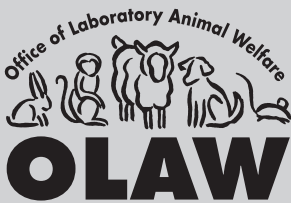




# Institutional Animal Care and Use Committee Guidebook

2nd Edition  
2002



2nd Edition  
2002

# Institutional Animal Care and Use Committee Guidebook

*This Guidebook is provided for informational purposes only.  
It neither establishes nor reflects a change in PHS Policy on  
Humane Care and Use of Laboratory Animals.*

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# Foreword

The original *OPRR/ARENA IACUC Guidebook* was published in 1992 and has served as a useful resource to the animal research community. This revised edition, the *ARENA/OLAW IACUC Guidebook*, continues to support the fundamental principle on which the animal care and use program is based: self-regulation with oversight. It clearly demonstrates the increased role of the Institutional Animal Care and Use Committee (IACUC) in ensuring the ethical and sensitive care and use of animals in research, teaching and testing.

This *Guidebook* is the product of an ARENA-established editorial board of knowledgeable individuals who have IACUC experience and are familiar with the evolution of IACUC issues and relevant documents published during the past decade. Sections from the original document have been updated, and new sections added to incorporate state of the art knowledge regarding the functioning of IACUCs and institutional animal care and use programs. This *Guidebook* does not create new or different interpretations of the *PHS Policy on Humane Care and Use of Laboratory Animals*, legislation, or USDA animal welfare regulations.

The most current knowledge and understandings were sought through distinguished authors with experience and expertise. New references, resources and contemporary scientific and “road tested” guidance have been incorporated. For example, the emphasis of the 1996 edition of the *Guide for the Care and Use of Laboratory Animals* on performance goals as opposed to engineering approaches is a theme that resonates throughout. Other new reports, such as the 1997 *Occupational Health and Safety in the Care and Use of Research Animals* and the 1998 *The Psychological Well-Being of Nonhuman Primates*, both published by the National Research Council have offered new insights and approaches that are reflected herein. The AVMA Panel on Euthanasia also published new guidelines in 2001.

Additional knowledge and changing trends in research have mandated broader and deeper coverage of topics in this *Guidebook*. New topic areas include training IACUC members, disaster planning, managing breeding colonies, and the use of transgenic animals. New federal requirements and directives



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# Abbreviations and Acronyms

## Abbreviations

**Guide** ILAR *Guide for the Care and Use of Laboratory Animals*  
**PHS Policy** *PHS Policy on Humane Care and Use of Laboratory Animals*

## Acronyms

### A

<b>AAALAC</b>	Association for Assessment and Accreditation of Laboratory Animal Care International
<b>AALAS</b>	American Association for Laboratory Animal Science
<b>AC</b>	Animal Care, APHIS, USDA
<b>ACLAM</b>	American College of Laboratory Animal Medicine
<b>AGRICOLA</b>	National Agricultural Library's Agricultural OnLine Access (USDA)
<b>APHIS</b>	Animal and Plant Health Inspection Service (USDA)
<b>ARENA</b>	Applied Research Ethics National Association
<b>ASLAP</b>	American Society of Laboratory Animal Practitioners
<b>AV</b>	Attending Veterinarian
<b>AVMA</b>	American Veterinary Medical Association
<b>AWA</b>	<a href="#">Animal Welfare Act</a>
<b>AWIC</b>	Animal Welfare Information Center
<b>AWRs</b>	<a href="#">Animal Welfare Regulations (USDA)</a>



**FOIA** Freedom of Information Act

**FR** *Federal Register*

## **G**

**GLP** Good Laboratory Practices

**GPO** Government Printing Office

## **H**

**HEPA** High-Efficiency Particulate Air Filter

**HREA** Health Research Extension Act, Public Law 99-158

**HVAC** Heating, Ventilation and Air Conditioning

## **I**

**IACUC** Institutional Animal Care and Use Committee

**IATA** International Air Transport Association

**IBC** Institutional Biosafety Committee

**ICLAS** International Council for Laboratory Animal Science

**IFA** Freund's Incomplete Adjuvant

**iiFAR** Incurably Ill for Animal Research

**ILAR** Institute for Laboratory Animal Research

**IO** Institutional Official

**IOM** Institute of Medicine

**IRAC** Interagency Research Animal Committee



**OMB** Office of Management and Budget

**OSHA** Occupational Safety and Health Administration

**OSTP** Office of Science and Technology Policy

***P***

**PHS** Public Health Service

**PRIM&R** Public Responsibility in Medicine and Research

***R***

**RSC** Radiation Safety Committee

***S***

**SCAW** Scientists Center for Animal Welfare

***U***

**USDA** U.S. Department of Agriculture

**USFWS** U.S. Fish and Wildlife Service, Department of Interior

***V***

**VA** Department of Veterans Affairs

***W***

**WHO** World Health Organization

**WVA** World Veterinary Association

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# **A. The IACUC**

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## **A.1. Timeline, Background and History**

### **Timeline**

- 1950 Formal establishment of Animal Care Panel.
- 1963 First edition of the *Guide for the Care and Use of Laboratory Animals (Guide)* developed by the Animal Care Panel.
- 1965 Incorporation of the American Association for the Accreditation of Laboratory Animal Care (AAALAC).
- 1966 Congress passed the Laboratory Animal Welfare Act (PL 89-544) and the USDA was named the responsible agency.
- 1967 Animal Care Panel changed its name to the American Association for Laboratory Animal Science (AALAS).
- 1971 NIH Policy on Humane Care and Use of Laboratory Animals for PHS Supported Institutions.
- 1971 USDA promulgated standards known as Subpart F, Stolen Animals (AWA).
- 1973 First Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals.
- 1974 Public Responsibility in Medicine and Research (PRIM&R) established.
- 1979 PHS Policy required each animal-using grantee institution to have a PHS Assurance and a committee to maintain oversight of its animal care program.
- 1979 USDA promulgated standards known as Subpart E, Identification of Animals (AWA).
- 1982 First PRIM&R Animal Care and Use meeting.
- 1985 U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training promulgated.
- 1985 Health Research Extension Act (P.L.99-158) passed by Congress.



## Background and History

Prior to the middle of the 20th century the responsibility for animals used in research in the United States was placed directly in the hands of the researchers and the quality of animal care and animal welfare varied tremendously among research institutions. Even within the same school or institution, research laboratories had inconsistent animal care policies and standards of care.

In 1961, a group of veterinarians working for research institutions in the Chicago area formed the Animal Care Panel (ACP). The ACP appointed a committee charged with establishing animal care and use guidelines for research facilities. Their product was the publication of the first edition (1963) of the *Guide for the Care and Use of Laboratory Animals* (referred to in this document as the *Guide*). Subsequent editions of this publication were supported by the NIH and developed under the auspices of the Institute of Laboratory Animal Resources (ILAR), which was subsequently renamed the Institute for Laboratory Animal Research. The National Academy Press, under the auspices of the National Research Council, published the most recent (seventh) edition in 1996. This single document serves as the primary source of laboratory animal care and use standards and guidelines in the United States. The 1996 edition has been translated and published in six languages, and over 400,000 copies have been distributed throughout the world.

In 1963, the ACP saw a need to evaluate the standards of animal care and use practiced in research institutions based on the *Guide*, and appointed an Animal Accreditation Committee. This Committee soon determined that it should function independently of the ACP, and in 1965 incorporated in the state of Illinois as the American Association for the Accreditation of Laboratory Animal Care. This independent accrediting agency changed its name in 1996 to the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

Prior to 1966, no U.S. federal law addressed laboratory animal welfare. Local humane societies actively promoted responsible treatment of pets and farm animals. Concurrently, the scientific community was improving the quality of animal care and well-being in the research laboratory. During this time the increasing need for dogs and cats in research was partially fulfilled by animal dealers who obtained these animals in various ways and sold them to research laboratories. A series of articles and news



to inspect the institution's animal facilities at least once a year and report its findings and recommendations to responsible institutional officials. Records of activities and recommendations were required to be available for inspection by NIH representatives.

The first PHS policy regarding animal care and use replaced the NIH policy on July 1, 1973 and continued to accept AAALAC accreditation in lieu of an institutional committee. The January 1, 1979 revision of the PHS policy required each animal-using grantee institution to have "a committee to maintain oversight of its animal care program" and expanded the definition of animal to include all vertebrates. The revised policy also required an institution to submit an Assurance statement to the Office for Protection from Research Risks (OPRR), now the Office of Laboratory Animal Welfare (OLAW), that it is committed to follow the *Guide*, the Principles and the PHS policy requirements, before receiving PHS support for studies in which animals or animal facilities were used.

Institutions were required to include in their Assurance a list of committee members with their position titles and credentials. Committees were composed of at least five members including at least one veterinarian. The members had to be knowledgeable regarding the care and use of animals used in research.

The 1979 PHS policy continued to accept AAALAC accreditation as a means of demonstrating conformance with the *Guide*, but an alternative was annual review of the animal facilities and procedures by the institution's IACUC. Institutions were required to report to NIH (OPRR) any nonconformance with the *Guide* or problems encountered in implementing the PHS policy, and submit annual reports indicating progress toward full conformance. Review of individual proposals or projects by the IACUC was encouraged but not required.

The most recent revision, officially the *PHS Policy on Humane Care and Use of Laboratory Animals* (referred to in this document as the *PHS Policy*), was promulgated in 1986 and reprinted in 1996 and 2000. It further defined and outlined requirements of an animal care and use program. This revised *PHS Policy* includes provisions of the Health Research Extension Act of 1985, enacted on November 20, 1985 as Public Law 99-158. The 1986 *PHS Policy* applies to both extramural and intramural PHS research and requires the Institutional Animal Care and Use Committee (IACUC) members to be appointed by the Chief Executive Officer of the institution. The



rights groups escalated and became more vocal in the early 1980s. This activity peaked in a series of illegal break-ins and vandalism and was brought to the forefront of public opinion soon after two incidents involving alleged “animal cruelty” and “insensitivity” in two well-known research institutions. This climate raised public concern and visibility of animals in research and served as a catalyst for amendments and clarifications of guidelines and regulations providing for animal welfare.

