Worksheet for Review of the Vertebrate Animal Section (VAS)

This worksheet is provided to assist applicants in preparing the VAS for submission to the NIH, and as guidance to reviewers in evaluating the VAS of applications and proposals. The responsibilities of extramural scientists and NIH staff are clarified on page 1. A worksheet to assist in preparing or evaluating the VAS is provided on page 2, with more detailed instructions provided on pages 3-4. An example of a complete VAS, coded as ACCEPTABLE, is presented on page 5.

I. Instructions for Applicants, Reviewers and NIH Staff

Overview of requirements

If live vertebrate animals are to be used, federal policy requires that the following five points are addressed by applicants in the VAS of applications and proposals. (A definition of research that involves the use of live vertebrate animals is on page 3.)

1. Detailed description of the proposed use of the animals, including species, strains, ages, sex and number to be used
2. Justification of the use of animals, choice of species, and numbers to be used
3. Information on the veterinary care of the animals
4. Description of procedures for ensuring discomfort, distress, pain and injury is minimized
5. Method of euthanasia and the reasons for its selection

Reviewers must evaluate information provided in the VAS. NIH staff will verify that any concerns are cited in the summary statement. Applicants are given the opportunity to resolve concerns prior to award. Applicants should be aware that NIH may release information contained in funded applications pursuant to a Freedom of Information Act request.

Applicant responsibilities

Each of the five points must be addressed in the VAS of NIH applications or proposals. All of the items must be addressed completely and evaluated by reviewers as appropriate for an application to be coded as ACCEPTABLE. Coding of the VAS as ACCEPTABLE is required prior to award.

Reviewer responsibilities

Members of scientific review groups (i.e., study sections) must evaluate the VAS to determine if it is complete, and if plans for the use of vertebrate animals are appropriate relative to the scientific work proposed. They must verify that procedures proposed in the VAS (e.g., anesthesia, housing, surgery, euthanasia) comply with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy).

NIH Staff responsibilities

***Review staff*:** a) performs an administrative review of each VAS, checking that all five points are addressed; b) provides reviewers with instructions for reviewing the VAS (e.g., worksheet), noting that all points must be evaluated as appropriate for the VAS to be ACCEPTABLE; c) subsequent to Initial Review Group (IRG) review, codes the application and includes reviewers' comments in the Resume at the end of 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 the IACUC approval date for the Investigator's protocol, if not previously provided.

II. Worksheet to Assist in Addressing the Required Five Points of the VAS

Performance site(s): The five points must be addressed for all performance sites.

__ If the applicant's institution is not where animal work will be performed, are all collaborative performance site(s) identified?

__ If more than one performance site is planned, are descriptions of animal care and use for each site provided?

Point 1 Describe the animals and their proposed use; address the following for all species to be used:

__ Species
__ Strains
__ Ages
__ Sex
__ Number of animals to be used
__ Provide a concise, but complete description of proposed procedures (i.e., sufficient information for evaluation)

Point 2 Provide justifications for:

__ The use of animals
__ Choice of species
__ Number of animals to be used (cite power calculations, if appropriate)

Point 3 Provide a general description of veterinary care, including veterinary support that is specifically relevant to the proposed procedures. Indicate the following:

__ A brief account of veterinary staff and their availability
__ The regular schedule of monitoring of animals by veterinary staff
__ If relevant to the procedures proposed (e.g., post-surgical), indicate any additional monitoring and veterinary support that may be required to ensure humane care
__ Indicators for veterinary intervention to alleviate discomfort, distress or pain, if relevant

Point 4 Describe procedures to minimize discomfort, distress, pain and injury. Indicate the following:

__ 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 special care or housing that may be necessary after experimental procedures
__ If survival surgeries are proposed, include plans for post-surgical care
__ Indicators for humane experimental endpoints, if relevant
__ Describe the use of restraint devices, if relevant

Point 5 Describe methods of euthanasia:

__ Describe the method(s) of euthanasia and rationale for selection of method(s)
__ Indicate if the method is consistent with AVMA Guidelines on Euthanasia
__ Provide a scientific justification for the choice of method if not AVMA recommended

III. Detailed Instructions for Preparation, Review and Coding of the VAS

Subsequent to evaluation of the VAS by an IRG (i.e., study section), all applications or proposals are coded as NO VERTEBRATE ANIMALS (10), NO CONCERNS/ACCEPTABLE (30) or CONCERNS/UNACCEPTABLE (44).

Coding as "NO VERTEBRATE ANIMALS" (10)
If animal tissue used in the study is obtained from other sources (e.g., tissue repository, animals euthanized for an unrelated purpose), the application is coded as "no vertebrate animals used." A statement indicating the source of the tissues is required in the VAS to validate the coding as "no vertebrate animals used."

