**Amendment**

To amend this protocol, please respond to Questions 1 and 3 below prior to opening and amending your protocol document.

1. **Briefly summarize the changes:**
   - Update the survival time to 400 days post inoculation
   - Decrease behavioral testing rate. Test monthly.
   - Decrease the types of behavioral tests. Only the rotarod test is used currently.

2. **For changes in Protocol, complete the change request by clicking on that section in the left navigation bar and completing the change in the Protocol Form.**
   - Adding, removing, or Updating Personnel - Personnel Section
   - Species - Species Section
   - Animal Housing Location - Species Section
   - Funding Source - Funding
   - Protocol rationale - Protocol Information Section
   - Adding or modifying procedures - Protocol Information Section
   - Other changes - see relevant section at left

3. **Briefly describe the rationale for the changes:**
   - We found that some mice did not develop ataxia (requiring euthanasia) until 370-380 days post inoculation
   - We found that monthly behavioral testing was sufficient.
   - We found that only the Rotarod test provided useful data.

4. **If you have any additional comments for IACUC consideration, please note here:**

List of sections (and questions) that have been changed/modified.

**Personnel Information**

Principal Investigator (PI)

<table>
<thead>
<tr>
<th>Name*</th>
<th>Pager</th>
<th>Department Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bryant, Damani</td>
<td></td>
<td>Veterinary Clinical Sciences</td>
</tr>
</tbody>
</table>
**Protocol Title**: Low dose aspirin as a prophylactic against the progression of scrapie in mice

<table>
<thead>
<tr>
<th>Internet ID/x.500</th>
<th>Fax</th>
<th>Dept ID</th>
<th>Job Title</th>
<th>Job Code Group</th>
<th>Job Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>dnbyrant</td>
<td></td>
<td>11652</td>
<td>Research Associate</td>
<td>Academic Professional</td>
<td>9702</td>
</tr>
</tbody>
</table>

**Employee/Student ID**: 5138207

**Email**: dnbyrant@umn.edu

**Mailing Address**: Veterinary Clinical Sciences Room 339 VetMedCtrS 6192A 1352 Boyd Ave St Paul MN 55108

**City / State / Zip**: St Paul / MN / 55108

**Works with Animals**: Yes

Is this person experienced with all species that he/she will use and all procedures he/she will be performing on this protocol? Y

Indicate with which procedures or species this person is not experienced and how they will be trained:

Click here for additional information about training.

Click to check ROHP Status

**Training Details**: No training data is available.

If you have completed training that is not indicated above, please describe training you received (include name of course provider, course number and brief description of coursework):

Alternate Submitter

Secondary Investigator
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

Name*: Seelig, Davis
Internet ID/x.500: dseelig
Employee/Student ID: 4828996
Email*: dseelig@umn.edu
Phone: 612/626-0471
Cell Phone: 612/626-0471

Department Name: Veterinary Clinical Sciences
Fax: 612/626-0471
Mailing Address: Veterinary Clinical Sciences Room 339 VetMedCtr St Paul 6192A 1352 Boyd Ave St Paul MN 55108

Works with Animals*: Yes
Is this person experienced with all species that he/she will use and all procedures he/she will be performing on this protocol?* Y
Indicate with which procedures or species this person is not experienced and how they will be trained.

Click here for additional information about training.

Training Details: No training data is available.

If you have completed training that is not indicated above, please describe training you received (include name of course provider, course number and brief description of coursework):

Additional Staff

*** Species ***

Common Name*: MICE
Housing Location*: St Paul / MN / 55108

Species Categories:
1. Check here if protocol is an Administrative Item or is for Custom Antibodies:
2. Pain Class Categorization (Check all that apply then add the number of animals by acquisition method)
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

1. Rationale for Species Selection
   a. Why are the species you have selected the most appropriate for these studies?
      We will use the C57bl/6 mouse, which recapitulates many of the pathogenic events of prion disease (Scrapie), including: 1) extensive peripheral prion protein accumulation, 2) progressive centrifugal neuroinvasion, and 3) stereotypic neuropathology. Since this mouse model is commonly used, our findings will be of use to the scientific community.