New USDA regulations based on the 1985 amendment to the AWA became effective between October 1989 and August 1991. These regulations require each registered research institution to appoint an IACUC of not less than three members, including a veterinarian, which “serves as the agent of the research facility that assures that the facility is in full compliance with the Act.” The regulations also require a member not affiliated with the institution representing community interests in the proper care and treatment of animals. These USDA Animal Welfare Regulations (AWRs) and the *PHS Policy* contain many common requirements.

The Scientists Center for Animal Welfare (SCAW) was instrumental in providing early guidance to institutions on IACUC functions and organization through regional conferences and workshops, culminating in a special 1987 American Association for Laboratory Animal Science (AALAS) publication entitled, “Effective Animal Care and Use Committees.” Since 1983, training and guidance of this type has also been provided through annual animal care and use conferences sponsored by Public Responsibility in Medicine and Research (PRIM&R) and the Applied Research Ethics National Association (ARENA), regional workshops supported by OLAW, and numerous similar activities. The first *Institutional Animal Care and Use Committee Guidebook* was written by a committee of experts under the auspices of ARENA and published by NIH in 1992. The present edition, published in 2002, is the first revision.

During the 1990s there was an evolution in the ways that IACUCs fulfilled their mandate. This was in part due to increased experience implementing the *PHS Policy* and AWRs, but may also be attributed to new reports, such as the 1996 *Guide* which emphasizes performance goals as opposed to engineering standards, and the 1997 ILAR report, *Occupational Health and Safety in the Care and Use of Research Animals*, that shifted the focus of occupational health programs to risk based systems. Other factors contributing to this evolution came from the research community, such as the development of transgenic animals and *in vitro* alternatives to the



## **A.2. Authority, Composition and Functions**

Each institution that receives PHS support for activities involving vertebrate animals or is subject to the authority of the Animal Welfare Act (AWA) must operate an animal care and use program with clear lines of authority and responsibility. The program must include:

- a properly constituted and functioning Institutional Animal Care and Use Committee (IACUC);
- procedures for self monitoring;
- an adequate veterinary care program;
- an occupational health and safety program (not required under the AWA);
- a personnel training program;
- an environment, housing and management program for animals; and
- appropriately maintained facilities for housing and support.

PHS requires an institutional Animal Welfare Assurance that provides details on the institutional program in order to award funds; USDA requires registration of facilities. [Section E.1.](#) and [E.1. Table B](#) include additional detail concerning PHS assurances and USDA registration.

### **Authority**

IACUCs derive their authority from the law. They are mandated by the Health Research Extension Act (HREA) of 1985 and the AWA. The laws require the Chief Executive Officer (CEO) of an organization to appoint the IACUC, whose responsibilities are delineated in the law and federal policy and regulations. Office of Laboratory Animal Welfare (OLAW) considers the CEO to be the highest operating official of the organization. The CEO may delegate authority to appoint the IACUC if the delegation is specific and in writing.

Once appointed, IACUCs report to a senior administrator known as the Institutional Official (IO). The IO must have administrative and operational authority to commit institutional resources to ensure compliance with the *PHS Policy* and other requirements. The CEO and IO may be the same



as such. The veterinarian with program responsibility must have training or experience in laboratory animal science and medicine or in the care of the species being used.

**Chair:** A knowledgeable and effective leader is crucial to an effective IACUC. This individual needs the full support of the IO. A chair with sufficient stature (e.g., seniority or tenure) can perform the functions of this position without jeopardy to his/her career. In the case of a large program of animal care and use a co-chair may be desirable.

**Nonaffiliated member:** The nonaffiliated member is intended to represent general community interests. An informed nonaffiliated member can bring significant value to the committee by bringing a non-institutional perspective to the research endeavor. This member has equal status to every other committee member and should be provided the opportunity to participate in all aspects of IACUC functions.

While in the majority of instances effective nonaffiliated members may be willing to serve without reimbursement, in other instances remuneration for expenses or compensation for time may allow for participation by effective individuals that would not otherwise be possible. OLAW and USDA maintain that nominal compensation is permissible without jeopardizing a member's non-affiliated status, if it is only in conjunction with service on the IACUC and if the amount of compensation is not so substantial that it could be considered to influence voting on the IACUC.

**Scientist and nonscientist:** *PHS Policy* requires that the IACUC include a practicing scientist experienced in research involving animals, and a member whose primary concerns are in a nonscientific area. Examples of the latter include, but are not limited to, ethicist, lawyer, member of the clergy, and librarian.

Institutions should consider persons with expertise in the disciplines involved in institutional research and teaching programs for service on their IACUCs. In addition to the required categories of membership, it is suggested that individuals with expertise in specific areas pertinent to protocol review and program oversight be considered (e.g., statisticians, occupational health experts, information resource specialists, animal health technicians, and scientific research staff).

There is no requirement that any particular member or category of members be present at all IACUC meetings. However, an institution must have a properly constituted IACUC in order for the IACUC to conduct valid



**Alternate members** may be appointed to the IACUC as long as they are appointed by the CEO or other official with authority to appoint members, and there is a specific one-to-one designation of IACUC members and alternates. An IACUC member and his/her alternate may not count toward a quorum at the same time or act in an official member capacity at the same time. Alternates should receive training similar or identical to the training provided to regular IACUC members.

### **Conflict of Interest**

Both the AWRs and *PHS Policy* state that no IACUC member “may participate in the IACUC review or approval of an activity in which that member has a conflicting interest, (e.g., is personally involved in the activity) except to provide information requested by the IACUC.”

If the investigator submitting a protocol believes that an IACUC member has a potential conflict, the investigator may request that the member be excluded. When a member has a conflict of interest, the member should notify the IACUC Chair and may not participate in the IACUC review or approval except to provide information. Members who have a conflict of interest may not be counted toward a quorum and may not vote.

Other possible examples of conflict of interest include cases where:

- a member is involved in a potentially competing research program,
- access to funding or intellectual information may provide an unfair competitive advantage, or
- a member’s personal biases may interfere with his or her impartial judgment.

### **Quorum Requirements**

Certain official IACUC actions require a quorum: full committee review of a research project (Policy IV.C.2. and AWR §2.31(d)(2)) and suspension of an activity (Policy IV.C.6. and AWR §2.31(d)(6)). “Quorum” is defined as a majority (>50%) of the voting members of the IACUC. Therefore, a protocol is approved only if a quorum is present, and if more than 50% of the quorum votes in favor. *PHS Policy* and AWRs require that in order



**A.2. Table B. Federally Mandated Functions of the IACUC**

PHS PHS Policy. IV.B.1-8	USDA 9 CFR. 2.31 (c) (1) – (8) and 2.31(d) (5) (6) & (7)
<p>1. Review, at least once every six months, the research facility's program for the humane care and use of animals, using the <i>Guide</i> as a basis for evaluation.</p>	<p>1. Review, at least once every six months, the research facility's program for humane care and use of animals, using title 9, chapter 1, subchapter A—Animal Welfare, as a basis for evaluation.</p>
<p>2. Inspect, at least once every six months, all of the institution's animal facilities (including satellite facilities) using the <i>Guide</i> as a basis for evaluation. Satellite holding facilities (a facility outside of a core facility or centrally designated area in which animals are housed for more than 24 hours) and areas in which surgical manipulations are performed must always be included.</p>	<p>2. Inspect, at least once every six months, all of the research facility's animal facilities, including animal study areas, using title 9, chapter 1, subchapter A—Animal Welfare as a basis for evaluation. Areas where animals are housed for more than 12 hours are defined as "study areas."</p>
<p>3. Prepare reports of the IACUC evaluations and submit the reports to the IO. The reports must contain a description of the nature and extent of adherence to the <i>Guide</i> and <i>PHS Policy</i> and identify specifically any departures from the provisions of the <i>Guide</i> and <i>PHS Policy</i> and state reasons for each departure. The IACUC may determine the best means of conducting an evaluation of its program and facilities. The IACUC may invite <i>ad hoc</i> consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report. Reports must distinguish significant deficiencies from minor deficiencies and must contain a reasonable and specific plan and schedule for correcting each deficiency. A significant deficiency is one that is or may be a threat to the health and safety of the animals. Reports must be made available to OLAW upon request.</p>	<p>3. Prepare reports of its evaluations (using the title 9, chapter 1, A – AWR) and submit to the IO. The IACUC may determine the best means of conducting evaluations of the research facility's programs and facilities, provided that no member wishing to participate in any evaluation is excluded. Reports must distinguish significant deficiencies from minor deficiencies and must contain a reasonable and specific plan and schedule with dates for correcting each deficiency. A significant deficiency is one that is or may be a threat to the health and safety of the animals. A significant deficiency remaining uncorrected beyond the scheduled correction date shall be reported in writing within 15 business days by the IACUC, through the IO, to APHIS and any federal agency funding that activity. Reports must be made available to APHIS and to officials of federal funding agencies for inspection and copying upon request.</p>
<p>4. Review concerns involving the care and use of animals at the institution.</p>	<p>4. Review, and if warranted, investigate concerns involving the care and use of animals resulting from public complaints and from reports of noncompliance received from laboratory or research facility personnel or employees.</p>

*continued on page 18*

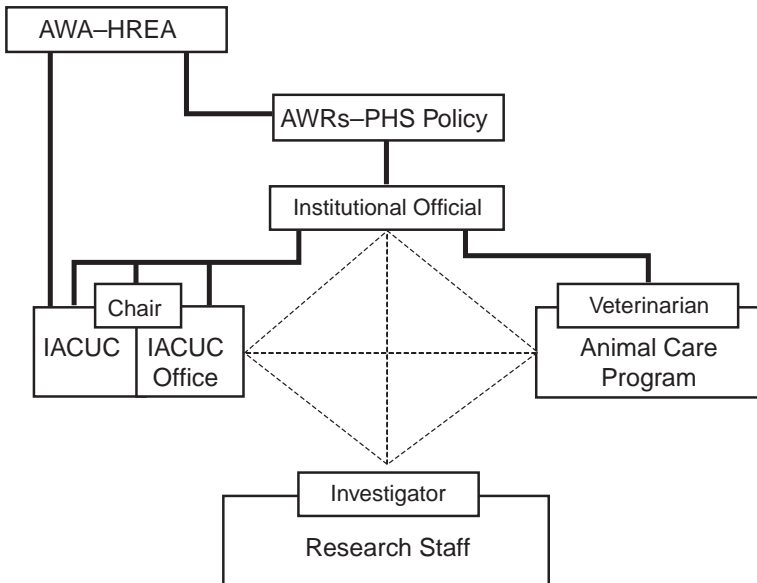


## A.3. Operation and Administration

### Institutional Responsibility for Animal Welfare

Assuring laboratory animal welfare necessitates a partnership among the Institutional Official (IO), the IACUC, the veterinarian and the investigators. Ultimately, accountability for assuring humane care and use of animals resides with the institution, but this may only be achieved when all of the players, i.e., the investigators and their research staff, the veterinary staff, animal caretakers and technicians, and the IACUC, contribute to a shared goal.

