



Key points to remember when preparing your Vertebrate Animals section for an NIH grant:

1. Address ALL 4 required points from the SF 424 guidelines (for more information, see page 2):
 - a. Detailed description of the procedures
 - b. Justifications for the choice of species, and why research goals cannot be accomplished using an alternative model
 - c. Minimization of Pain and Distress
 - d. Method of euthanasia to be used (only if not consistent with AVMA guidelines)
2. While it is acceptable to have a "Pending" IACUC approval at the time of application, NIH will ask for the approval at Just-in-Time. In order to avoid delays, it is a good idea to write and submit your protocol before the grant is reviewed.
3. Remember, only the IACUC committee can approve amendments to your pre-existing IACUC approval. Sometimes what the PI deems as an amendment, the IACUC committee deems as an entirely new IACUC protocol. Start your amendment early to avoid delays if this happens.
4. Make sure that the Vertebrate Animals section for an NIH grant corresponds with pre-existing IACUC protocol, if you plan to use that IACUC approval.

Worksheet for the Vertebrate Animals Section (VAS)

This is a worksheet to assist applicants in preparing the VAS for submission to the NIH, and to assist reviewers in evaluating the VAS of grant applications and cooperative agreements. It provides an overview of the requirements, applicant and reviewer responsibilities, a checklist, detailed instructions, and an example of an acceptable VAS.

Applicability

A VAS is required if the work proposed in a grant application or cooperative agreement involves live vertebrate animals, including animals obtained or euthanized for tissue harvest and generation of custom antibodies.

The criteria in the VAS must be addressed for work proposed at every performance site – this is the site (institution) where procedures with animals will be performed. If the applicant institution is not the site where animal work will be performed or if the work will be performed at several sites, these performance sites must be identified.

Requirements

If live vertebrate animals are to be used, federal policy requires applicants to address the following criteria:

- 1. Description of Procedures.** Provide a concise description of the proposed procedures to be used that involve vertebrate animals in the work outlined in the Research Strategy section. Identify the species, strains, ages, sex, and total number of animals by species to be used in the proposed work. If dogs or cats are proposed, provide the source of the animals.
- 2. Justifications.** Provide justification that the species are appropriate for the proposed research. Explain why the research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro).
- 3. Minimization of Pain and Distress.** Describe the interventions including analgesia, anesthesia, sedation, palliative care, and humane endpoints to minimize discomfort, distress, pain, and injury.

Note, for applications with due dates on or after May 25, 2016: (1) the method of euthanasia is eliminated from the VAS and is addressed in the FORMS-D Cover Page Supplement or PHS Fellowship Supplemental forms; (2) a description of veterinary care is no longer required; and (3) the justification for the number of animals has been eliminated from the VAS and should now be addressed in the Research Strategy as part of experimental design.

Applicant Responsibilities

Each of the criteria must be addressed in the VAS of NIH applications or proposals. All of the items must be evaluated by reviewers as appropriate for an application to be rated as ACCEPTABLE. Failure to address the criteria will result in the application being designated as incomplete and it will not be reviewed. The VAS must not be used to circumvent page limits.

Reviewer Responsibilities

Members of scientific review groups (SRGs) must evaluate the VAS to determine if plans for the use of vertebrate animals are appropriate relative to the scientific work proposed. An application will be rated UNACCEPTABLE if all required items are not addressed adequately or found inappropriate. Reviewers will assess the VAS for applications proposing the use of chimpanzees as they would any other application.

NIH Staff Responsibilities

- **Review staff** a) performs an administrative review of each VAS, checking that all criteria are addressed; b) provides reviewers with instructions for reviewing the VAS (e.g., worksheet), noting that all criteria must be evaluated as appropriate for the VAS to be ACCEPTABLE; c) subsequent to SRG review, codes the application and includes reviewers' comments in the summary statement.
- **Program staff** a) obtains additional information or clarification to resolve concerns for any application found to be UNACCEPTABLE if it is to be recommended for funding; b) works with the applicant to provide information to the Office of Laboratory Animal Welfare (OLAW) allowing resolution of the animal welfare concerns.
- **Grants Management staff** a) verifies that the institutional Animal Welfare Assurance number is provided; b) obtains verification of IACUC approval.

Checklist

Performance sites:

- ___ If the applicant's institution is not where animal work will be performed, are all collaborative performance sites identified?
- ___ If more than one performance site is planned, are descriptions of animal use addressing the required criteria provided for each site?

1. Describe the animals and their proposed use. Address the following for all species to be used:

- ___ Species
- ___ Strains
- ___ Ages
- ___ Sex
- ___ Total number of animals by species to be used
- ___ Concise, complete description of proposed procedures (i.e., sufficient information for evaluation)
- ___ Source, only if dogs or cats are proposed

2. Provide justifications for:

- ___ Choice of species
- ___ Why research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro)

3. Describe interventions to minimize discomfort, distress, pain, and injury. Examples of the kinds of items that may be appropriate to include are:

- ___ Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain, or injury
- ___ Procedures to alleviate discomfort, distress, pain, or injury
- ___ Identify (by name or class) any tranquilizers, analgesics, anesthetics, and other treatments (e.g., antibiotics) and describe their use
- ___ Provisions for palliative care or housing that may be necessary after experimental procedures
- ___ Plans for post-surgical care, if survival surgeries are proposed
- ___ Indicators for humane experimental endpoints, if relevant

Instructions

Typically, all of the required elements for the VAS can be addressed within 1-2 pages. The VAS must not be used to circumvent page limits. Applicants should be aware that NIH may release information contained in funded applications pursuant to a Freedom of Information Act request.

