The IACUC Protocol Review Form: One of the Keys to a Successful Review

Ernest D. Prentice, David A. Crouse, Michael D. Mann

The Public Health Service (PHS) policy on Humane Care and Use of Laboratory Animals (1), the amended Animal Welfare Act (2) and the United States Department of Agriculture (USDA) Animal Welfare Regulations (3) require every research institution in the United States to establish an Institutional Animal Care and Use Committee (IACUC). The IACUC, in part, is charged with the responsibility for reviewing and approving research protocols involving animals. To comply with this federal mandate, institutions across the United States are in the process of establishing and refining their IACUC protocol review system. Because this is a new experience in many institutions, it is not surprising that developmental "pains" and problems are fairly common.

One key to a successful review process is the form used for submitting protocols which provides the informational base for IACUC review. Other important factors in the development of the review process include the provision and use of institutional animal care and use guidelines (which include methods of anesthesia, analgesia, and euthanasia as well as pain criteria and other resource literature), the organization of a dedicated and qualified IACUC, and adequate administrative support. Herein, we describe the system for protocol review and the protocol review form developed by the IACUC at the University of Nebraska Medical Center (UNMC). Since its inception in 1986, this system, including the form, has undergone several revisions which reflect an evolving review process driven by public and scientific awareness of the ethics of research involving animals, as well as a clearer understanding of the PHS and USDA requirements.

The IACUC Protocol Review System

The IACUC review system is patterned after the University's Institutional Review Board (IRB) for the Protection of Human Subjects (4). The IACUC uses, with some degree of flexibility, two systems for review: i) subcommittee review by mail, and ii) full committee review in session. The decision is based on an assessment of the ethical implications of the proposed research. The type of review required by a particular protocol depends on its classification according to the IACUC's Categories of Animal Use (A-D) defined in Table 1. These categories are patterned on those established by Orlans (5) and use the pain associated with routine venipuncture as a base level. In completing the protocol review form, the investigator must identify the category of animal use which best characterizes the protocol. After submission, an IACUC administrative officer performs a preliminary review and determines if the protocol qualifies for subcommittee review or requires review by the full committee. If a protocol involves only category A procedures (no pain or momentary slight pain) and/or B procedures (minor short-term pain treated with anesthetics/analgesics), the protocol may qualify for review by a specially appointed IACUC subcommittee consisting of the staff veterinarian and one or two committee members. Pursuant to the requirements of the PHS policy and USDA rules, each eligible A and B protocol is mailed to the entire IACUC for review and comment. However, the subcommittees, which act bi-monthly, are empowered to approve A and B protocols if no other member of the IACUC refers the protocol to a full committee meeting for action. Both the subcommittees and the remaining IACUC members are given 7 working days to complete their review of A and B protocols. Any protocol referred for full committee review is considered at the next monthly meeting of the full IACUC.

Table 1. Category of Research

Category	Description
A	The research involves either no pain or potentially involves momentary, slight pain, discomfort, or distress. Includes simple invasive procedures (e.g., injection, blood sampling), terminal anesthetics surgery, collection of tissues preceded by standard euthanasia, behavioral testing without stress.
B	The research potentially involves minor short-term pain, discomfort, or distress which will be treated with appropriate anesthetics/analgesics. Includes minor survival surgery with anesthesia and without significant post-op pain (e.g., biopsy), implantation of minor chronic catheters (e.g., femoral arterial and venous catheters, flow probes, etc.), short-term physical restraint (<60 min) of awake animals, induction of minor behavioral stress.
C	The research involves chronic maintenance of animals with a disease/functional deficit and/or procedures potentially inducing moderate pain, discomfort, or distress which will be treated with appropriate anesthetics/analgesics. Includes major survival surgery with anesthesia and/or inducement of a functional deficit (e.g., orthopedic surgery on femur, amputation, bowel resection, cardiac surgery, adrenalectomy, non-painful small tumor inducement, use of immunological adjuvants), physical restraint (>60 min) of awake animals, induction of more than minor behavioral stress.
D	The research potentially involves pain, discomfort, or distress (greater than that attending routine injections) which cannot/will not be alleviated through the administration of appropriate anesthetic, analgesic or tranquilizer drugs. Example include pain research, radiation testing, toxicity testing, and lifetime carcinogenesis experiments.