Each institution should provide a framework with appropriate resources for an animal care and use program that is managed in accordance with the *PHS Policy*, the *Guide*, and the Animal Welfare Regulations (AWRs). Organizations that function effectively have simple, clear and direct lines of responsibility and corresponding authority.



**Components of an animal care and use program.** Heavy lines represent the mandate from the Animal Welfare Act and Health Research Extension Act that the Secretaries of Agriculture and Health and Human Services develop guidelines for the use of animals in research and for IACUCs, and require established lines of authority from the IO to the IACUC, IACUC staff, and veterinarian. Dotted lines represent the need for cooperation and communication among components.



## Role and Responsibilities of the IACUC Staff

The nature of the institution and the volume of animal-based research determine the staffing requirements of an IACUC and the animal care program. Institutions with a high volume of proposals involving animals may require full time IACUC staff. A professional staff with expertise in animal welfare laws, regulations and policies is especially important to provide stability and continuity to animal care and use programs where IACUC chairs and members serve on a rotating basis.

The role of the IACUC staff is to provide administrative support to the IACUC and the IO. It is important however, that neither the IO nor the IACUC Chair over-invest authority or responsibility in the IACUC staff.

The IACUC staff often serve as the gatekeepers of information and communications for the IO, the IACUC Chair and members, the veterinarian, the animal resource program, the investigators, and other offices within the institution such as public relations and sponsored research. It is important that training and continuing education be provided to program staff so they are knowledgeable of current animal care and use policies and regulations and aware of proposed changes. OLAW workshops, ARENA and PRIM&R annual meetings, ARENA IACUC 101 Training, and SCAW meetings, are examples of useful training and educational opportunities.

IACUC staff responsibilities range from clerical and administrative to professional, depending on the size and complexity of the program.

Some examples of **clerical tasks** are:

- data entry;
- screening protocols for completeness;
- preparing agendas and distributing protocols and other materials to IACUC members;
- sending out reminders of protocol expirations and approval letters;
- maintaining records of protocols and minutes of the meetings, policies and procedures, program reviews and facility inspection reports; and
- coordinating and scheduling the IACUC's meetings, facilities inspections and laboratory site visits.



reflected in the grant application, then the PHS funding component must be notified in the follow-up certification of IACUC approval.

Institutions are required to provide PHS with the date of IACUC approval. There is no provision for providing a contingent approval date; the date provided must signify full approval by the IACUC. If an institution has a PHS Assurance, then in most cases the PHS allows a 60-day grace period following the receipt deadline date during which the investigator may secure IACUC approval; otherwise, the application cannot be peer reviewed. If the IACUC review occurs subsequent to the grant submission, then a letter verifying IACUC approval, and stating any modifications required by the IACUC, must be submitted to the funding agency. This grace period is non-existent for some non-federally funded projects and investigators are required to submit evidence of IACUC approval coincident with the grant or contract submission.

If an institution does not have a PHS Assurance, the signature of the official signing the grant application for the organization constitutes a declaration that the institution will submit an Assurance and verification of IACUC approval upon request by OLAW.

## **Responsibility for Collaborations and Subcontracted Research**

Collaborations between institutions can sometimes create ambiguity regarding responsibility for animal welfare. In cases where an individual investigator has appointments at several institutions, or where collaborations occur between institutions, it is advisable to have a formal written agreement, contract or memorandum of understanding between the institutions. This document should originate from the primary collaborative institution (i.e., the institution primarily responsible for directing and/or funding the research) and be signed by the secondary institution.

When an institution receiving PHS funds contracts with a commercial vendor using animals to produce a product, there may need to be IACUC involvement. If a company produces standard antibodies for general sale, that company is not required to file an Assurance with OLAW. However, if a supplier or contractor produces antibodies in animals using an antigen provided by or at the request of an investigator, the antibodies are considered “custom” and the vendor must have an Assurance on file. The vendor Assurance must be identified on the PHS grant application, and the awardee institution is responsible for verifying that the work is done at an Assured institution.



- Another possible collaboration, that may or may not involve sub-contracting, occurs if an awardee institution does not have an animal program or facility and is therefore not assured, but the investigator will use the facilities of an assured institution. Under these circumstances OLAW requires an “Interinstitutional Agreement Assurance” whereby both IOs agree that the project will be conducted in accordance with the assured institution’s Assurance and the investigator will abide by the determinations of the assured institution’s IACUC. The effect of such an agreement is to extend the IACUC’s oversight to include the particular project, and to meet the *PHS Policy* requirement that the grantee institution be assured.

### **References**

Garnett, N.L., and W.R. DeHaven. Commentary: Protocol Review—Who’s to Blame? *Lab Animal* 28(7), 1999.

*NIH Guide for Grants and Contracts*, Notice OD-01-017, February 12, 2001.

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## A.4. Training for Members

For the IACUC to discharge its responsibilities a program of education and training is essential. A well-defined and implemented program, while primarily directed to the IACUC member, would also be of value to researchers, administrators and others with responsibilities associated with research involving animals.

It is the responsibility of the institution to provide suitable orientation, appropriate materials, adequate resources and training to enable IACUC members to carry out their duties consistent with the *Guide*, the *PHS Policy* and the Animal Welfare Regulations (AWRs). It is important to provide the tools necessary to assist members in understanding and evaluating issues that are brought before them. Appropriate training depends on the size, scope and needs of the research facility, but must incorporate the federal mandates of the IACUC.

Local institutional policies and procedures need to be a part of the training and education program. Frequently, new members find it confusing to understand the differences between the federal policies and requirements and institutional policies and procedures. It is useful to provide an institutional policy manual as well as the Web sites for pertinent federal rules and regulations.

Although the plan for training and education can take many different forms, a recommended syllabus with suggested topics for the orientation module and the continuing education module follows.

In addition, ARENA sponsors a basic one-day training course for new IACUC members and persons with IACUC responsibilities – ARENA IACUC 101 – and ARENA IACUC 101 “On the Road.” To learn more about this training program, contact the ARENA office at (617) 423-4112 or OLAW at (301) 496-7163, or visit the ARENA or OLAW Web sites (see [Appendix A](#)).



- 2.3.2 Protocol changes (amendments)
- 2.4 Records
- 2.5 Semiannual reviews
  - 2.5.1 Animal care and use program
  - 2.5.2 Institutional animal facilities
- 2.6. Handling animal welfare concerns
- 2.7. Roles, responsibilities, relationships
  - 2.7.1. IACUC
  - 2.7.2. IACUC Program office
  - 2.7.3. Veterinarian
  - 2.7.4. Animal Care Program (e.g., Department of Comparative Medicine or Laboratory Animal Resources)
  - 2.7.5. Institutional Official (IO)
  - 2.7.6. Office of Laboratory Animal Welfare (OLAW), NIH
  - 2.7.7. Animal and Plant Health Inspection Service (APHIS), USDA
  - 2.7.8. Project sponsor/grantor
  - 2.7.9. Community

### **Suggested Resource Materials**

- *Public Health Service Policy on Humane Care and Use of Laboratory Animals*. NIH. Reprinted 2000.
- Health Research Extension Act, P.L.99-158.
- Animal Welfare Act – P.L. 89-544 as amended by P.L. 94-279, P.L. 99-198, P.L. 91-579 and P.L. 101-624.
- Animal Welfare Regulations. 9 CFR.
- *Institutional Administrator's Guide for Animal Care and Use*. NIH. 1988.
- *Guide for the Care and Use of Laboratory Animals*. NRC. 1996.
- *ARENA/OLAW Institutional Animal Care and Use Committee Guidebook*. 2002.
- Institutional IACUC Policies and Procedures Manual.

For additional suggestions see the Core Module in the National Research Council's *Education and Training in the Care and Use of Laboratory Animals – A Guide for Developing Institutional Programs*, pages 11 through 15.



## A.5. Legal Concerns

The functions and activities of IACUCs are based on two federal laws: the Health Research Extension Act of 1985 (P.L.99-158) (HREA) and the 1985 amendments to the Animal Welfare Act (AWA), the Improved Standards for Laboratory Animals Act of 1985 (P.L. 99-198). In addition, other federal rules may pertain to IACUCs, such as the Occupational Safety and Health Administration (OSHA), Food and Drug Administration (FDA), and Good Laboratory Practice (GLP) regulations, and the Endangered Species Act (ESA). Committee members need to be aware of the legal obligations of their institutions, the responsibilities of the IACUC in relation to these institutional commitments, and the regulatory requirements for which they may be personally accountable.

Many states have statutes and regulations in place relevant to laboratory animals as well. Institutional Officials (IOs) and IACUC administrators should ensure that procedures are in place to enable IACUCs to be cognizant of and compliant with state and local laws and regulations that may affect their institution's animal care and use program. A useful reference is the National Association for Biomedical Research (NABR) publication, *State Laws Concerning the Use of Animals in Research*.