   b. Will you be conducting the same experiment in multiple species? N
      If Yes, Please Justify

   c. Check all of the statements below that apply:
      - This model has previously been used.
        Provide citations, specify and explain why the citation is applicable to your study:
        Scrapie:
        This citation reviews standardized methodology for the use of mouse models of scrapie.
        Low Dose Aspirin in mouse drinking water.
        Coe, LM., Denison, JD., and McCabe LR. (2011) Low dose aspirin therapy decreases blood glucose levels but does not prevent Type 1 Diabetes-Induced bone loss. Cellular Physiology and Biochemistry 28:923-932
        Bulkaen et al., (2008) Low-dose aspirin prevents age-related endothelia dysfunction in a mouse model of physiological aging
        Am J Physiolo Heart Circ Physiol. 294: H1562-H1570
        These citations detail consequences of low dose aspirin exposure for mice.
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

The results will be directly applicable to the health, care, or study of the species used. Describe how they will benefit in item.

This study will test the hypothesis that low dose aspirin has a prophylactic effect on the progression of Scrapie. Low dose aspirin is already used by humans in other contexts. This project may provide useful information that could ultimately improve the quality of life for people with Creutzfeldt-Jakob Disease, the human form of scrapie.

This is a new model. Describe the features of the species (e.g., anatomic, physiologic, genetic, etc) that make it desirable for this model. Contrast with other available models, if any. (RAR veterinarians are available for consultation on new model development)

Administrative Items (Collaborative Agreement, VA, Umbrella/Training Grants, Inter-Institutional Agreements)

2. Justification for Number of Animals

How did you determine how many animals were needed for the activities described in this protocol? A statistical analysis should be used to justify animal numbers whenever possible. Statements such as “The study requires 50 animals or 50 experiments.” is not sufficient.

Check all that apply and provide specific answers to the associated questions:

- Pilot study or preliminary project, group variances unknown at present. Describe the information used to estimate how many animals are needed.

  The number of animals used in this preliminary study is based on 1) previous work in our laboratory examining the neuropathologic consequences of prion disease in mice, and 2) previous published studies evaluating the efficacy of novel therapeutics in rodent models of prion disease.

- Group sizes determined statistically. Describe the statistical analysis used to estimate the number (N) of animals needed. A common approach is to estimate N from a simple power analysis for the most important measurement in the study. This is usually based on the expected size of the treatment effect, the standard error associated with the measurement, and the desired statistical power. Data analysis methods should not be submitted unless directly applicable to the estimate of N.

- Group sizes based on quantity of harvested cells or amount of tissue required. Explain how much tissue is needed based on the number of experiments you will conduct and how much tissue you expect to obtain from each animal. Example: Need 10 g tissue. Can get 2 g tissue per animal = Need 5 animals.

- Product Testing. If the number of animals needed is based on FDA guidelines, provide the citation from the regulations, the IND tracking number, or relevant FDA correspondence:

- Other - Elaborate, indicating method used to determine group size:

- Administrative Items (Collaborative Agreement, VA, Umbrella/Training Grants, Inter-Institutional Agreements)
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

☐ Administrative Items (Collaborative Agreements, VA, Umbrella/Training Grants, or Inter-Institutional Agreements)

☐ Controlled Substances

☐ Teaching/Classroom Activities

Please name all the Courses and their Course IDs:

Potentially Hazardous Agents in Animals

☐ Laboratory Safety Plan And Annual Safety Training
☐ Hazardous Waste
☐ Anesthetic Gases
☐ Chemicals
☐ Radiation
☐ Human blood, body fluids, normal or neoplastic tissue
☐ Infectious Agents
☐ Biologically-Derived Toxins
☐ Recombinant DNA

☐ Client-Owned Animals

If privately owned animals are used by University investigators for research, the owner or client should sign a consent form. The IACUC must review and approve the "client consent form" prior to the investigator obtaining the client's consent. Please read the instructions and attach the "client consent form" in the Attachments section.

☐ This is a clinical trial using client owned animals to evaluate a drug or device.

You must complete at least one of the following:

☐ FDA approval for IND or IDE #
☐ NADA, CNADA, ANADA #
☐ Describe safety and/or efficacy data to justify use of this drug/device in client-owned animals:

☐ Wildlife

Please state the length of time wildlife will be held and attach your wildlife permit. Also, if wildlife will be collected/harvested, indicate what the potential effect on the population status of the species will be.

☐ Non-Pharmaceutical Grade Compounds

☐ Potential for Animals to enter the human or animal food chain.

