Research Involving Animals

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1. Introduction

If using animals, provide all information required by this appendix. Any and all subcontractors using animals must also provide the information required by this appendix.

DOD definition of **animal: Any live nonhuman vertebrate.**

The DOD Directive 3216.1, dated April 17, 1995, provides policy and requirements for the use of animals in DOD-funded research. **These requirements may differ from those of other funding agencies.** Each of the following items **must** be addressed in a proposal appendix entitled "Research Involving Animals." Questions concerning animal use should be directed to Ms. Joyce O'Brien:

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Fax: 301-619-4165
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ATTN: MCMR-RCQ-AR
504 Scott Street
Fort Detrick, MD 21702-5012

2. Alternatives to Painful Procedures:

A painful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which that procedure is applied. The Animal Welfare Act regulations specifically state that the Principal Investigator (P.I.) must provide a narrative description of the methods and sources, (e.g., the Altweb (Johns Hopkins Center for Alternatives to Animal Testing), MEDLINE, Life Sciences Abstracts, AGRICOLA, and BIOSIS) that he/she used to determine that alternatives to the painful/distressful procedure, including those procedures in which pain/distress is alleviated, were not available. The minimal written narrative must include: databases searched or other sources consulted, date of the search and the years covered by the search, key words and/or search strategy used and a discussion of what alternatives were considered but not used. Where Federal law requires specific testing procedures, state the appropriate CFR or legal guidance that requires this testing. (The USAMRMC reserves the right to request evidence that a literature search for alternatives to painful procedures was performed.)

3. Literature Search for Unnecessary Duplication:

This search must be performed to prevent unnecessary duplication of previous experiments. A search of the following databases is required: Biomedical Research Database (BRD) at http://www.scitechweb.com/acau/brd/ and the Computer Retrieval of Information of Scientific Projects (CRISP) at http://www.crisp.cit.nih.gov/ or the Federal Research in Progress (FEDRIP) at http://grc.ntis.gov. Additional searches in databases specific to the area of research performed in your proposal are highly recommended.

Information on your search for duplication must include databases searched, keywords or search strategy used, period of search, and date search was performed.

4. Rationale for Using Animals:

Provide a scientific justification for using animals in the proposed research. State alternatives to animal use that you considered, such as computer modeling or cell cultures, and explain why these alternatives cannot be used to obtain the research objectives. **It is USAMRMC policy that alternatives to the use of animals be thoroughly investigated prior to submission of any proposal involving animals.**

5. Species Identification and Rationale:

Identify the species of animals used. If using mice, rats or guinea pigs, state the strain. If using dogs, cats or rabbits, state the breed. Provide a scientific justification for their use. Explain why you selected this particular animal model. What unique morphological and physiological characteristics does this animal model possess that make it the best choice?

6. Number of Animals Used:

State number of groups, number of animals in each group and the total number of animals used by species. Per USDA Animal Care Policy 11, 14 April 1997, "A painful/distressful procedure is defined as any procedure that would reasonably be expected to cause more than slight or momentary pain and/or distress in a human being to which the procedure is applied."

a. State the common names and number of animals used in research involving no more than slight or momentary pain or distress.

b. State the common names and numbers of animals used in research involving pain or distress that is relieved with anesthetics and/or analgesics.

c. State the common names and numbers of animals used in research involving pain or distress that is NOT relieved with anesthetics and/or analgesics.

7. Rationale for the Number of Animals Required:

Describe the statistical methodology used to determine group size and total number of animals used. Include animals necessary for controls, technique development, expected losses, etc. Explain how **these numbers were statistically determined to be the minimum** required to obtain valid scientific results. State the statistical test(s) planned or describe the strategy intended to evaluate the data. Where Federal law or regulations require specific group sizes, state the appropriate CFR or reference.

8. Experimental Design:

Provide a complete description of experimental design to include a summary table of experimental groups and a flowchart indicating sequence of experimental events. Succinctly outline the formal scientific plan and direction of experimentation. If several

experiments or sequential studies are included in the protocol, describe the experimental design of each separately. The number of animals listed in this section must correspond to the total number of animals requested in paragraph 6.

9. Technical Methods (Animal Procedures):

Provide a complete description of all procedures the animals will experience. Include surgical procedures, biosamples (i.e., frequency, volume, harvest site, and collection method), adjuvants, tissue sampling for DNA analysis (i.e., age of sampling, amount of tissue taken, anesthetic use) and injections (i.e., agent, dosage, route, and anatomical site of administration). State frequency of animal observation once experimental procedures start and describe health status assessment criteria used. When using Complete Freund's Adjuvant and/or *in vivo* production of monoclonal antibodies, provide a scientific justification and state what alternatives you considered and why they were not used. If prolonged restraint, food or water restriction, or multiple major survival surgeries are performed during the protocol, provide a scientific justification.