Institutions are responsible for informing IACUC members of their responsibilities, providing training relative to their role on the IACUC, and ensuring that members have the information necessary to fulfill their duties as IACUC members:

- IACUC members should be provided with documents such as the PHS Assurance with the Office of Laboratory Animal Welfare (OLAW), NIH, the *PHS Policy*, the *Guide* and the Animal Welfare Regulations (AWRs). Committee members should be aware of their institutional registration with the U.S. Department of Agriculture (USDA) and reports of inspections and other interactions with Animal and Plant Health Inspection Service (APHIS).
- IACUC members should be free to request through the IACUC Chair or IO, guidance from the institution's legal counsel with regard to Committee actions.
- IACUC members should be provided with information regarding their obligation to treat material as privileged or confidential, especially prior



Information about federally conducted or supported research projects, PHS Assurance documents, USDA annual reports filed by research facilities, and inspection reports of USDA, Environmental Protection Agency (EPA) and FDA, are generally available to the public under FOIA.

Many states have public records laws and/or open meetings acts, known as “sunshine” laws, which may permit public access to information reviewed and generated by the IACUC, and public attendance at IACUC meetings. However, even in some “sunshine” law states, the IACUC, because it serves in an advisory capacity to the IO, may hold closed sessions. IACUC members need to be aware of specific state laws regarding these issues and should always seek legal counsel if necessary to ensure compliance with applicable laws.

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## **B. Oversight of the Animal Care and Use Program**

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## **B.1. Program and Facility Review**

The *PHS Policy* and Animal Welfare Regulations (AWRs) stipulate that the IACUC must review the program for humane care and use of animals at least once every six months, using the *Guide* as the basis for evaluation for the *PHS Policy* and title 9, chapter I, subchapter A-Animal Welfare for the U.S. Department of Agriculture (USDA). Federal requirements also state that the IACUC must inspect all institutional animal facilities at least once every six months.

### **Benefits of the Reviews**

- Reviews provide an ongoing mechanism for ensuring that the institution maintains compliance with applicable animal care and use policies, guidelines and laws.
- Reviews serve as an opportunity for constructive interaction and education for the animal care personnel, research staff and IACUC members.
- Reviews can help an institution prepare for subsequent visits by outside evaluators, such as USDA inspectors, Office of Laboratory Animal Welfare (OLAW) staff and Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) site visitors.

A summary of recurring IACUC issues related to semiannual program review and facility inspection identified by AAALAC during site visits is provided in Appendix C.

### **Resources**

OLAW has developed a sample format for the program review and facility inspection that may be modified to meet the institution's needs (see the [OLAW Web site](#)). The Table of Contents of the *Guide* or an institution's AAALAC Program Description can also serve as an outline for the semi-annual evaluation.



are conducted may be evaluated by other means such as random inspections. However, the institution, through its IACUC, is still responsible for all animal-related activities regardless of where animals are maintained or the duration of the housing. The IACUC must have reasonable access to these areas for the purpose of verifying that activities involving animals are being conducted in accordance with the proposal approved by the IACUC.

## **Staffing and Scheduling the Facility Inspections**

The IACUC must conduct inspections of facilities at least once every six months. This may be accomplished by assigning specific facilities to sub-committees, which must consist of at least two IACUC members (AWRs). No IACUC member should be excluded should she or he wish to participate in an inspection. *Ad hoc* consultants may be used although the IACUC remains responsible for the evaluations and reports. The inspection team should have a working knowledge of the *Guide* and AWRs in order to fully evaluate the facilities that are being inspected. [Section B.2.](#) of this Guidebook also provides general guidance in this regard.

## **Categories to be Inspected**

It is helpful for the inspection team to use a list of categories such as:

- sanitation,
- food and water provisions,
- animal identification,
- waste disposal,
- animal health records,
- controlled and/or expired drugs,
- environmental control,-
- occupational health and safety concerns,-
- staff training,
- knowledge of applicable rules and regulations, and
- security.



## Use of AAALAC Activities as Program Evaluation

Provisions permitting use of *ad hoc* consultants may be invoked by IACUCs to make use of either of the two AAALAC assessment programs (Program Status Evaluation or Accreditation), or pre-assessment preparation activities, to meet the requirements for an IACUC semiannual program evaluation and subsequent report. In order to utilize one of these AAALAC related activities as a semiannual evaluation, the IACUC must ensure that the report complies with IV.B.3. of the *PHS Policy*, and officially endorse the report and submit it to the IO. If an institution is covered by the AWRs, the report must comply with §2.31(c) of the AWRs, at least two IACUC members must participate, no member wishing to participate may be excluded, and the report must be signed by a majority of the IACUC members and include any minority views.

## Documentation

A written report of the semiannual program review and facility inspection must be prepared. The AWRs require the report to be signed by a majority of the IACUC. The report must describe the institution's adherence to the AWRs, the *PHS Policy*, and the *Guide*, and identify specifically any deviations from these documents.

Any deficiencies identified in these reviews must be designated by the IACUC as minor or significant. A significant deficiency is defined as a situation that is or may be a threat to animal health or safety. The IACUC, through the IO, must promptly report to OLAW any serious or continuing noncompliance with the *PHS Policy* or any serious deviation from the provisions of the *Guide*. For both categories of deficiencies, a reasonable and specific plan and schedule with dates for correction must be included in the final report. All individuals to be involved in the corrections should be consulted to ensure that the plan is realistic. If the institution is unable to meet the plan, the IACUC, through the IO, must inform Animal and Plant Health Inspection Service (APHIS) officials within fifteen business days of the lapsed deadline (AWRs). If the activity is federally funded, the relevant funding agency also must be informed.



## **B.2. Animal Environment, Housing and Management**

This section provides an overview of the IACUC's role regarding animal environment, housing and management. The *Guide* provides recommendations that are written in general terms and require the application of sound professional judgment (i.e., current best practices). The use of performance standards, or an outcome approach, will direct decisions to optimizing animal well-being while providing a refined animal model for the researcher. Variances from *Guide* recommendations in animal care and husbandry should be based on clear scientific justification, or rationale for an alternative approach to accomplish a performance based *Guide* standard, and must be approved by the IACUC.

### **B.2.a. General**

The *Guide* states:

Proper housing and management of animal facilities are essential to animal well-being, to the quality of research data and teaching or testing programs in which animals are used, and to the health and safety of personnel. A good management program provides the environment, housing, and care that permit animals to grow, mature, reproduce, and maintain good health; provides for their well-being; and minimizes variations that can affect research results. Specific operating practices depend on many factors that are peculiar to individual institutions and situations. Well-trained and motivated personnel can often ensure high quality animal care, even in institutions with less than optimal physical plants or equipment.

Animals should be housed in a manner that facilitates the expression of species-typical behavior and minimizes stress-induced behaviors. For social species, housing systems should be designed to accommodate pair or group housing of animals. The *Guide* places responsibility with the IACUC for the review and approval of housing systems; it further recommends follow-up objective evaluations to ensure the housing system is appropriate for the health and well-being of the species and consistent with research objectives.



The range of daily temperature fluctuations should be kept to a minimum (e.g.,  $\pm 2^\circ$  F) to avoid large demands on the animals' metabolic and behavioral processes. Relative humidity should also be controlled (e.g., 30% to 70%). In general, an air exchange rate of 10 to 15 changes per hour is considered an acceptable standard.

Light intensity, duration of exposure, wavelength of light, light history of the animal, pigmentation of the animal and other factors should be considered when establishing an illumination level in the animal room.

Because sound exposure can have variable effects on animals, noise generators (e.g., human activities, noisy animals, equipment) should be minimized in animal areas. Environments should be designed to accommodate animals that make noise, rather than resorting to methods of reducing the noise made by animals.

A review of an animal care and use program should include consideration of environmental standards adopted for the facilities with adequate justification for deviations, which are reviewed and approved by the IACUC. While environmental control in outdoor facilities is much less stringent, acceptable ranges in temperature for several species are specified in the AWRs. Reliable methods for monitoring environmental control systems should be in place, including an after-hours monitoring and response program. Back-up heating, ventilation, air conditioning, and lighting systems are highly desirable.

### **B.2.c. Husbandry**

#### ***Animal Identification***

It is imperative that research animals be adequately and appropriately identified and that records pertaining to individuals or groups of animals be maintained. A wide range of acceptable identification methods can be employed, including:

- cage cards,
- subcutaneous transponders,
- ear notches and tags,
- collars,
- colored stains, and
- individual animal tattoos.



Small quantities of food may be kept in animal rooms if stored in tightly covered, leak- and vermin-proof containers; these should not be moved from room to room.

Food should be provided in receptacles that are accessible to all animals in a cage or pen and placed so as to minimize contamination. More than one receptacle may be necessary for some socially housed animals. Food receptacles should be easily cleaned and sanitized, and those functions should be performed on a schedule that meets *Guide* and AWR requirements. With limited exceptions, (e.g., neonatal animals or animals with limited mobility) food should not be placed on the bottom of the cage. Although some species may prefer this presentation, it results in waste and contamination of the food.

### **Watering**

Potable drinking water should be available continuously or provided as often as necessary for the health and well-being of the animal, considering the animal's species, age, condition, and any research requirements. Water may be provided in receptacles (e.g., bowls, bottles or via automatic watering systems). Whatever method is used, care should be taken to ensure that water does not become contaminated and is actually available. Water may be treated or purified to eliminate contaminants; however, some water treatments may cause physiologic changes, alter microflora, or affect experimental results. Sipper tubes and automatic watering devices should be checked daily for patency and cleanliness. Animals occasionally need to be trained to use automatic watering devices. Water bottles generally should be replaced and sanitized rather than refilled.

### **Bedding**

Bedding may be used in the housing of a variety of commonly used laboratory animals. Bedding material should be absorbent and free of any substances that might harm the animals or alter research data. Cedar and untreated softwood products can affect an animal's metabolism (e.g., liver enzymes), which may in turn affect immunologic or other physiologic parameters, and can increase the incidence of cancer. Bedding should be stored off the floor.