☐ None of the Above

*** Funding ***
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

How will the work covered in this protocol/agreement be funded? (Please include All funding sources)*

☐ No Funding.

Sponsored Projects Funding

Internal University Of Minnesota Funding

Internal Funding Source(s)

Departmental Funding

Fund Source(s) Outside The University

*** Rationale ***

Project Title *

Low dose aspirin as a prophylactic against the progression of scrapie in mice

Rationale

Note: Use language understandable to a layperson as you answer questions in this section. Avoid overly technical terms and define abbreviations. The readability should be similar to a newspaper article.

1. Study Objectives

Address the following four points:

a Background and significance (1-2 sentences)

Prion diseases are a group of progressive and fatal neurological diseases that occur in a number of species, including humans. Available evidence suggests that Aspirin may protect the brain by interfering with harmful cellular pathways activated by prions.

b What is the question the research addresses? (1-2 sentences)

The long range goal of this proposal is test the hypothesis that acetylsalicyclic acid (Aspirin)slows the behavioral progression of Scrapie in a mouse model system.

c How will the results of this study be used? (1-2 sentences)

This data will be submitted for publication in the scientific literature. The results will be used to apply for federal funding.

d Summarize the specific aims (derived from the grant proposal)
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

1. Determine whether low dose Aspirin pretreatment and/or intervention slows the progression of the behavioral symptoms of Scrapie.
2. Determine if there are any epigenetic changes in the brain associated with exposure to low dose Aspirin and/or Scrapie

*** Procedures ***

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>Procedure Title</th>
<th>Species</th>
<th>Pain Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administration of Biological Agents to rodents</td>
<td>Intraperitoneal Administration of scrapie prions</td>
<td>MICE</td>
<td>A</td>
</tr>
<tr>
<td>Dietary or Fluid Modifications</td>
<td>Ad Lib administration of low dose aspirin in drinking water</td>
<td>MICE</td>
<td>A</td>
</tr>
<tr>
<td>Behavior</td>
<td>Inverted Screen</td>
<td>MICE</td>
<td>A</td>
</tr>
<tr>
<td>Behavior</td>
<td>Rotorod motor coordination assay</td>
<td>MICE</td>
<td>A</td>
</tr>
</tbody>
</table>

*** Procedure Description ***

Procedure Type: Administration of Biological Agents to rodents

Procedure Title: Intraperitoneal Administration of scrapie prions

Species: MICE

Number of Animals of this Species used for this procedure: 30

Procedure Location: Room Number: 1234

Will you be moving Animals from Primary Housing for this Procedure? N

From where to where will animals be transported?

Via what route will the animals be transported?

Who will transport the animals?

What equipment will be used to transport them?

At what time(s) of day will transport occur?
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

Administration of biological materials to rodents

Biological materials include: rodent cells, non-rodent cells (including human cells), tumors, hybridomas, other tissues, body fluids, and rodent antiserum. Biological materials are potential sources of infectious agents that may severely impact research results when introduced into rodents and may be transmitted to other rodents. Biological materials must be tested for rodent pathogens prior to being administered to rodents. Commercial vendors do not routinely screen biological materials for rodent pathogens.

List the biological materials to be administered to rodents on this protocol:
Scrapie prion positive brain homogenate

Please select among the following options (choose all that apply):

- The biological materials to be used were derived from donor rodents housed in an RAR-managed housing facility with the same or higher health status as the recipient animals and have not been passaged through rodents of a lower health status, nor exposed to rodent cells, tissues of body fluids from animals with a lower health status.
- The biological materials have previously been used in an RAR-managed rodent housing facility with the same or higher health status and were neither passed through rodents of a lower health status nor exposed to rodent biological materials from animals with a lower health status.
- The biological materials to be used will only be administered to rodents that will be housed in either ABSL-2 or ABSL-3 housing facilities.
- These are non-rodent cells which have NOT been passed through rodents and have NOT been exposed to rodent biological materials such as serum.

If you selected any of the above choices, you are not required to test your biological samples for rodent pathogens.

- None of the above apply. You are required to have your biological materials tested prior to administration to rodents housed in a RAR-managed facility. Contact the RAR Diagnostic Lab at 612.624.3961 or 612.624.5406 for details about sample submission and the cost of testing.