In order for a protocol to qualify as category A, B, or C, appropriate anesthetics/analgesics must be used if the animal will experience more than momentary slight pain. Momentary slight pain is defined as no greater than the level and duration of pain attending a routine injection. Alternately, the animal must be immediately euthanized upon evidence of such pain or the protocol classified as category D.

A or B protocols involving nonhuman primates in any research other than non-stressful behavioral studies do not qualify for subcommittee review. This more careful scrutiny reflects both the endangered status of nonhuman primates and the greater sensitivity of animal rights groups and the general public to the welfare of this

Continued on page 14.

The authors are affiliated with the Department of Anatomy and the Department of Physiology and Biophysics at the University of Nebraska Medical Center, Omaha, Nebraska. Reprints can be ordered from Dr. Prentice at the Division of Graduate Studies and Research, 600 South 42 Street, Omaha, NE 68198-6810.

With all the controversy currently surrounding the use of animals in biomedical research, the public has been inundated with charges and counter charges from those who use animals and those who oppose that use, but they rarely hear from those who care for the animals. So, whenever you get a chance, tell everyone who will listen about what you do and how much you care about what you do. Tell them that caring people care for the animals in your institution and that you are one of those caring people. In short, Blow Your Own Horn, brag about yourself, don't be shy about what you do. If enough of us blow our own horns, the collective sound will be heard by the public. AALAS is like an orchestra in that we need a few soloists to stand out front to play selected tunes, but we need all the musicians working together to provide the backup so that the audience is listening when the soloists stand up to play their tune.

Maybe AALAS should adopt a catchy phrase that we can put on bumper stickers and pins and tee-shirts. Something like, Laboratory Animal Science: Where Caring People Care for Animals. This might help individuals define their own position within this debate.

As individual members of a branch or the national, you do not have to worry about speaking out about what you know and do best, which is care for animals. You needn't address the other issues unless you choose to do so and then only after you have done your homework. Let other organizations address the other issues.

The Role of the Other Organizations

Other scientific and professional organizations can speak for themselves. Let the psychologists explain behavioral research, the oncologists explain cancer research, and the cardiologists explain cardiovascular research.

We should support groups like FBR and iiFAR, both literally and figuratively. By figuratively, we should make donations so that they can do the things we as individuals and as an association have neither the time nor the resources to accomplish.

In another article in the Bulletin, I talked about being President of AALAS and how it had exposed me to people and organizations that I would otherwise not have known. I used iiFAR as an example and then encouraged the AALAS membership to support the organization through donations. Why did I do this? Because, iiFAR can do a better job than we can of winning the overall debate. When I was President of AALAS, there was no iiFAR, there was only an FBR, and at that time I questioned why AALAS should develop brochures, tapes, and other materials that FBR could produce better and faster. Then I encouraged our members to support FBR.

Now when people ask what we can do to help win this debate, I say support iiFAR and FBR who are better equipped to deal with the issues than is AALAS. In addition, do not be afraid to stand up and be counted as Caring People Who Care For Animals.

References

1. **American Veterinary Medical Association.** 1990. AVMA Policy on Animal Welfare and Animal Rights. American Veterinary Medical Association.
2. **Russell, W. M. S., and R. L. Burch.** 1959. Principles of Humane Experimental Techniques. p. 64. Methuen & Co., Ltd. London.

Editor's Note: *Viewpoint provides AALAS members with an opportunity to express responsible opinions. The opinions expressed here do not necessarily reflect the views of AALAS or its members.*

REQUEST FOR REVIEW OF RESEARCH/BIOLOGICAL TESTING PROTOCOL

SECTION 1

I. APPLICATION DATA

TITLE OF PROTOCOL: _____

_____

STARTING DATE: _____ PROJECTED COMPLETION DATE: _____

PRINCIPAL INVESTIGATOR: _____

SECONDARY INVESTIGATOR(S): _____

TECHNICIANS/STUDENTS: _____

DEPARTMENT/COLLEGE: _____

ADDRESS: _____ ZIP CODE _____ TELEPHONE: _____

II. CATEGORY OF RESEARCH: The investigator should check the appropriate category(ies) of experimentation.

____A **The research involves either no pain or potentially involves momentary, slight pain, discomfort or distress.** Includes simple invasive procedures (e.g., injection, blood sampling), terminal anesthetic surgery, collection of tissues preceded by standard euthanasia, behavioral testing without stress.