Animals may be placed directly on bedding material, a common practice with many rodent species, or bedding may be placed under a slat-bottom cage. Bedding should be used in sufficient amounts and changed as often as necessary to keep the animals clean and dry and the animal room



If waste must be stored while awaiting disposal, the storage area should be outside the animal holding and clean equipment areas. Animal carcasses and tissues require a separate cold storage area and regularly scheduled removal. Hazardous waste, including carcasses of animals exposed to radioactive or biohazardous agents, must be adequately sterilized and/or contained prior to removal and disposal.

### ***Pest Control***

The research animal facility is an active place, with frequent movement of personnel, animals, equipment, containers, and food and bedding, creating ideal conditions for the introduction of pests, including arthropods, birds and wild rodents. Pest control programs are complicated by the potential for harm to animals and personnel, as well as interference with research data by many commonly used pesticides. A regularly scheduled, documented pest control and monitoring program should be implemented, which effectively combines elimination of all entry and harborage sites with good waste disposal and personnel training. If traps are used, methods should be humane.

### **B.2.e. Emergency, Weekend and Holiday Care**

Laboratory animals must be observed by qualified personnel every day, including weekends and holidays to ensure their health and well-being, as well as to promote sound research practices. Skilled assistance, including veterinary care, must be readily available at all times. Names and telephone or pager numbers of those assigned these responsibilities should be prominently displayed in the facility. A disaster plan should be part of the overall facility safety plan which takes into account both personnel and animals (see [Section B.6.](#)).

### **B.2.f. Behavioral Management for Laboratory Animals**

There are varying requirements for attention to the behavioral management of laboratory animals, depending on the species of animal and the reference document.

The *Guide* provides recommendations for:

- increasing the complexity of the structural environment,
- addressing the social environment of animals, and



## **Oversight**

The IACUC should provide oversight of the behavioral management program in a manner similar to its oversight of other husbandry components of the animal care and use program, and evaluate program outcomes during semiannual reviews.

To adequately discharge this responsibility, the IACUC should have access to training or other orientation materials that will assist the IACUC members in evaluating the adequacy of the program (Bayne 2000). Formal, written plans for nonhuman primate environmental enrichment and canine exercise, established to provide a framework to the behavioral management program, should be approved by the IACUC and reviewed periodically. The committee should identify who is responsible for keeping the plan current and implementing the plan (e.g., an enrichment committee, the AV, etc.). The NRC publication, *The Psychological Well-Being of Nonhuman Primates* (1998), adopted by the Association for Assessment and Accreditation of Laboratory Animal Care International as a Reference Resource for accredited institutions, advises a team approach to development and oversight of the behavioral management program to include investigators, veterinarians and the IACUC.

## **References**

- NRC. 1998. *The Psychological Well-Being of Nonhuman Primates*. National Academy Press, Washington, DC.
- Bayne, K. 2000. Laboratory animal enrichment. In: *The IACUC Handbook* (J. Silverman, M.A. Suckow and S. Murthy, eds.). CRC Press. New York.

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## **B.3. Role of the Veterinarian**

Adequate veterinary medical care is an essential component of an animal care and use program and is required by the *PHS Policy* and Animal Welfare Regulations (AWRs). Institutions with smaller programs may opt for a part-time consulting veterinarian; the veterinarian's overall responsibilities remain the same in all cases.

It is the institution's responsibility to support ongoing improvements in the animal care and use program through the development and implementation of procedures and policies (e.g., IACUC guidelines) that enhance the health of the animals (ACLAM 1996). Clear provisions should be made to give the veterinarian appropriate authority to execute a program of adequate veterinary care, including access to all animals.

### **Qualifications**

The veterinarian participating in a laboratory animal care and use program must have training or experience in laboratory animal science and medicine, or in care of the species of animals maintained by the institution. Veterinarians can demonstrate the breadth and relevance of their expertise by achieving certification as a Diplomate of the American College of Laboratory Animal Medicine (ACLAM) or through other work experience and career accomplishments. Specialty training programs are available at a number of government, academic and commercial institutions to prepare graduate veterinarians to pursue ACLAM certification. Alternatively, veterinarians may qualify for ACLAM certification by working in a laboratory animal resource program and meeting other specified criteria.

The veterinarian providing support to a laboratory animal care and use program must meet applicable state veterinary practice acts, inclusive of licensure requirements, particularly in the discharging of certain official duties, such as signing interstate health certificates or verifying rabies vaccination or tuberculosis status of animals.



These programs include:

- immunization against infectious pathogens;
- surveillance of colonies for specific infectious microbial agents;
- disease prophylaxis utilizing pharmaceutical agents;
- isolation and quarantine of incoming animals; and
- separate housing of animals according to species, source or different background microbial floras.

While preventive medicine programs are successful in reducing the incidence of disease, illness and injury may still occur in laboratory animal colonies. The veterinarian is responsible for monitoring animal health, providing adequate diagnostic support through clinical assessments, laboratory diagnosis and necropsy when required, and treating animals when illness or injury necessitates veterinary medical care. Using a documented process, the veterinarian may delegate responsibility for care to trained technical staff but must always be available to provide rapid diagnosis and treatment.

The AWRs stipulate that the veterinarian attend to not only the physical health of animals, but also the psychological well-being of nonhuman primates, and exercise for dogs. The plan for canine exercise must be approved by the Attending Veterinarian (AV) before it can be implemented. Additionally, animals that are exempted from either the canine exercise plan or the nonhuman primate psychological well-being enhancement plan for health, condition or behavioral reasons must be documented by the AV and, unless a permanent condition exists, reviewed by the AV every 30 days.

Specific areas requiring the veterinarian's attention and guidance are:

- the selection and utilization of suitable anesthetic and analgesic agents and methods of euthanasia;
- appropriate selection of species for research projects; and
- proper performance of surgical procedures and adequate pre-operative, surgical, and post-operative care.



many institutions. However, institutions should also be aware that the domination of IACUC activities by the veterinarian(s) may foster or be symptomatic of the disengagement of other members, thereby resulting in a less cohesive and effective IACUC.

The veterinarian should keep abreast of current literature on comparative medicine and laboratory animal science. The knowledge gained often leads to suggestions for alternative techniques, models or species that may enhance animal well-being, augment the study design and help ensure the completion of the proposed study.

### ***Reference***

American College of Laboratory Animal Medicine. 1996. Report of the American College of Laboratory Animal Medicine on Adequate Veterinary Care in Research, Testing and Teaching.

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## **B.4. Occupational Health and Safety**

The health and safety of individuals working in animal care and use programs is an area of institutional concern requiring commitment from the senior officials of the institution. The goal of the occupational health and safety program (OHSP) is to prevent occupational injury and illness by avoiding, controlling or eliminating hazards in the workplace. The emphasis of such a program is the prevention of illness and injury, but it also includes provisions for early diagnosis and treatment when necessary.

### **The IACUC's Responsibility for Occupational Health and Safety**

The *PHS Policy* places responsibility for ensuring a safe working environment for personnel involved in the animal care and use program with the institution. An effective OHSP interdigitates with many separate institutional components including animal care and use, research, environmental health and safety, occupational health, and administration and management. A natural point of convergence for these functionally distinct institutional elements at many institutions is the IACUC. Assurance of a safe working environment is one of the topics the IACUC should consider in each animal use proposal and as part of the semiannual program evaluation. It is generally necessary to involve health and safety specialists in the design and implementation of the IACUC review guidelines.

### **Role of the IACUC in the Occupational Health and Safety Program**

Procedures should be developed for conducting a health and safety review of research activities that present hazards. These procedures should be incorporated into the IACUC protocol review process. Procedures to identify and address non-experimental hazards (e.g., during semiannual facility inspections and program reviews) should also be implemented. Communication and other procedural links between the IACUC and the environmental health and safety professional or office should be established, maintained and documented. In some institutions, IACUCs defer review of OHSP to an office of health and safety review.



- susceptibility of personnel; and
- history of occupational illness and injury in the workplace.

Health and safety specialists should be involved in the assessment of risks associated with hazardous activities.

### **Education and Training**

There are ethical and legal requirements to inform individuals of health risks that affect them and appropriate precautions. The objectives of an institution's OHSP can be achieved only if employees are appropriately trained to understand the hazards associated with their work area and job duties, and how those risks are mitigated through institutional policies, engineering controls, work practices, and personal protective equipment.

Training should include information about:

- zoonoses,
- chemical safety,
- microbiologic and physical hazards (e.g., allergens, radiation),
- hazards associated with experimental procedures,
- handling of waste materials, and
- personal hygiene.

Proficiency in work assignments through education and training will also contribute to a safer work environment. Training should be a continuous process, and records of OHSP training of personnel should be maintained.

### **Preventive Medicine and Provision of Medical Care**

The principal means of preventing occupationally acquired illness or injury is by controlling or eliminating hazards. The efficacy of the prevention program will depend on the institution's resource allocation to hazard control and the cooperation or compliance of personnel who are potentially at risk. The quality of the preventive medicine program can also be increased if its development and implementation involves input from trained health professionals.



reduce the potential development of laboratory animal allergy and possibly alter its severity.

Infectious diseases also pose a significant risk depending on the species and health status of animals involved and the level of exposure to them by animal care personnel.

Infectious diseases to which animal care personnel may be exposed include:

- viral infections, such as contagious ecthyma, the hepatitises, and *Cercopithecine herpes virus 1* (Herpes B);
- rickettsial diseases, such as Q fever and cat scratch fever;
- bacterial diseases, such as tuberculosis, salmonellosis, and shigellosis;
- protozoal diseases, such as toxoplasmosis, giardiasis, and cryptosporidiosis; and
- fungal diseases, such as dermatomycosis.

In addition to infections acquired from live animals, animal tissues and excreta can serve as sources of zoonoses. Careful monitoring and quarantine of any animals with potential viral or bacterial infections or parasitic infestations are crucial components of any animal care and use program. It is important to immunize animal care personnel against tetanus. Routine tuberculosis testing is essential and measles vaccination may also be appropriate for workers exposed to nonhuman primates.