Procedure Type: Dietary or Fluid Modifications

Procedure Title: Ad Lib administration of low dose aspirin in drinking water

Species: MICE

Pain/Distress Category: A

Number of Animals of this Species used for this procedure: 30

Location: Room Number: [Redacted]

Will you be moving Animals from Primary Housing for this Procedure? N

From where to where will animals be transported?

Via what route will the animals be transported?

Who will transport the animals?

What equipment will be used to transport them?

At what time(s) of day will transport occur?
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

*** Procedure Description ***

Dietary or Fluid Modifications

Please select diet modification type (check all that apply):

- Food
- Fluid

FOOD
Indicate whether dietary manipulations are:

- Restricted
- Modified (Not restricted)

Describe Dietary Manipulations:

Describe the expected impact of this manipulation on the animal’s health and the potential for discomfort or distress. Explain what will be done to alleviate or minimize these potential adverse effects.

Describe frequency of animal health monitoring during periods of food restrictions.

Describe length of time animals will be on experimental diet.

Will neonates be fasted beyond 8 hours, ruminants beyond 48 hours, or other mammals beyond 24 hours?

FLUIDS

Will animals be provided less than ad lib fluids or drinking water for experimental reasons?

- Yes, provide details including amount/day, monitoring methods, criteria used to determine well-being of animals.

Describe length of time animals will be on fluid modification.

Will fluids be withheld for more than 24 hours or more than 5 hours for rodents?

- Yes, provide details including the amount/day, rationale and monitoring methods:

Describe the expected impact of this manipulation on the animal’s health and the potential for discomfort or distress. Explain what will be done to alleviate or minimize these potential adverse effects.

Describe frequency of animal health monitoring during periods of water restrictions.

Do you need an exception to the weekly weighing policy?

Procedure Type: Behavior

Procedure Title: Inverted Screen
### Protocol Details

**Protocol Title**: Low dose aspirin as a prophylactic against the progression of scrapie in mice

<table>
<thead>
<tr>
<th>Species: *</th>
<th>MICE</th>
<th>Pain/Distress Category: *</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Animals of this Species used for this procedure: *</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Procedure Location: *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Will you be moving Animals from Primary Housing for this Procedure? *</td>
<td>N</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From where to where will animals be transported? *</td>
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<tr>
<td>Via what route will the animals be transported? *</td>
<td></td>
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<tr>
<td>Who will transport the animals? *</td>
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<tr>
<td>What equipment will be used to transport them? *</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>At what time(s) of day will transport occur? *</td>
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<td></td>
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</tbody>
</table>

**Behavior**

* * * Procedure Type * * *

**Please provide procedure details:**

For the Inverted Screen assay, mice will be placed on a wire grid which is then inverted directly (less than 1 inch) over a foam pad. The latency to fall will be recorded. This assay will be conducted weekly for all mice.

<table>
<thead>
<tr>
<th>Procedure Type: *</th>
<th>Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure Title: *</td>
<td>Rotorod motor coordination assay</td>
</tr>
<tr>
<td>Species: *</td>
<td>MICE</td>
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<tr>
<td>Pain/Distress Category: *</td>
<td>A</td>
</tr>
<tr>
<td>Number of Animals of this Species used for this procedure: *</td>
<td>50</td>
</tr>
<tr>
<td>Procedure Location: *</td>
<td></td>
</tr>
<tr>
<td>Will you be moving Animals from Primary Housing for this Procedure? *</td>
<td>N</td>
</tr>
<tr>
<td>From where to where will animals be transported? *</td>
<td></td>
</tr>
<tr>
<td>Via what route will the animals be transported? *</td>
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<td></td>
</tr>
<tr>
<td>At what time(s) of day will transport occur? *</td>
<td></td>
</tr>
</tbody>
</table>
Behavior

Procedure details:
Mice will be placed onto a horizontal rotating rod which accelerates over the course of a trial. A single trial lasts from the time the animal is placed on the rod until it falls off or until 5 minutes have elapsed. Animals will be tested monthly throughout the study period.

1. Check here when you have completed entering all the procedures
2. In the text box below, provide a complete, sequential, and accurate description of what procedures will be performed on/with the animals. You are strongly encouraged to provide a diagram or chart to explain complex designs or sequential procedures. Enter description below, if additional space is needed, please add attachment.