____B **The research potentially involves minor short-term pain, discomfort or distress which will be treated with appropriate anesthetics/analgesics.** Includes minor survival surgery with anesthesia and without significant postop pain (e.g. biopsy), implantation of minor chronic catheters (e.g. femoral arterial and venous catheters, flow probes, etc.), short-term physical restraint (<60 min) of awake animals, induction of minor behavioral stress.

____C **The research involves chronic maintenance of animals with a disease/functional deficit and/or procedures potentially inducing moderate pain, discomfort or distress which will be treated with appropriate anesthetics/analgesics.** Includes major survival surgery with anesthesia and/or inducement of a functional deficit (e.g. orthopedic surgery on femur, amputation, bowel resection, cardiac surgery, adrenalectomy, non-painful tumor inducement, use of immunological adjuvants), physical restraint (>60 min) of awake animals, induction of more than minor behavioral stress.

____D **The research potentially involves pain, discomfort or distress (greater than that attending routine injection) which cannot/will not be alleviated through the administration of appropriate anesthetic, analgesic or tranquilizer drugs.** Examples include pain research, radiation testing, toxicity testing and lifetime carcinogenesis experiments.

In order for a protocol to **qualify** as category A, B or C **appropriate** anesthetics/analgesics **must** be used **if** the animal will experience **more** than momentary slight pain. Momentary slight pain is defined as pain **no greater** than the **level** and **duration** of pain attending a routine injection. Alternately, the animal **must** be immediately euthanized upon evidence of such pain or the protocol classified as category D.

III. ANIMAL CHARACTERISTICS: The investigator should state the required number of animals to be used in the research project.

Species	Sex	Age/Weight	Animal Vendor	Location of Housing	Total

IV. BIOHAZARDOUS MATERIAL: If the animal use involves biohazardous materials the appropriate category should be checked and approval obtained from other required review committees:

Infectious Agents____; Carcinogens____; Radioisotopes____; Recombinant DNA____; Other _____

ARC-7 (Rev. 10/90)

SECTION 2

INSTRUCTIONS: The ARC requests the information described in the following section pursuant to its charge by the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals. Submit all information **using the headings** listed below in **boldface** type. Address each item independently, without reliance on information covered under other items. Subheadings (e.g., a, b, c, d) of points VII, IX, XII, XIII and XIV **must** be included and addressed in sequence. Include sufficient information to allow reviewers to judge whether the research merits the use of animals and whether the animals will be treated humanely. Do **not** submit major sections of your grant proposal or excessive detail of assays not related to the use of animals (e.g., chemical assays, molecular biology, in vitro tests). All abbreviations and terms not part of common usage should be clearly defined. Remember that not all reviewers are familiar with your area of research. Consult the ARC Guidelines during completion of this form. Section 2 has a limit of **5 pages** excluding references.

I. **Purpose of the Study.** State the specific scientific objectives (aims) of the research.

II. **Potential Value of the Study.** State the potential value of the study with respect to human or animal health, the advancement of knowledge or the good of society. Identify the information gaps the project is intended to fill. If the research duplicates previous experiments, explain why the duplication is necessary. If it does not duplicate previous research, this should be stated.

III. **Alternatives to Animal Use.** What alternatives to the use of live animals did you consider? What reasons did you have for rejecting them? If specific alternatives to live animal use do not exist, this should be stated and justified appropriately. In general, a simple statement that there are no alternatives will **not** suffice.

IV. **Species Justification.** State how you selected which species to study.

V. **Justification of the Number of Animals Requested Based Upon the Experimental Design.** Provide detailed justification for the number of experimental and control animals requested. Include a brief description of the experimental design and state the number and species/strain of animals per group/subgroup in each experiment/procedure. A table or block design can facilitate the review of this section.

VI. **Previous ARC Approved Protocols.** Does this project contain procedures which have been approved in previous protocol applications? If yes, please indicate the ARC approval number(s) and points of overlap/similarity with the present protocol. Do **not** omit material from this protocol because it was discussed in a previous protocol. Reviewers will not, in general, consult previous protocols.