### **Common Occupational Health and Safety Program-wide Pitfalls\***

- Instead of being based on hazard identification and risk assessment, the program identifies personnel risk based on animal contact time or frequency.
- There is inadequate training on occupational health and safety topics (e.g., zoonoses, allergies).
- Not all personnel at risk (e.g., students, visiting scientists) are offered inclusion in the program.
- Hazard identification covers experimental hazards, but does not address hazards intrinsic to animal care and use.
- There is inadequate linkage between the IACUC and the institutional safety committee(s).

\*From data collected by AAALAC International.



## B.5. Personnel Training and Education

All staff working with laboratory animals must be qualified to do so in order to ensure the humane treatment of animals. Training is a classic performance standard where the emphasis is on the outcome (i.e., all personnel qualified to do their jobs). Although the *PHS Policy* and Animal Welfare Regulations (AWRs) do not specify a particular program or the frequency with which a program should be offered, the requirement for competence is mandatory.

The AWRs, in Sec. 2.32 (a) and (b), specify:

It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel. Training and instruction shall be made available, and the qualifications of personnel reviewed, with sufficient frequency to fulfill the research facility's responsibilities....

The *PHS Policy, Section IV.C.1.f.* places responsibility specifically with the IACUC to ensure that personnel conducting procedures on research animals are appropriately qualified and trained in those procedures.

Personnel training in the care and use of research animals is an important aspect of the alternatives concept (replacement, reduction and refinement) described in [Section C.2.a](#). Training in the recognition and alleviation of animal pain, distress, and abnormalities addresses refinement. Similarly, training in the conduct of animal procedures prepares staff to work without causing unnecessary harm to the animal. Technical proficiency also invokes reduction by avoiding wasted animal lives through failed procedures.

Personnel training should be seen as one of the pillars supporting the animal research program. Training of staff is essential for safeguarding the quality of the animals as a tool of research or testing. A lack of training may



All staff should have exposure through training to regulatory requirements for animal welfare and occupational health and safety considerations. Staff who work directly with animals should have training that supports the humane care and use of animals in the course of day-to-day procedures.

The AWRs, in Sec. 2.32 (c), require that training and instruction of personnel must include guidance in at least the following areas:

- (1) Humane methods of animal maintenance and experimentation, including:
  - (i) The basic needs of each species of animal;
  - (ii) Proper handling and care for the various species of animals used by the facility;
  - (iii) Proper pre-procedural and post-procedural care of animals; and
  - (iv) Aseptic surgical methods and procedures;
- (2) The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress;
- (3) Proper use of anesthetics, analgesics, and tranquilizers for any species of animals used by the facility;
- (4) Methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility.
- (5) Utilization of services (e.g., National Agricultural Library, National Library of Medicine) available to provide information:
  - (i) On appropriate methods of animal care and use;
  - (ii) On alternatives to the use of live animals in research;
  - (iii) That could prevent unintended and unnecessary duplication of research involving animals; and
  - (iv) Regarding the intent and requirements of the [Animal Welfare] Act.

Training programs should also include information on occupational health and safety. Specific recommendations for general training objectives may be obtained from *Education and Training in the Care and Use of Laboratory Animals: A Guide for Developing Institutional Programs*. Recommendations for general training objectives are outlined in [Table A](#) for each type of staff.



## **Personnel Training Records and Documentation**

Although there is no specific requirement to document individual training activities, training records demonstrate that staff have met the training requirements related to their responsibilities in the research animal program, and regulatory or other oversight authorities often request to inspect personnel training records as evidence of an effective program.

Training records have value in tracking the range of topics offered, the frequency of training sessions, and the participation of institutional staff. Such records may include training received in informal settings, e.g., one-on-one instruction, common for teaching animal use methodologies.

Training records may be archived with the IACUC, a training coordinator, research departments or individual laboratories. Whatever the location, training records should be accessible to inspection by any oversight authority, including the IACUC. If training records of research staff are stored in laboratories, a good practice would be to include a brief review of training records among the objectives for the IACUC's semiannual inspection of facilities.

## **Training Personnel**

Many institutions with a large research program have a training coordinator to oversee the training program for all personnel with animal care and use training needs. The training coordinator should be involved in IACUC meetings when institutional training issues are discussed.

Training coordinators should not be the only ones with training responsibilities. The facility staff, (e.g. veterinarians, veterinary technicians, facility managers and animal care technicians), also should be involved in training activities to the greatest extent possible. Their training activities, either with individuals or groups, should be acknowledged as a valuable contribution to the animal research program. In this way, individual expertise is fully utilized and every contact with facility staff offers a training opportunity.

In addition, other staff or outside consultants with specialized expertise can be incorporated into the training program. For example, occupational health professionals may be invited to take part in training on safety related issues. Training in specialized animal methodologies may be best performed by researchers who are accomplished in these techniques. Training program staff, if available, should participate in or oversee the training by outside experts to ensure that the training content is appropriate.



## **B.6. Emergency Preparedness**

### **B.6.a. Security and Crisis Management**

Anti-animal research activities during the past several years against institutions using animals in research, testing and teaching programs have included demonstrations, break-ins, vandalism, life threats and harassment by mail or telephone, arson, and bomb threats. Since the IACUC has responsibility for the welfare of animals at its facility, it shares responsibility for the security of the animals and personnel who care for and use these animals with other units within the institution, such as the units responsible for security, public information, and governmental relations. Institutions receiving federal funds have an obligation to protect the federal investment in research by exercising due diligence in this area. The IACUC can serve a key role in advising the IO and the institution of potential risks and vulnerabilities, and in developing a plan for responding to potential or real threats.

In all cases the IACUC must consider allegations of noncompliance or animal welfare issues as concerns that must be addressed in accordance with relevant *PHS Policy* provisions and Animal Welfare Regulations (AWRs) (see [Section D](#)).

There are four key elements to an institution's preparedness:

- an animal care and use program of impeccable integrity;
- a security program based on risk assessment;
- an integrated communication plan with descriptions of research projects in lay terminology, spokespersons and a telephone tree; and
- an internal and external community outreach program that includes legislators and funding agencies.

#### ***Crisis Management Team***

The establishment of a crisis management team before a crisis occurs is important in order to respond in a timely manner. This team may be comprised of individuals representing the following areas: security, public information, laboratory animal resources, the IACUC, management/research administration (including the IO), legal affairs, and governmental relations. It



- d. Identify ongoing investigations by regulatory agencies.
  - e. Limit access of delivery persons within animal care facilities.
  - f. Keep duplicate physical layout plans available off site.
  - g. Share information with security personnel about activism at other research organizations.
  - h. Develop a document that will provide pertinent information to the police in the event of an incident such as type of incident, location, animals or property destroyed or stolen, people involved, time, method of entry, and need to check for hazardous materials.
5. Organize a communication plan in the event of an incident during the day, after hours, weekends and holidays.

### ***Communications and Risk Reduction***

Institutions using animals need to communicate effectively and on an ongoing basis with the internal and external community and the media. It is important to build these relationships over time and to keep individuals in all of these areas informed about the significance of the work in which animals are used, and the institution's commitment to scientific standards through quality animal care and use. Being proactive by conveying significant advances in research using animals ethically and humanely can reduce the potential for negative public reactions in a crisis situation.

The IACUC Chair and members can interact with institutional public information officers, researchers, veterinarians, technicians and the research administration to identify spokespersons to address animal research issues. These spokespersons should be provided adequate training. Fact sheets should be readily available about the institution's policies and commitment to humane and appropriate animal care and use, the quality of its animal care and use program (including accreditation), and brief summaries of the value and importance of any specific animal use under scrutiny. Written materials need to be written in language understandable to nonscientists. Institutions must be prepared to respond to allegations honestly (i.e., if real noncompliance with relevant policies or regulations is substantiated then the institution must take appropriate action and should be forthcoming about the situation).

In the event of a crisis the facility that is prepared can respond quickly through its spokespersons with accurate and factual information. It is also important for the institution to notify OLAW in such an event so they can confirm



Agency (FEMA). FEMA is an independent federal agency founded in 1979 that reports directly to the President. FEMA's mission is *to reduce loss of life and property and protect our nation's critical infrastructure from all types of hazards through a comprehensive, risk-based, emergency management program*. FEMA considers an effective emergency management program to consist of four parts:

- *Mitigation* (activities related to preventing future emergencies or minimizing the effects of emergencies that occur);
- *Preparedness* (incorporation of the planning and preparations required to handle an emergency, including the Disaster Plan);
- *Response* (the Disaster Plan put into action when an emergency occurs); and
- *Recovery* (the actions needed to return to normal after an emergency occurs.)

### ***Segments of a Disaster Plan***

This section focuses on the Disaster Plan because it is the component of an emergency management program that the IACUC should review as a part of its semiannual program review. The content and scope of the Disaster Plan will be shaped and determined by the individual program and facility. The following approach is one way to create a Disaster Plan and can be useful to the IACUC in evaluating the facility's plan.

A suggested organization method includes:

- developing a planning team,
- defining emergencies,
- identifying critical functions and systems,
- defining resources and contacts,
- developing policies and procedures, and
- training staff and testing emergency equipment.

### ***Developing a Planning Team***

The Disaster Plan is best completed by the group of individuals that would respond to an emergency. The emergency response planning team should be comprised of individuals of various backgrounds and expertise, including certain animal facility staff and investigators, as well as representatives



being made. If electrical power is lost, and the facility is relying on emergency back-up generators, there may be refueling problems when the fuel reserves are exhausted and delivery trucks can't reach the site. This example shows how the planning exercise can provide valuable modeling information useful in disaster preparation.

### ***Identifying Critical Functions and Systems***

Fundamentally, the Disaster Plan should address ways to maintain or cope with the loss of critical functions and systems in the animal facility. To do this, it is important to rigorously identify all critical animal facility specific functions and systems. The critical functions and systems fall into two general categories: mechanical systems and personnel functions (see [Table B](#)). It is helpful to compare the list of primary and secondary effects of the different emergencies ([Table A](#)) and review their impact on the critical functions and systems. Different scenarios can become the basis for action plans and preparedness activities.