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1. Description of Procedures

Investigators must include a concise, complete description of the proposed procedures. While additional details may be included in the Research Strategy, a coherent, albeit brief, description of the proposed use of the animals must be provided in the VAS. The description must include sufficient detail to allow evaluation of the procedures.

Examples of the types of procedures that may be described include:

- Blood collection
- Surgical procedures
- Administration of substances
- Tumor induction
- Post-irradiation procedures

In describing the animals, investigators must provide the following information:

- Species
- Strain
- Ages
- Sex
- Total number of animals to be used by species
- Source of the animals, if dogs or cats are proposed

2. Justifications

Investigators must justify the use of animals in the proposed research. [U.S. Government Principles](#) require grantees to consider mathematical models, computer simulation, and in vitro biological systems. The justification should:

- Indicate why the research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro).
- Provide rationale for the choice of species must be provided (e.g., advantages of the species chosen and why alternative species are not appropriate).
- Discuss why less highly evolved or simpler animal models are not appropriate. For example, the use of non-human primates, dogs, or cats should be thoroughly justified.

3. Minimize of Pain and Distress

Investigators should identify procedures or circumstances that may result in more than momentary discomfort, distress, pain, or injury and describe:

- Interventions to alleviate discomfort, distress, or pain should.
- Name or class of pharmacological agents, if used.
- Any additional (e.g., non-pharmaceutical) means to avoid discomfort, distress, pain, or injury, including palliative care.
- Manner, circumstances, and duration of all post-surgical provisions and care.

- Special housing following surgery or manipulations, if necessary.
- Procedures (e.g., pharmacological, surgical) that might lead to severe discomfort, distress, pain, or injury.
- Indicators for humane endpoints and euthanasia (e.g., severe infection, respiratory distress, failure to eat, tumor size).

All of these issues are particularly important for survival surgeries. If multiple surgeries are proposed, these should be well justified and provisions to avoid any potential complications may be described.

Resources

- [Frequently Asked Questions](#)
- [Grant Application VAS Worksheet](#) (PDF) – an optional tool for grant application review
- [Contract Proposal VAS Worksheet](#) (PDF) – an optional tool for contract proposal review
- [VAS Factsheet](#) (PDF)
- [What Investigators Need to Know About the Use of Animals](#) (PDF)
- [NOT-OD-16-006](#): Simplification of the Vertebrate Animals Section of NIH Grant Applications and Contract Proposals

References

The guidance in this worksheet is based on Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy) and federal requirements. The PHS Policy incorporates the standards in the *Guide for the Care and Use of Laboratory Animals* and the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*, and requires that euthanasia be conducted according to the *AVMA Guidelines for the Euthanasia of Animals*. Additional background information and references are available on the OLAW website (<http://olaw.nih.gov>).

- PHS Policy
<http://grants.nih.gov/grants/olaw/references/phspol.htm>
- U.S. Government Principles
<http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples>
- Guide for the Care and Use of Laboratory Animals
http://www.nap.edu/catalog.php?record_id=12910
- AVMA Guidelines for the Euthanasia of Animals
<https://www.avma.org/KB/Policies/Documents/euthanasia.pdf>

Example

(This VAS has been modified from the original. It addresses all required criteria.)

F. Vertebrate Animals

Aims 1-3 will be addressed in vitro; Aim 4 will be addressed using a mouse model of ocular infection.

1. Description of Procedures: Male and female Balb/c mice will be used to determine if virions treated with enzyme can cause viral keratitis, and to test the in vivo efficacy of the test articles. The studies will require 700 mice, 4 to 6 weeks old. Ocular infection is accomplished by scratching the cornea of anesthetized mice with a sterile needle and exposing the scarred portion of the cornea to inoculum. Test articles are applied directly to the scarified cornea as liquid or cream. Following inoculation and recovery, mice are monitored for 30 days. With the mice under anesthesia, the eyes will be examined at intervals, microscopically, and are flushed with medium with 2% serum to determine viral titers. Thirty days post-infection, with the mice under deep anesthesia, the trigeminal ganglia are removed aseptically for viral assay, followed immediately by euthanasia.

2. Justifications: The proposal is to study mechanisms for the prevention of ocular disease caused by viral infections, a leading cause of blindness in the US. Mice are needed for these experiments because no alternative in vitro model incorporates all elements of the mammalian ocular immune system; too little is known about this system for the development of computer simulations or for clinical studies to be considered. Mice are a well-accepted model for studying viral keratitis, assessing the virulence of viral strains, and testing the efficacy of antivirals. Mice provide several advantages over other models for these studies: a) The murine ocular immune system is similar enough to that of humans to allow extrapolation of the results; b) Their small size allows the use of smaller amounts of drugs for testing; and c) The entire mouse genome is known and easily manipulated genetically, allowing extension of the work in future genetic studies. Balb/c mice will be used because they have intermediate resistance to infection.

3. Minimization of Pain and Distress: Mice will be anesthetized with isoflurane (3-5%) during the infection process, when treatments are administered, and titer samples are collected. This eliminates the need for restraint devices and topical anesthetics that would interfere with the infection and disease process. For post-procedural pain relief, we will administer buprenorphine twice daily for the duration of the experiments (i.e., approximately two weeks post-inoculation). Death is not an endpoint for the studies; the Balb/c strain was chosen because of its resiliency and resistance to this particular virus. Our goal is to avoid severe infections leading to death. Though unlikely, if an animal reacts severely, it will be euthanized, based on humane indicators (e.g., failure to groom or feed). These experiments involve no post-surgical survival animals.