VII. **Procedures.** Describe the animal-related procedures by addressing the following in sequence under the subheadings (a, b, c) indicated. This section must clearly reflect how the purpose of the study will be approached.

a) Using boldfaced subheadings identifying the procedures, describe sequentially with a reasonable degree of detail **all** procedures (surgical and non-surgical) to be carried out on live animals. When chemical agents are administered, specify the dose and route of administration. The end-points of procedures and the time frame must be clearly defined. For chronic as well as acute experiments, the length of time the animals will be maintained prior to euthanasia must be estimated.

b) If live animals will be maintained outside of their normal housing facility for greater than 12 hours, identify why, where and how long the animals will be used at that location.

c) If survival surgery will be performed, identify where the surgery and postoperative recovery will take place.

VIII. **Alternatives to Painful Procedures.** If the research involves procedures that may cause **more** than momentary or slight pain or distress to the animal, the investigator must consider alternative procedures that cause less potential pain or distress. Address why alternative procedures either do not exist or were rejected. State the method(s) and/or sources that were used to determine that alternatives are not available and/or are scientifically unacceptable.

or

If the procedure is acute this should be so stated.

IX. **Restraints.** Describe any proposed restraint (other than short-term hand-held restraint) to be used on awake animals by addressing the following in sequence under the **boldfaced** subheadings indicated.

a) **Justification.** Justify the need for restraint.

b) **Description.** Identify or describe the restraint(s).

c) **Duration.** State the duration of the restraint period.

d) **Conditioning.** Describe steps to be taken to condition the animals to the restraining device and assure the comfort and well-being of the animals.

or

If restraints will not be used this should be stated.

X. **Pain Control During the Procedure(s).** For **each** procedure that causes more than momentary slight pain, identify the procedure, specify the preoperative preparation (e.g., antibiotics, tranquilizers, etc.) and specify the anesthetic(s) to be used during that procedure. Include dose (e.g., mg/kg) and route (e.g., IM, IV) of administration of all agents:

or

SECTION 2 *(continued)*

If anesthetics are indicated but will not be administered, strong justification for withholding anesthetics must be provided in this section;

or

If pain control during procedures is unnecessary this should be stated and **justified.**

XI. **Estimation of Potential Postoperative/Intervention Pain.** If a procedure (e.g., thoracotomy, administration of drugs, chemicals) or induced condition (e.g., tumor, pancreatitis) will potentially cause more than momentary slight pain, estimate the magnitude and duration of any pain, discomfort or distress the animals may potentially experience;

or

If animals will not experience postoperative/intervention pain, discomfort or distress in association with any specific procedure(s) or condition this should be stated and **explained.**

XII. **Post-Procedure/Chronic Care.** Describe the proposed care of the animals by addressing the following in sequence under the **boldfaced** subheadings indicated. Alternatively, if post-procedure care is unnecessary this should be so stated and **justified.**

a) **Post-Procedure Monitoring.** State the frequency and length of time over which post-procedure examinations/ monitoring of the animals will be performed.

b) **Criteria for Pain.** State the specific criteria that will be used to measure/monitor acute and chronic pain.

c) **Analgesic(s).** If it is anticipated that an animal may be subjected to more than slight pain, discomfort or distress specify the analgesic(s) which will be used to **prophylactically** treat the animal. Include dose (e.g., mg/kg), route (e.g., IM, IV), frequency and duration of administration;

or

If analgesics will **not** be administered **routinely/prophylactically** state the specific criteria for administration of analgesics. In addition, specify the analgesic(s) including dose (e.g., mg/kg), route (e.g., IM, IV) and frequency of administration;

or

If analgesics are indicated but will not be administered (category D), strong justification for withholding analgesics must be provided in this section.

d) **Antibiotics.** Specify any antibiotic to be used. Include dose (e.g., mg/kg), route (e.g., IM, IV), frequency and duration of administration. If antibiotics are not necessary this should be so stated.