### ***Defining Resources and Contacts***

The Disaster Plan can also include lists of available resources and contacts to be used during emergency events. The lists can include various emergency equipment, spare parts, equipment capacities, levels of redundancy built into the mechanical equipment systems and ways to put the equipment into use. Additionally, this section might include critical vendors that can supply services during an emergency, such as a supplier to perform periodic refueling of emergency generator fuel tanks, as well as up to date emergency personnel notification lists, including criteria for contacting specific individuals. More advanced plans stage the level of an emergency and clearly prescribe the type of response for each level. Other pertinent items such as floor layouts, mechanical equipment plans, the names and numbers of national, regional and local emergency response organizations (FEMA, Red Cross, Police, etc.) and local weather information resources, can be included.

### ***Developing Policies and Procedures***

The core elements of a Disaster Plan are the policies, guidelines and procedures that are put into action during an emergency. The plan should address very specific emergencies and/or give general outlines for action steps in response to an emergency. Many plans will also focus on coping







### ***Suggested Reading***

Anderson, S. 1998. Hazard Analysis: Preparing for Natural Disasters, *Lab Animal* 27(1):24-29.

Federal Emergency Management Agency (FEMA) Web site: [www.fema.gov](http://www.fema.gov).

“Animal in Disaster” a two module training program by FEMA.

Vogelweid, C. M. Developing emergency management plans for university laboratory animal programs and facilities. *Contemporary Topics on Laboratory Animal Science* 37(5):52-56.

*Resources for Crisis Management in Zoos and other Animal Care Facilities*. 1999. Published by the American Association of Zoo Keepers. Editors: Chan S. D., W. K. Baker, and D.L. Guerrero. Topeka, Kansas.

Heath, S. E. 1999. *Animal Management in Disaster*. Mosby Year Book. St Louis, MO.

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# **C. Review of Proposals**

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## C.1. Fundamental Issues

The IACUC is responsible for overseeing and evaluating all aspects of animal care and use, and is charged with reviewing proposals\* that involve animals to ensure that the criteria established in the *PHS Policy* and the Animal Welfare Regulations (AWRs) are implemented. In its review of proposals, the Committee's primary goal should be to facilitate compliance with applicable laws, regulations and policies consistent with the performance of appropriate and productive scientific endeavors.

### Protocol Review Criteria

[Table A](#) lists each review criterion of the *PHS Policy* and AWRs along with the applicable US Government Principles. Since the *PHS Policy* further requires that the provisions of the *Guide* apply, there are many other aspects of research that an IACUC should review, such as food and water deprivation, use of noxious stimuli, and physical restraint. The *Guide* provides useful guidance on these and other practices. [Section C.2](#). Protocol Review Criteria addresses many of the subjects described below in greater detail.

If the IACUC does not have the scientific and technical expertise to evaluate all aspects of a proposal it may bring in outside expert consultants to provide information. Such consultants may not vote. In all cases, the onus should be on the investigator to justify and explain his or her proposed experiments to the satisfaction of the IACUC.

*\*This Guidebook generally uses the term "proposal" to describe the proposed use of animals. In some cases the term "protocol" is used for ease of readability. For the purposes of this Guidebook "proposal" is interchangeable with the commonly accepted use of the term "protocol."*







**C.1. Table A. Regulatory Criteria Applicable to Protocol Review as Defined in PHS Policy and USDA Regulations** *(continued)*

U.S. Government Principles	PHS Policy on Humane Care and Use of Laboratory Animals	USDA AWR 9 CFR Part 2, Subpart C
<p><i>Principle IX:</i> Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.</p>	<p>See <a href="#">C.1.</a> above.</p>	<p>See <a href="#">§2.31(d)</a> above.</p>
	<p>D.1.: Applications and proposals... that involve the care and use of animals shall contain the following: ...c) a complete description of the proposed use of the animals...</p>	<p>§2.31(e): A proposal...must contain the following: ... (3) A complete description of the proposed use of the animals...</p>
	<p>D.1.: Applications and proposals...that involve the care and use of animals shall contain the following: ...d) a description of procedures designed to 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 tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals.</p>	<p>§2.31(e): A proposal...must contain the following: ... (4) A description of procedures designed to assure that discomfort and pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, including provision for the use of analgesic, anesthetic, and tranquilizing drugs where indicated and appropriate to minimize discomfort and pain to animals.</p>

*Continued on page 90*



## Proposal Review Procedures

The procedural review requirements of the *PHS Policy* or the AWRs take precedence even though they may differ from some commonly used parliamentary procedures. Institutions may develop their own meeting procedures as long as the procedures do not contradict or are not inconsistent with the requirements of the *PHS Policy* or the AWRs.

If a proposal may cause more than momentary or slight pain or distress to animals, the AWRs specifically require investigators to consult with the AV or his or her designee during protocol development. Some committees find it helpful to assign a member a given proposal for in-depth review and liaison with the investigator prior to committee review. Still other committees assign this task to professional IACUC staff. The investigator may choose to consult with these individuals and request a preliminary review before formally submitting a proposal.

The *PHS Policy* and AWRs recognize two methods of review: full committee review and designated member review. The following pertains to review of initial protocols as well as to review of proposed significant changes in previously approved protocols.

- **Full committee review**

Full committee review of proposals requires a convened meeting of a quorum of the IACUC members. The *PHS Policy* and AWRs are explicit that proposals reviewed by the full committee must receive the approval vote of a majority (>50%) of the quorum present in order receive approval (see [A.2. Quorum requirements](#)).

Some committees designate a specific member or members to serve as primary or primary and secondary reviewers. These individuals, usually chosen for their expertise or familiarity with a given topic, are responsible for an in-depth review of a proposal and sometimes take responsibility for describing the proposal to the full committee and answering questions about the proposal during review by the Committee. Primary and secondary reviewers can also take the initiative to contact the investigator prior to the meeting for clarifications, additional information, or in anticipation of questions the IACUC may raise. The use of primary



have the opportunity to request full committee review of any proposal. If no member requests full committee review, the Chair designates one or more qualified members to review the proposal (or proposed amendment). These designated members have authority to approve, require modifications in (to secure approval), or request full committee review.

IACUCs with a large volume of proposals to be reviewed find the designated member review option may allow for efficient management of the IACUC workload as well as timely turnaround of requests from investigators for protocol review. Some committees prefer to reserve the designated member review option for certain classes of protocols or amendments; conversely, some IACUCs have devised categories of research activities that must be reviewed by the full committee, e.g., nonhuman primate studies, survival surgeries, etc. If the designated member review method is to be used by PHS-supported institutions then the IACUC's specific procedures for using the method should be described in its PHS Assurance.

### **Categories of IACUC Actions**

As a result of their review of a protocol, an IACUC may take one of several different actions depending upon the findings of the committee: approval, modifications required to secure approval, or withhold approval. An IACUC may also defer or table review if necessary.

The *PHS Policy* and AWRs require the IACUC to notify investigators and the institution in writing of its decision to approve or withhold approval, or of modifications required to secure approval. If approval is withheld the IACUC must provide the reasons for its decision and give the investigator an opportunity to respond.

- **Approval**

When the IACUC has determined that all review criteria, based on the *PHS Policy* and AWRs, have been adequately addressed by the investigator, the IACUC may approve the proposal, thus providing the investigator permission to perform the experiments or procedures as described.

An IACUC-approved proposal may be subject to further appropriate review and approval by institutional officials due



- **Withhold approval**

When the IACUC determines that a proposal has not adequately addressed all of the requirements of the *PHS Policy* and AWRs as applicable, the committee may withhold approval. A designated reviewer may not withhold approval; this action may only be taken if the review is conducted using the full committee method of review.

As indicated above, a higher institutional authority may not administratively overrule an IACUC decision to withhold approval of a proposal.

- **Defer or table review**

If the proposal requires clarification in order for the IACUC to make a judgment, committee members with certain expertise are not present, the IACUC wishes to seek external consultation, or any of a number of other reasons prevent the IACUC from conducting its review, then the IACUC may wish to defer or table review. Good communication between the IACUC and the investigator can ensure that this action is needed infrequently. However, should it be necessary, the investigator should be informed so that he or she can respond or plan accordingly.

## **Review of Changes to Approved Protocols**

Significant changes to an IACUC-approved protocol must be reviewed and approved by the IACUC before they occur (*PHS Policy* IV.C.1., and AWR §2.31[d][1]). It is prudent for an IACUC to develop a policy on the kinds of changes that are considered significant in order to avoid ambiguity. OLAW has identified the following kinds of significant changes that may serve as examples to guide the IACUC in its determinations:

- change in objectives of a study;
- proposals to switch from nonsurvival to survival surgery;
- change in degree of invasiveness of a procedure or discomfort to an animal;
- change in species or in the approximate number of animals used;
- change in personnel involved in animal procedures;
- change in anesthetic agent(s) or in the use or withholding of analgesics;



## C.2. Protocol Review Criteria

### C.2.a. Alternatives – Replacement, Reduction and Refinement

There is significant interest in the application of alternatives to animals used in research, education and testing. The *PHS Policy* and the AWRs require research institutions to ensure that investigators have appropriately considered alternatives to procedures that can cause more than slight or momentary pain or distress in animals, consistent with sound research design. Through U.S. Government Principle III (Appendix F), the *PHS Policy* further requires that the minimum number of animals be used and that non-animal methods be considered.

#### ***The “3 Rs”***

Alternatives are framed within the context of the “3 Rs” articulated originally by Russell and Burch in 1959; they include:

1. **Replacement**, or utilizing non-animal models;
2. **Reduction** of numbers of animals used; and
3. **Refinement**, or elimination or reduction of unnecessary pain and distress in animals.

**Replacement** alternatives utilize:

- living systems,
- non-living systems, or
- computer simulations.