Within each species and for each group (treatments within a study, etc.) of animals, describe all procedures performed on/with the animals and indicate how often and when these procedures will be performed within a study. Be certain to identify the pain classification (A, B, or C) of each animal group and make sure this corresponds to the information you provided in the species section of this protocol.

Include an indication of how long (endpoint) animals within each group will participate in the study. These endpoints could be based on the end of a particular experiment, when animals are sacrificed for tissue collection, how long they are maintained after surgery, etc. Include dose ranges (in mg/kg) and routes and frequency of administration of any drugs to be administered. You may provide a minimum/maximum range of endpoints, doses, routes of administration for committee consideration.

Describe methods to be used in behavioral studies (including use of noxious stimuli or other methods of positive or negative reinforcement).

Surgery should be briefly described here only as it relates to the study design.

For animals used in agricultural projects, you do not need to describe specific details of animal care and management if they do not differ from those described in the approved Standard Operating Procedures for the agricultural facility being used. In this situation, simply report the IACUC protocol number for the agricultural unit SOP and state that your study animals will be managed as described in the SOP. Be sure to identify any exceptions. For each species list your experimental and control groups and the number of animals in each. A summary table format is highly recommended, and may be added as an attachment to this submission.

BE SURE THAT INFORMATION PROVIDED SUFFICIENTLY DESCRIBES WHAT WILL HAPPEN TO EACH ANIMAL.

There are 5 experimental groups in this study.

Group 1. Aspirin Pretreatment/Scrapie. Ten mice (5 female, 5 male) will drink low dose aspirin (30ug/ml, Bulkaen et al., 2008) containing drinking water for 7 days prior to a single IP injection of 5-10% brain prion homogenate. Aspirin containing drinking water will be changed weekly by the investigator. These mice will receive aspirin for the duration of the study. All mice (Groups 1-5) will be weighed, behaviorally tested(rotarod,inverted screen)weekly and sacrificed at 400 days post inoculation.

Group 2. Scrapie/Aspirin intervention. Ten mice (5 female, 5 male) will receive as single IP injection of 5-10% brain homogenate at the same time as group 1. These mice will receive 30ug/ml Aspirin in their drinking water
Low dose aspirin as a prophylactic against the progression of scrapie in mice

at the onset of behavioral/clinical (described later in the protocol) symptoms of scrapie.

Group 3. Scrapie. Ten mice (5 female, 5 male) will receive a single IP injection of 5-10% brain homogenate at the same time as groups 1 and 2.

Group 4. Aspirin. Ten mice will receive low dose (30ug/ml) aspirin in their drinking water at the same time as group 1.

Group 5. Control. Ten mice (5 female, 5 male) will be weighed and tested as described above.

*** Housing ***

<table>
<thead>
<tr>
<th>Species</th>
<th>Housing Location</th>
<th>MHA Building</th>
<th>MHA Room Number</th>
<th>MHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MICE</td>
<td></td>
<td></td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

** Health and Monitoring **

Please provide Species - Specific responses to the questions below

a. List the anticipated specific study-induced or related adverse health conditions that the animals might experience (i.e. pain, distress, complications, etc) or any health problems that will or might result from the genotype or phenotype of the animal. Note that momentary pain or distress does not need to be described (eg venipuncture or injections).

The intraperitoneal (IP) inoculation of scrapie prions will be associated minor, transient discomfort. The onset of disease in IP-infected mice is, based upon previous publications, expected to occur prior to approximately 400 days post inoculation.

b. How will pain and/or distress be monitored? Provide the specific clinical signs which will be monitored as well as the frequency of monitoring by personnel on this protocol and indicate if this monitoring will include weekends and holidays.

We do not expect pain as part of these studies. The development of progressive neurologic disease is expected and the mice will be monitored as follows:

Mice will be monitored over the course of the experiments as follows:

1. Weekly neuromuscular assessment using the inverted grid and rotarod assays as described.
2. Regular assessment for signs of clinical disease. Prion disease will be diagnosed using previously established and published criteria, which are summarized below.

a. Possibly affected: Hyperexcitability, increased tail tone, weight gain, or roughened hair coat.
b. Definitively affected: Truncal ataxia, head bobbing or tilting, kyphosis, incoordination, or hind limb paralysis.

c. Explain what steps will be taken to alleviate any pain, distress or discomfort the animals may experience. Provide the dose (in mg/kg), route of administration, frequency, and type of analgesic or tranquilizers to be administered. Consider warming pads, fluids, soft bedding, etc. You may provide a range of doses, frequencies, and drug classes for committee consideration.