XIII. **Euthanasia/Disposition of Animals.** Describe euthanasia of the animals by addressing the following in sequence under the **boldfaced** subheadings indicated:

a) **Method of Euthanasia.** Specify the method(s) of euthanasia including the dose (e.g., mg/kg) of any injectable agents. Describe the criteria for determining that euthanized animals are dead. Simply stating that they will be put into 100% CO_2 or the like is not sufficient.

b) **Criteria.** Describe the criteria for euthanasia of the animals (e.g., end-point of experiment, specific time period, tumor size, etc.)

c) **Criteria for Premature Euthanasia.** For category C and D experiments specify the criteria for premature euthanasia of the animals (e.g, significant pain or sickness, inability to feed, etc.).

If animals will **not** be euthanized, state the final disposition.

XIV. **Investigator(s) Qualifications/Experience.** For **each** individual listed in Section I, describe the expertise and experience **related to this project** by addressing the following in sequence under the **boldfaced** subheadings indicated.

a) **Knowledge of Species.** Address familiarity with behavioral/physiological/anatomical characteristics of the selected species.

b) **Relevant Experience.** Describe experience with regard to the specific procedures to be applied to live animals, methods of pain control, postoperative care and euthanasia.

c) **Responsibilities.** State the individual's specific role/responsibility in this project.

XV. **References (optional).** Provide a list of *key* references (maximum of five) that support the statements contained in Section 2 (II. Potential Value of the Study) of this form.

XVI. **Investigator Comments.** Include any additional comments relevant to the proposed study and/or attach any relevant material the ARC should consider during the review process.

SECTION 3

CHECKLIST: Check the appropriate boxes and provide the information requested.

I. Anticipated Funding Source

_____PHS
_____NSF
_____Nebraska State Grant Funds (LB506)
_____Departmental/Internal Funds
_____Other External Funds _____

II. Status of Grant Application

_____Application submitted on _____
_____Application to be submitted on _____
_____Not applicable _____

III. Certification of Principal Investigator

_____ _____ _____
Signature Date Position

Signature certifies that the principal investigator will conduct the project in full accordance with the PHS Policy on Humane Care and Use of Laboratory Animals, USDA rules and University of Nebraska regulations governing the use of live vertebrate animals for research or teaching purposes. It is understood that ARC approval is valid for a period of 60 months following the date of original approval and release with annual update required. It is further understood that should this project be submitted for external funding the information presented on the Request for Review form reflects accurately the animal use in the full grant application.

IV. Certification of Review by Student's Advisor (required for all protocols submitted by students)

_____ _____ _____
Signature Date Position

NOTE: The ARC requires one (1) original and three (3) copies in order to process the proposal for full committee review. Protocol categories A or B which qualify for expedited review require 20 copies. Insufficient information may result in delay of the review process. The ARC reserves the right to request additional information.

group of animals. This same careful scrutiny is also applied to any A or B protocol involving relatively large numbers of animals. Category C protocols automatically require full committee review because the procedures potentially involve moderate pain (that will be relieved/minimized), production of a disease or functional deficit or both. Category D protocols involve pain that will not be relieved. These protocols must be reviewed by the full committee and require strong justification that is referenced to the scientific literature.

To achieve a greater consistency of review in both the subcommittee and full committee systems, the UNMC IACUC uses a protocol review guide (6). This guide encourages committee members to sequentially apply the same evaluation criteria and serves to decrease the individual and collective variation in ethical reasoning that leads to IACUC decisions. The protocol review guide is keyed to the protocol review form, and is based on the UNMC Code of Ethics for Animal Use (7). This code, which constitutes the protocol review criteria employed by the IACUC, consists of those ethical principles which govern the use of animals in research, testing or teaching.

The Protocol Review Form

The UNMC IACUC review form (see page 11) includes three sections which solicit the information required by the committee, as mandated by the PHS policy, USDA rules, and our own perception of animal welfare. Sections 1 and 3 are for general application data such as identification of the principal and co-investigators, participating students and technicians, the animal vendor, the species and strain of animal(s), the location of animal housing, anticipated funding, source and status of the grant, and the principal investigator's certification of compliance with PHS policy and USDA rules. Section 2, provides information for fourteen points of review. These fourteen points were selected on the basis of federal requirements as well as the institution's need to maintain documentation that clearly supports the value and humaneness of all research involving animals conducted by our faculty, students, and staff.