10. Anesthesia/Analgesia/Tranquilization

Describe the methods or strategies planned to effectively relieve pain and distress. If analgesics are used for pain/distress relief provide the time schedule for administration and the observation criteria utilized to determine if the animals are experiencing pain and/or distress. State the drug's name, dosage, frequency, route, and anatomical site of administration. Additional scientific justification is required if the following agents are used: neonatal hypothermia, chloral hydrate, alpha-chloralose, ether or urethane. If anesthetic/analgesic agents are not used, provide an explanation.

11. Study Endpoint:

State the projected study endpoint for the animals (e.g., recovery, euthanasia, use in another protocol). Define specific health assessment criteria used to determine early study endpoints for euthanasia (e.g., percentage of weight loss, tumor size, number of abdominal taps, abdominal distention, anorexia, decreased activity, ruffled fur).

12. Euthanasia or Final Disposition:

Describe the method of euthanasia by agent, dosage, route, and anatomical site of administration. If animals are not euthanized, state final disposition of the animals.

13. Institutional Animal Care and Use Committee(s) (IACUC) Approval(s):

Provide written documentation of protocol approval in the form of a letter on institutional stationery signed by the IACUC chair or the IACUC administrator. An IACUC approval letter is required from the facility where the animal research is performed to include any subcontracted facilities. If IACUC approval is pending provide a statement to this effect. Evidence of IACUC review and approval may follow proposal submission, but must be provided prior to the start of animal experimentation.

14. U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service Animal Care Inspection Report:

Include a copy of the most recent annual USDA Facility Inspection Report for any and all facilities where animal research is performed to include any subcontracted facility.

15. Qualifications:

List all personnel working with animals under this protocol and all procedures (e.g., surgery, euthanasia, pre and post-operative care), manipulations (e.g., injections, phlebotomy, restraint), and observations each individual will perform. Provide each individual's training, experience, and qualifications to perform these duties. Training should include required institutional courses as described in the Animal Welfare Act regulations (9 CFR paragraph 2.32(c)). Qualifications should include educational degrees.

16. Accreditation:

For each applicable item, provide the following information for each facility where the animal research will be conducted:

a. A copy of the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) letter stating the institution's current accreditation status (e.g., full, provisional, probationary, or revoked).

b. A copy of the current Institutional Letter of Assurance of Compliance with the "Public Health Service Policy on Humane Care and Use of Laboratory Animals," revised September 1986.

c. In the event that items 16.a. and 16.b do not apply to your institution, provide a statement signed by the Institutional Official that the care and use of animals will be performed according to the National Research Council 1996 "Guide for the Care and Use of Laboratory Animals" and applicable Federal regulations.

17. Principal Investigator Assurances:

The law specifically requires several written assurances from the P.I. Please read and sign the assurances as indicated (this page may be photocopied and signed).

As the Principal Investigator on this protocol, I acknowledge my responsibilities and provide assurances for the following:

A. Painful Procedures: I assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research and that analgesic, anesthetic, and/or tranquilizing drugs will be used where indicated and appropriate to minimize pain and/or distress to animals.

B. Animal Use: The animals authorized for use in this protocol will be used only in the activities and in the manner described herein, unless a modification is specifically approved by the IACUC and the U.S. Army Medical Research and Materiel Command prior to its implementation.

C. Duplication of Effort: I have made a reasonable, good faith effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

D. Statistical Assurance: I assure that I have consulted with a qualified individual who evaluated the experimental design with respect to the statistical analysis, and that the minimum number of animals needed for scientific validity will be used.

E. Training: I verify that the personnel performing the animal procedures/manipulations/observations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused to the animals as a result of the procedures/manipulations.

F. Responsibility: I acknowledge the inherent moral, ethical and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to conduct this study in the spirit of the fourth “R”, which the DOD has embraced, namely, “Responsibility” for implementing animal use alternatives where feasible, and conducting humane and lawful research.

G. Scientific Review: This proposed animal use protocol has received appropriate peer scientific review, and is consistent with good scientific research practice.

_____	_____
(Principal Investigator Printed Name)	(Principal Investigator Signature and Date)

NOTE: For proposals that require the use of nonhuman primates, companion animals, marine mammals, or for research deemed warranted by the USAMRMC, a site visit shall be conducted as necessary by the USAMRMC Animal Care and Use Review Officer or designees.