, species-specific information, humane techniques for animal procedures, and other appropriate information relevant to the experimental procedures being used). IACUC could provide the PIs with PowerPoint slides on the UMMS IACUC Animal Care and Use Program upon request. Please note that these slides do not cover Federal Regulations, Occupational Health Hazards and Species Specific information.	☐ Yes ☐ No
b. Do you recommend the trainees complete the UMMS training program instead of the training lecture? The trainees could complete the online "training course" available to the New Animals Users at UMMS to meet all the training requirements. Please follow the link below: http://inside.umassmed.edu/uploadedFiles/On-line%20training%20for%20new%20animal%20users.doc	☐ Yes ☐ No
K3. Are the trainees going to perform SURVIVAL SURGERY? **If the trainees are going to perform survival surgery, they are required to undergo a surgery training provided by the Dept of Animal Medicine. Please see follow the link to for details:** **http://inside.umassmed.edu/uploadedFiles/Hands-on%20Training.doc**	☐ Yes ☐ No

The PIs are required to provide a list of trainees on or before the day of training to the IACUC office. Please see next page for a template for listing trainees. The list should include the names, affiliation and contact information, and evidence for completion of the above requirements (K1 to K3). Failure to submit a list of participants prior to the training session may be considered a protocol violation.

TRAINING PARTICIPANT LIST (template; make additional copies if necessary)

Note: Do not have to fill this out at the time of protocol submission; to be submitted to the IACUC Office (hardcopy or pdf) on or before the day of training

PI Name:	
Docket Number:	
Name of personnel conducting the training session if other than PI:	
Date of training:	

TRAINING PARTICIPANTS

Name	Indicate if affiliated to UMMS, OR provide the name and address of the non-UMMS affiliation	Contact information (Email and phone number)	Occupational Health Evaluation and clearance to work with animals, OR Informed Consent singed (check applicable box below)			Training (check applicable box below)		
			By the Employee Health Service	By a qualified physician [1]	Informed Consent Form [2]	Online training courses	Classroom instruction	Surgery Training (if performing survival surgery)

[1] Please submit copies of Heath Clearance certificate to the IACUC Office
[2] Please submit copies of the Informed Consent Form to the IACUC Office

WORKSHEET 1

Animal number worksheet (addendum to section IV)-*add on more rows as needed*

Use this worksheet to show the details of animal numbers to be used for 3 years

Species:---------- (please use one sheet/species)

A	B	C	D	E	F	G	H	I			J			
#	Experiment or procedure[1]	Number of animals per group[2]	Number of groups	Total number of animals per experiment or procedure	Estimated number of additional animals to compensate for possible death or protocol failure	If animals are going to be bred in house, list the additional animals you may need[3]	Total number of animals requested (Sum of E, F and G)	Source of animals			Pain level			
								To be bred (should agree with column J of worksheet II)	To be purchased	To be transferred from another protocol	B	C	D	E
Grand total														

[1] The specific experiment(s) and procedure(s) listed here should be referenced in the Experimental Design (section IV)
[2] Should be based on justification (power analysis, previous publications, etc.) for the number of animals as described in section IV
[3] Estimated number of animals used for mating and the progeny that cannot be used in experiment due to undesired genotype

WORKSHEET 2

Breeding worksheet (add more rows if needed)

Species:---------- (please use one sheet/species)

A	B		C	D	E	F	G	H	I	J
#	Animal strain, genotype, phenotype, etc.		**Number of animals from outside source used in mating [1]**	**Number of matings**	**Expected litter size**	**Total number of pups expected**	**Number of pups expected to be used in experiments**	**Number of pups which may not be used in experiments (due to undesired genotype)**	**Number of pups to be used for continued breeding**	**Total number of animals (sum of columns C and F)**
	Offspring	Parents								
Grand total				**Not applicable**						

[1] Animals purchased or obtained from other investigators used in breeding, do not use animals bred in house used for breeding in this column