Section 2 of the protocol review form logically begins with a consideration of the purpose and potential value of the proposed study. The IACUC is charged by PHS policy with assuring that, when live animals are used in research or biological testing, there is reasonable expectation that such use will contribute to the enhancement of human or animal health, the advancement of knowledge, or the good of society. Therefore, pursuant to this charge, the committee requests information about the scientific objective(s) and potential value of the proposed study. The IACUC, in compliance with the PHS policy, requests a statement that the investigator has considered alternatives to the use of live animals, including the use of non-animal models, and the reasons for rejecting such alternatives. In addition, the investigator is requested to explain why the particular species selected is appropriate for the proposed studies.

Both the PHS policy and USDA Animal Welfare regulations require that the number of animals used in research be minimized consistent with sound scientific and statistical standards. Determining the appropriate number of animals to be used in an experiment

can be complicated, involving statistical, economic, contractual, and welfare issues (8). Indeed, the most common cause for delaying approval of a protocol by the UNMC IACUC has been the inability of the committee to determine the distribution of animals among experimental and control groups (stratification and substratification of design) particularly with respect to block size (N) for a given intervention. The protocol review form we currently use attempts to correct this problem by recommending that investigators submit requests for animals in the form of a table, clearly specifying all experimental and control groups and the number of animals required in each group or subgroup.

The UNMC IACUC asks investigators to provide reasonably detailed descriptions of the procedures to be applied to live animals, including experimental end-points and the duration of the experiment. Because pain is a particularly important consideration, investigators, as mandated by USDA regulations, are required either to state that alternative procedures that cause less pain do not exist or explain why existing alternatives were rejected. Considerations of pain and discomfort also demand information about restraints, pain control during the procedure, estimated post operative pain, and post operative care. With regard to the latter, the IACUC requires specifics about post-operative monitoring, the method for recognizing and monitoring pain, and the circumstances for using of analgesics and antibiotics, including the types, dosages, and routes of administration.

The ultimate disposition of the animals is almost as important as the way in which they are to be used. The committee requests detailed information on the method of euthanasia, as well as the criteria for euthanasia, including criteria for premature euthanasia. When the animals will not be euthanatized at the end of the experiment, the committee is vigilant for additional unrelated survival surgeries which are not permitted. Finally, the IACUC asks investigators to provide their pertinent credentials including knowledge of the species, relevant experience and specific responsibility. The same information is required for technicians and other personnel who will work on the project.

Discussion

The basic ethical premise upon which prior review of animal research is founded is shared responsibility. Other persons, in this case the IACUC members, who are independent of the research should share with the investigator the responsibility for making the ethical decisions regarding the use of animals. In the past, scientists planned and conducted experiments in relative isolation with little pre- or post-experimental accountability for animal welfare. Ethical issues were a matter of individual conscience rather than discussion and debate. While this did not necessarily lead to unethical behavior, it did eventually become a major target of the animal rights movement. A concomitant growing concern of the public, the community of animal researchers, and the federal government resulted in the establishment of IACUCs charged with the ethical review of research which proposes to use animal subjects. The advancement of science and the fulfillment of a moral responsibility to animals now depends on the decisions of investigators and the IACUCs, who seek jointly to establish the appropriate balance between research needs and animal welfare. The IACUC offers the scientific community an opportunity to express its own concern for the welfare of laboratory animals and to refute the often inaccurate and emotional propaganda generated by the more radical antivivisectionists.

The question that each institution and its IACUC must address is how the IACUC can best fulfill its responsibility. A recent survey involving 32 IACUCs, who reviewed four hypothetical protocols, indicated the existence of considerable variation in approval criteria. The committees were uniform in their concerns about justification of animal use, but varied in their approaches to evaluating of this justification (9). Because federal guidelines allow IACUCs considerable autonomy in terms of the design of the protocol review process and because they have failed to provide clear statements of the type and degree of evidence required to justify their standards, it is not surprising that significant variation exists among institutions. Variability may be increased further by local issues such as the presence of animal rights activity. The fundamental role of the IACUC must, however, remain constant. The IACUC has a scientific and social obligation to ensure that meaningful and justifiable research is conducted in accordance with humane standards. This means that the review process should consider the scientific priorities of the investigators, the welfare of experimental animals, and potential benefits to society. Local review must be flexible but it should be based on predetermined published criteria and structured according to the potential levels of pain, discomfort and distress associated with the procedures. In addition, issues related to reducing the number of animals used, alternatives to live animal usage and refinement of techniques should be addressed.