Vertebrate animals:
If animals are manipulated prior to euthanasia or obtained specifically for tissue harvest as part of the proposed research, this constitutes using animals and is classified as "use of live vertebrate animals." The generation of custom antibodies is coded as "use of live vertebrate animals."

Coding as "NO CONCERNS/ACCEPTABLE" (30) or "CONCERNS/UNACCEPTABLE" (44)
Coding is based on peer review of the five required points for each of the performance sites.

Performance site(s): This is defined as the institutions where procedures with animals will be performed. If the applicant institution is not the site where animal work will be performed, the performance site must be identified. If there is more than one performance site, the description of animal care and use at each site must be included and must address the five points.

Preparation of the VAS:
Typically, all of the required elements for the VAS can be addressed within 1-2 pages. Following the detailed guidelines below, an example of a concise, but complete VAS section is included on the last page of this document.

Point 1 Description of animals and how they will be used
A concise, complete description of the proposed procedures must be included in the VAS. While additional details may be included in the Methods section of the Research Plan, a coherent, albeit brief description of the proposed use of the animals must be provided within the VAS. The description must include sufficient detail to allow evaluation of the procedures. Examples of the types of procedures that should be described include blood collection, surgical procedures, administration of substances, tumor induction and post-irradiation procedures. In describing the animals, investigators must provide the following information for each species or strain:

- Species
- Strain
- Ages
- Sex
- Number of animals to be used

Point 2 Justifications for use of animals
Investigators must justify the use of animals in their research. The justification must indicate why alternatives to animals (e.g., computer models, cell culture) cannot be used, and should indicate the potential benefits and knowledge to be gained. In addressing this point, researchers are encouraged to consider means to "replace, reduce and refine" the use of animals. Rationale for the choice of species must be provided. The rationale should indicate the advantages of the species chosen and why alternative species are not appropriate. If less highly evolved or simpler animal models are available, justification must be provided for using more advanced species. For example, the use of non-human primates (NHP), dogs or cats should be thoroughly justified. If

NHP species are to be used, a comparison to other NHP species may be appropriate. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and the number of animals used.

Estimates for the number of animals to be used should be as accurate as possible. Justification for the number of animals to be used should include considerations of animal availability, experimental success rate, inclusion of control groups and requirements for statistical significance; cite power calculations where appropriate.

Point 3 Veterinary care

Descriptions of veterinary care should indicate the availability of veterinarians or veterinary technicians. For example, the VAS might indicate the number of veterinarians and veterinary technicians associated with the applicant institution, and their proximity to the performance site(s). The frequency with which veterinary staff observe or monitor animals should be stated.

If survival surgeries are proposed, veterinary involvement or post-surgical monitoring should be described. For example, if animal use involves invasive approaches that might result in discomfort, distress or pain, the investigator should indicate if or when veterinary care is necessary. The indicators for veterinary intervention to alleviate discomfort, distress or pain should be described. The ways in which veterinary staff may intervene should be described.

Point 4 Provisions to minimize discomfort, distress, pain and injury

Procedures or circumstances that may result in more than momentary discomfort, distress, pain or injury should be identified. Methods to alleviate discomfort, distress or pain should be described. If pharmacological agents are used, the agent(s) should be specified by name or class. Any additional means to avoid discomfort, distress, pain or injury should be described briefly. The manner, circumstances and duration of all post-surgical provisions and care should be described. If special housing is necessary following surgery or manipulations, the VAS should describe these provisions, the duration, and type of monitoring provided. If procedures (e.g., pharmacological or surgical) 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) should be described. All of these issues are particularly important for “survival surgeries.” If multiple surgeries are proposed, these must be well justified and provisions to avoid any potential complications must be described. Describe how restraining devices will be used, if applicable.

Point 5 Euthanasia

The method(s) of euthanasia must be described and must comply with the AVMA Guidelines on Euthanasia. If the method(s) do not comply with AVMA recommendations, the rationale and scientific justification for use of the method(s) must be provided. The indicators for euthanasia (i.e., termination of experiment or humane endpoints) should be stated. It is not sufficient to state simply that humane methods will be used, that are consistent with the recommendations of the AVMA Guidelines on Euthanasia or the Institutional Animal Care and Use Committee (IACUC).

References

Information within this document is based on PHS Policy and federal requirements. The PHS Policy incorporates the standards in the Guide for the Care and Use of Laboratory Animals and requires that euthanasia be conducted according to the AVMA Guidelines on Euthanasia. Additional background information and references are available on the Office of Laboratory Animal Welfare website (http://olaw.nih.gov).

- PHS Policy - http://grants.nih.gov/grants/olaw/references/phspol.htm
- Guide for the Care and Use of Laboratory Animals - http://www.nap.edu/openbook.php?record_id=5140
- AVMA Guidelines on Euthanasia - http://www.avma.org/issues/animal_welfare/euthanasia.pdf

IV. Example VAS (Under development)