Mice that are definitively affected (see above) by scrapie will be euthanized. Mice will be euthanized for humane reasons at the onset of severe weight loss (15-20% loss) or if suffering is apparent from any non-experimental-related clinical symptoms.

d. For animals housed in RAR, species specific environmental enrichment is routinely provided. Do these provisions interfere with your study?*

* If "Yes", please provide justification for exception request in the Guidelines Section.

e. Do you need an exception to social (group) housing of animals?*

* Controlled Substances *

1. Select Controlled Substance(s) being used on this protocol:

Name of Controlled Substance*

Guidance for using controlled substances for research can be found on the OVPR-REO website at: http://www.research.umn.edu/riop/controlsubst.htm

Questions: Contact Research Education and Outreach (OVPR-REO) at OVPRREO@umn.edu for information on controlled substances used for research.

*** DEHS, IBC & OHS ***

Note: Complying with the guidelines and expectations of DEHS and/or OHS to ensure appropriate safety procedures is a condition of IACUC approval to conduct activities associated with potentially hazardous agents listed in Appendix G. Representatives from DEHS and OHS review all IACUC submissions and may contact you for further information or guidance about your lab safety training, agent specific SOPs or other health and safety issues related to the conduct of activities in this protocol. DEHS, OHS and/or IBC will determine if hazardous agent administration in animals requires notification to RAR (or other animal care staff if animals are not housed in RAR). Such notification
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

would be needed a minimum of two weeks in advance of administering a hazardous agent to an animal. Information about the agent and exposure control procedures must be provided to the animal facility staff and safety-training offered as needed. To request information on appropriate safety procedures on any of the sections below call DEHS at 612-626-6002, or visit the web at http://www.dehs.umn.edu. For occupational health questions, call OHS at 612-626-5008, or visit the web at http://www.ohs.umn.edu.

1. Laboratory Safety Plan And Annual Safety Training - Please verify that the following requirements are in effect:

   Your laboratory personnel must have read and have access to your department’s current (updated within the last calendar year) Laboratory Safety Plan. The departmental Laboratory Safety Plan can be obtained from your Research Safety Officer (RSO). Information and templates are available from DEHS (612-626-6002) or on the web at http://www.dehs.umn.edu/ressafety_rsp.htm. All laboratory workers (including PI) listed on this protocol must have completed their annual update laboratory specific safety training.

   [ ] Yes, this laboratory has a current laboratory safety plan and personnel are current on lab safety training requirements.

   Note: To self-report training in PeopleSoft, log onto http://hrss.umn.edu/, click on Training Registration/History in the right hand column of the gray shaded box, click on Personal Training Record in the right hand side of the page under “Track your Training History”, scroll down to bottom and click on "Report completed training...", and follow the instructions.

2. Hazardous Waste - Any hazardous wastes generated by your research activities will require special handling and disposal. All University personnel that generate hazardous wastes must complete annual Hazardous Waste training.

   [ ] Yes, this Laboratory has verified that all personnel are current on Hazardous Waste training requirements.

   [ ] No, this protocol will not generate hazardous wastes.

You indicated that you are using the following potentially Hazardous Materials. Please add details below

3. Anesthetic Gases - Please verify that all halogenated anesthetic gas use is in accordance with DEHS Policy: http://www.dehs.umn.edu/PDFs/AnestheticGases.pdf. A training module on the safe use of anesthetic gases is available at: http://www.dehs.umn.edu/PDFs/WAG%20training.pdf. All personnel that use anesthetic gases must receive training and a record of the training must be available or accessible in your laboratory.

   Anesthetic Gases

   [ ] Yes, this laboratory has verified that all anesthetic gas use complies with DEHS policy and all relevant personnel have been trained on the safe use of anesthetic gases.

4. Chemicals - List all chemicals, drugs, nanoparticles, etc. that may cause adverse human health effects due to exposure during research, including those that could cause treated animals or their excrement to be...
hazardous. Types of chemicals that should be listed include: agents that require specific prophylactic measures, specific pre-placement or surveillance measures, have specific contraindications such as pregnancy or immunosuppression, have potential for significant human health effects, or that require specific work practices, engineering controls or personal protective equipment to prevent human health effects. Contact DEHS, 612-626-6002, dehs@umn.edu, if you have questions regarding what to include.