While protocols require equally careful scrutiny, not all protocols necessarily require the same magnitude of review. For example, research involving terminal surgery under general anesthesia or minor procedures such as biopsies and venipunctures, particularly when employing small numbers of animals other than nonhuman primates, do not necessarily require, either ethically or scientifically, a detailed review by all of the members of the IACUC at a convened meeting. Indeed, to require such a review would significantly increase the work- load of the committee which should be focusing its attention on protocols involving large numbers of animals or invasive survival procedures, or protocols which may potentially produce more than minor short-term pain, discomfort and/or distress. Therefore, we contend that a small subcommittee of the IACUC consisting of a veterinarian and one or two knowledgeable and dedicated members should be empowered to review and approve category A and B research protocols subject to final endorsement by all members of the IACUC via a declination to refer the protocol for further review by the full committee. However, any protocol that involves large numbers of animals, a

significantly invasive survival procedure, or pain that is greater than the level and duration of pain attending routine injection should automatically be reviewed by the full IACUC at a regular meeting which promotes a thoughtful confirmation and discussion of all relevant issues. Because the potential value of the research must clearly balance or outweigh the level of pain to which animals are subjected, the IACUC has an ethical obligation to provide both the animal subjects and the investigator with the benefits of its collective wisdom. In other words, as the ethical cost of the research increases, so does the responsibility of the IACUC and the significance of its decisions. Therefore, there is clearly a need to share this responsibility among all committee members.

Regardless of the category into which an experiment fits, the protocol review system must be designed to provide the information necessary for the IACUC to fulfill its legal and ethical obligations. The University of Nebraska Medical Center does not presume to have the ideal review system. Indeed, our protocol review form has undergone six revisions over the years, and it is likely that further revision will be required. However, we do believe that our system is, for the present, adequate and that it addresses the ethical imperatives of animal welfare review as we understand them. As society's understanding of ethics related to animal use grows, our review system and the systems employed by other institutions will undoubtedly change. Perhaps, by a greater sharing of experiences and problems, all IACUCs will be able to increase their effectiveness through achieving an appropriate balance between research needs and fulfillment of our moral obligation to animals.

References

1. **National Institutes of Health.** 1986. PHS Policy on Humane Care and Use of Laboratory Animals. NIH Guide for Grants and Contracts. 14(8): June 25, 1985. OPRR PHS Animal Welfare Policy. Revised September 6, 1986.
2. **United States Department of Agriculture.** 1985. The amended Animal Welfare Act (Health Research Extension Act of 1985, Public Law 99-158).
3. **Federal Register.** 1989. USDA Animal Welfare Regulations. 9 CFR parts 1 and 2. Fed. Regist. 54(168/Tuesday, August 31, 1989).
4. **Prentice, E. D., and R. K. Zetterman.** 1983. Evolution, Structure and Function of the Institutional Review Board. Nebraska Medical Journal. **68**(8):293-295.
5. **Orlans, F. B.** 1987. Research Protocol Review for Animal Welfare. Invest. Radiol. **22**:253-258.
6. **Prentice, E. D., D. A. Crouse, and R. W. Rings.** 1990. Approaches to Increasing the Ethical Consistency of Prior Review of Animal Research. Invest. Radiol. **25**:271-274.
7. **Prentice, E. D., I. H. Zucker, and A. Jameton.** 1986. Ethics of Animal Welfare in Research: The Institution's Attempt to Achieve Appropriate Social Balance. The Physiologists. **29**(2):April.
8. **Mann, M. D., D. A. Crouse, and E. D. Prentice.** 1991. Appropriate Animal Numbers in Biomedical Research in Light of Animal Welfare Considerations. Lab. Animal Sci. **41**(1):9-17.
9. **Dresser, R.S.** 1989. Developing Standards in Animal Research Review. JAVMA. **194**:1184-1191.