Chemicals

Note: When normal laboratory practices, consistent with your department’s lab safety plan, are insufficient to protect personnel from potential health effects of exposure to high hazard agents, you may be notified by DEHS or OHS to submit agent specific SOP(s) for review. Information describing the classes of high hazard chemicals and materials that might require an SOP may be found at [www.dehs.umn.edu/Docs/High_Hazard_Chemicals_and_Materials.doc](http://www.dehs.umn.edu/Docs/High_Hazard_Chemicals_and_Materials.doc)

5. Radiation - Contact Radiation Protection (612-626-6764) for radiation protection forms or assistance, or visit the web at [http://www.dehs.umn.edu/rad.htm](http://www.dehs.umn.edu/rad.htm)

   Name of approved radioisotope permit holder or source owner:

   Duration of permit:

Radiation

Describe safety procedures for animal care staff handling animals/cages/bedding:

6. Human blood, body fluids, normal or neoplastic tissue (including human cell lines) (Please select ‘Human blood, body fluids, normal or neoplastic tissue’ under ‘Potentially Hazardous Agents in Animals’ in Protocol Checklist to answer ‘Human blood, body fluids, normal or neoplastic tissue’):

   Will human tissue, human cells, blood or body fluid be used in your research?
   Note: Universal Precautions must be followed when handling human blood, body fluids, or tissues.

   Yes - Yes, this laboratory has verified that all relevant personnel have completed Bloodborne pathogen training and immunizations

   NOTE: Use of any of the items identified in sections (7-9) requires an application to, and approval from, the Institutional Biosafety Committee (IBC) prior to IACUC approval. If you are unsure or have questions, please contact the IBC at 612-626-6664.

7. Infectious Agents (Including bacteria, viruses, parasites, prions).

Infectious Agents
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

Name of Agent*: Prions
Biosafety Level*: 2
Animal Species*: Mouse
Route of Administration*: Intraperitoneal

8. Biologically-Derived Toxins (derived from plants, bacteria, fungi, etc).

Biologically-Derived Toxins

9. Recombinant DNA (Please select 'Recombinant DNA' under 'Potentially Hazardous Agents in Animals' in Protocol Checklist to answer 'Recombinant DNA')

*** Euthanasia ***

Euthanasia/Disposition of Animals

1. Identify and explain the rationale for the specific endpoint(s) for each animal or group of animals used in this protocol. The endpoint is when an animal or a group of animals will no longer be used in the protocol. This could be associated with time after administration of a compound, collection of a final blood sample, when animals are sacrificed for tissue collection, how long they are maintained after surgery, etc. Make sure the endpoints match those identified in your response to question 3B. You may provide a range of endpoints for committee consideration.

The proposed studies are, in part, focused on the longitudinal evaluation of the progressive clinical and neuropathologic consequences of animals infected with scrapie prions. The specific endpoints proposed are based upon the previously-published incubation period for scrapie in this model system.

2. Indicate the disposition of each species. For approval of multiple euthanasia methods per species, re-enter the species for each requested method. "Not euthanized" and "Other Euthanization Method" are options.

Euthanasia Method
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

Species: MICE
Method of Euthanasia: Carbon dioxide
IACUC criteria for CO2 Euthanasia Guidelines will be followed: Y
Method to ensure euthanasia (optional): Decapitation

3. Animals that are experiencing unrelieved pain or distress prior to the defined experimental endpoint must be humanely euthanized, unless doing so would interfere with, or compromise the scientific goals of the experiment.

Do the IACUC Criteria for Euthanasia interfere with your experimental objectives?
- If "Yes" please provide justification for exception request in the Guidelines Section.
- Y No. All of the personnel on this study have read and will comply with the IACUC Guidelines for early euthanasia.
- N/A. Client owned animals - the decision to euthanize a client-owned animal is between the owner and their veterinarian and cannot be required as an endpoint for clinical studies.

4. Will death or moribund condition be used as the experimental endpoint?
- Yes (Select "Death" or "Moribundity" below and provide justification for exception request in the Guidelines Section.)
- □ Death
- □ Moribundity will be used as the experimental endpoint. These animals are classified as pain Class C
- Y No. IACUC Criteria for Euthanasia guidelines will be followed

5. Food Chain Approval
Describe the treatment to be administered.
Note that separate sections are provided for chemicals, biologics, and devices. Chemicals (part A) include drugs and hormones. Biologics (part B) include innoculants (i.e. bacterial or viral suspension, vaccine) and antibodies. Devices (part C) include transponders or other electrical or mechanical devices that might be implanted, retained in the digestive tract, etc. In some instances, more than one section may need to be filled out. For example, use of implantable items, such as the Alzet minipump, would require completion of part A (chemicals) or B (biologics) depending upon the item being administered and part C for the device.

Chemicals / Biologics

Devices (transponders, pumps, etc.)
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

***Attachments***
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

*** Guidelines ***

FOR STAFF USE ONLY:

- USDA
- AAALAC
- Neither

Guidelines - Mandatory and Non-mandatory

**Mandatory**

- Food/water restriction recordkeeping or weekly weighing (a)

**Non-Mandatory**

- Tumor Endpoint Criteria
- Environmental Enrichment
- Social Housing
- Non-Pharmaceutical Grade Compounds
- Anesthesia/Surgical Recordkeeping/monitoring (a): (IACUC Policy on Anesthesia, Surgery and Post-Procedural Records)
- Anesthesia/Surgical Recordkeeping/monitoring (b)
- Food/water restriction recordkeeping or weekly weighing (b)
- Three-Days Post-Op Analgesia
- Euthanasia (criteria, decapitation/cervical dislocation, CO2 Methodology)
- Administration of Biological Materials to Rodents
- Blood Collection
- Immunization
- Drug Recommendations from RAR
- Physical Restraint
- Special Diet/Water Recordkeeping
- Tail Biopsy
- Toe Clipping
- Sanitation Frequency
- Primary enclosure size/space
- Acclimation Time
- Blood Collection Method
- Decapitation via Scissors
- Animal Transport
- Other
- Multiple Surgery Guideline

**AGREE**

**NA**

**Request Exception**

**ADDITIONAL POLICY WEBLINKS**

**NIH, USDA, AAALAC**

- The UMN's USDA Registration Number is 41-R-0005.
- The UMN's NIH Animal Welfare Assurance Number is A3456-01
- AAALAC Accreditation Letter - Note: AAALAC accreditation applies only to facilities in the AHC, CLA, and the Hormel Institute.
Protocol Title: Low dose aspirin as a prophylactic against the progression of scrapie in mice

NIH Vertebrate Animal Section Template

REGULATORY LINKS
- Public Health Service Policy on Humane Care and Use of Laboratory Animals
- U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
- Guide for the Care and Use of Laboratory Animals (The Guide)
- Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching (Ag Guide)
- NIH Office of Laboratory Animal Welfare (OLAW)
- USDA Animal Welfare Act Regulations (AWAR) - Federal Law

UNIVERSITY LINKS
- Board of Regents Policy on Animal Care and Usage
- Research Animal Resources
- Office of Occupational Health and Safety (The Guide)
- Office of the Vice-President for Research (OVPR)
- Institutional Animal Care and Use Committee (IACUC)
- Institutional Biosafety Committee (IBC)

*** Assurance ***

Principal Investigator(s)

As Principal Investigator, I agree to execute all activities as described; request approval from the IACUC for changes; comply with the guidelines set forth by the IACUC, Research Animal Resources, Environmental Health & Safety; and be responsible for the supervision, training, documentation of training, and work of staff listed on this protocol. I affirm that the activities described in this study do not unnecessarily duplicate previous experiments and that this form accurately and completely reflects the animal use in the full grant application, if applicable. I will notify the funding agency of any subsequent protocol amendments that represent a change in the scope of the grant.

Conflict of Interest

Please remember that you were required to file a Report of External Professional Activities (REPA) in February. If you have not completed that process, do so as soon as possible.

Please also remember that you are required to file a new REPA within 30 days of a "substantial change" in a financial or business interest that relates to your University expertise or responsibilities, or a change in your University responsibilities that relates to an existing business or financial interest. Should you have questions, the FAQ on the Conflict of Interest Program website may be helpful to you.

http://www.compliance.umn.edu/conflictHome.htm

I (we) certify that I (we) understand the University of Minnesota Code of Conduct policy and agree to abide by the rights and responsibilities as identified therein.

☒ The Principal Investigator(s) has read and agrees to abide by the above assurances.
**Event History**

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