*Living systems* include *in vitro* methods that utilize organ, tissue or cell culture techniques. Invertebrate animals, such as the fruit fly, have long been used in research and represent another type of living alternative to vertebrate animals. Finally, microorganisms and plants represent living alternatives for some types of research and testing. *If no invertebrate model is appropriate, use of species lower on the phylogenetic scale may be considered a replacement alternative.*



**Refinement of technique** to reduce or eliminate unnecessary pain and distress in study animals is the most commonly practiced of the 3 Rs, although it is not always recognized as one of the applications.

Investigators are required to consider alternatives to painful procedures, and to avoid or minimize discomfort, distress and pain, consistent with sound scientific practice and the goals of the research. This requires an understanding of the potential of pain or distress in the animals (see [Section C.2.d.](#)).

When there is no consensus among IACUC members as to whether a certain procedure actually causes pain or distress in the affected animals, U.S. Government Principle IV should be applied. This Principle states, “Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.”

To assist in this deliberation, the IACUC may need to utilize one or more of the following:

- pilot studies,
- evaluations of clinical signs,
- clinical pathology,
- gross and histological necropsy studies,
- review of comparable literature, and
- consultation with experts.

If there remains any doubt about the presence of pain or distress, the IACUC should err on the side of protecting the animals against the potential of unnecessary pain or distress.

Some refinement opportunities include:

- pain-relieving drugs,
- non-pharmacologic techniques,
- new diagnostic and therapeutic techniques,
- environmental enrichment programs, and
- establishment of more humane endpoints.



### ***USDA Requirements for Consideration of Alternatives***

USDA AWRs require that investigators consider alternatives to procedures that may cause more than momentary or slight pain or distress and provide a written narrative of the methods used and sources consulted to determine availability of alternatives. Animal Care Policy 12 provides guidance on the requirements for the written narrative, which should include adequate information for the IACUC to assess that a reasonable and good faith effort was made to determine the availability of alternatives or alternative methods. Resources in the area of alternatives include the USDA Animal Welfare Information Center (AWIC); ALTWEB, a Web site maintained under the auspices of the Johns Hopkins University Center for Alternatives to Animal Testing; and the University of California Center for Animal Alternatives (see [Appendix A](#)).

### **C.2.b. Euthanasia**

“Euthanasia means the humane destruction of an animal accomplished by a method that produces rapid unconsciousness and subsequent death without evidence of pain or distress, or a method that utilizes anesthesia produced by an agent that causes painless loss of consciousness and subsequent death” (AWR). The choice of a method depends on species, age, availability of restraint, skill of the individuals performing euthanasia and other considerations. In a research setting, the method of euthanasia must be consistent with the research goals.

The *PHS Policy* and the AWRs require that an IACUC review and approve methods of euthanasia. The *PHS Policy* specifically states that methods of euthanasia must be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless scientific justifications for alternative methods are presented in writing by the investigator and approved by the IACUC. The most recent Panel convened in 2000, and published its Report in March 2001.

The criteria used as the basis for the Panel’s recommendations include:

- minimum pain, distress, anxiety or apprehension;
- minimum delay until unconsciousness;
- reliability and irreversibility;
- safety of personnel; emotional effect on personnel;



Methods described as conditionally acceptable are considered acceptable when used in deeply anesthetized animals. Some euthanasia methods (e.g., KCl or formalin by intracardiac injection, or exsanguination) are acceptable only under deep general anesthesia.

For more information on methods of euthanasia see [Appendix D](#).

### **C.2.c. Humane Endpoints**

Animals used in research and testing may experience pain from induced diseases, procedures, and toxicity. The *PHS Policy* and AWRs state that procedures that cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. However, research and testing studies sometimes involve pain that cannot be relieved with such agents because they would interfere with the scientific objectives of the study. Accordingly, federal regulations require that IACUCs determine that discomfort to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, and that unrelieved pain and distress will only continue for the duration necessary to accomplish the scientific objectives.

The *PHS Policy* and AWRs further state that animals that would otherwise suffer severe or chronic pain and distress that cannot be relieved should be painlessly killed at the end of the procedure, or if appropriate, during the procedure.

#### ***Developing Humane Endpoints***

Criteria used to end experimental studies earlier in order to avoid or terminate unrelieved pain and/or distress are referred to as humane endpoints. An important feature of humane endpoints is that they should ensure that study objectives will still be met even though the study is ended at an earlier point. Ideally, humane endpoints are sought that can be used to end studies before the onset of pain and distress.

It is important to understand that stress may lead to distress when major shifts in biologic function, to which the animal cannot adapt, threaten the animal's well-being. If pain and distress are anticipated, a detailed plan for when and how these will be alleviated should be provided in the protocol.



Various clinical signs are indicative of a moribund condition in laboratory animals. These typically include one or more of the following:

- impaired ambulation which prevents animals from reaching food or water,
- excessive weight loss and emaciation,
- lack of physical or mental alertness,
- difficult labored breathing, and
- inability to remain upright.

Animals should be observed frequently enough to detect signs of impending death so they can be euthanized in a timely manner. When increased morbidity or mortality is expected, a minimum of twice daily observation is recommended. Animals not likely to survive until the next scheduled observation should normally be euthanized. In situations where animals are often found dead, closer and more frequent observation for moribund animals should be considered to reduce spontaneous deaths. Euthanasia of animals that are moribund or experiencing severe pain and distress should always be done in a manner that produces the least possible amount of additional pain and distress.

### ***Other Humane Endpoints in Research***

Animals used to study tumor biology, to develop new cancer therapies, and to evaluate the carcinogenic potential of substances may experience pain and distress. Frequent and appropriate monitoring of animals during tumor development is necessary to allow for appropriate intervention before significant deterioration or death. Effective monitoring systems and endpoints should include limits on tumor size and severity of tumor-associated disease. Altered physiologic, biochemical, and other biomarkers may be potentially more objective and reproducible endpoints than clinical signs for such studies.

Genetically engineered animal models are sometimes accompanied by unintended and unpredicted alterations that adversely affect animal well-being. Investigators need to establish a plan for addressing unanticipated adverse outcomes for genetically altered animals. There should be a plan for systematic characterization of phenotypes to facilitate assessment of their possible utility and timely decisions on disposition or retention. IACUCs should provide oversight of such studies to ensure that animal welfare problems are handled in an effective and prompt manner.



The use of death as an endpoint is discouraged and must always be justified. Endpoints other than death must always be considered and should be used whenever the research objective can be attained with non-lethal endpoints. Use of death as an endpoint must be justified in writing in proposals and its use must be approved by the IACUC prior to beginning a study.

**C.2.c. Table A. Examples of Humane Endpoints for Studies with Potential Lethality**

<b>Endpoint</b>	<b>Characteristics</b>	<b>Applications</b>
Tumor growth or effects	Tumor exceeds 10% of normal body weight; necrosis, infection, ulceration, interference with ambulation or eating/drinking	Subcutaneous or intraperitoneal tumors and hybridomas
Prolonged inappetence/ Cachexia	Rapid loss of weight (>20% of normal body weight) and/or condition	Metastatic disease, chronic infectious disease
Inability to ambulate	Prolonged recumbency	Many
Signs of severe organ or system involvement	Respiratory: rapid or labored breathing, coughing, rales  Cardiovascular: shock, hemorrhage, anaphylaxis  Gastrointestinal: severe diarrhea or vomiting  Peripheral Nervous System: flaccid or spastic paralysis  CNS Signs: circling, blindness, dementia, convulsion	Toxicity testing; systemic disease
Progressive hypothermia	Decrease of 4-6°C in body temperature in rodents	Infectious disease studies; vaccine potency studies
Moribund or pre-moribund state	Define with specific clinical signs and euthanize when reached	Many



Stokes W.S., and R.N. Hill. 2000. The Role of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) in the Evaluation of New Toxicological Testing Methods. In: Proceedings of the 3rd World Congress on Alternatives and Animal Use in the Life Sciences, Bologna, Italy, August 31-September 2, 1999. New York: Elsevier Sciences (Forthcoming).

Tannenbaum J. 1999. Ethics and pain research in animals. *ILAR J* 40:97-110.

Toth L.A. 2000. Defining the moribund condition as an experimental endpoint for animal Research. *ILAR J* 41:72-79.

UKCCCR [United Kingdom Coordinating Committee on Cancer Research]. 1997. Guidelines for the Welfare of Animals in Experimental Neoplasia. London: UKCCCR.

Wallace J. 2000. Humane endpoints and cancer research. *ILAR J* 41:87-93.

### **C.2.d. Minimization of Pain and Distress**

It is the responsibility of the IACUC to critically evaluate all research protocols for the potential to cause pain or distress and assess the steps that are to be taken to enhance animal well-being.

As required by the *PHS Policy* and the AWRs, and reiterated in the *Guide*, the IACUC is mandated to review protocols to ensure that pain and distress are minimized in laboratory animals. The AWRs stipulate that the IACUC determine that the principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animal and has provided a written narrative description of the methods and sources used to determine that alternatives were not available. Additional guidance from the USDA on this subject is provided in their policies. The *Guide* states that the IACUC should ensure the protocol addresses:

- appropriate sedation, analgesia, and anesthesia;
- criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and
- details of postprocedural care.

The protocol must provide adequate information for the IACUC to assess the potential animal pain and/or distress resulting from the study and the effectiveness of the pain- and distress-relieving agents proposed for use. Criteria for re-dosing the animal should also be established. The AV must be consulted for any procedure that has the potential to cause more than momentary pain or distress.



observations with the aid of descriptors. It is often useful to start with a general set of observations for assessing pain and distress such as change in body weight, physical appearance/posture or changes in unprovoked and provoked behavior. The assessment system should then be modified on a case-by-case basis using specific changes that may be anticipated in a particular study.

### ***Alleviation of Pain and Distress***

Accepted best practices for dealing with the possibility of unrelieved pain and distress should be considered and incorporated into protocols unless there is a sound scientific rationale for deviation from those practices. The investigator must also provide an assurance that unrelieved pain will continue for only the minimum period of time necessary to attain the study objectives.

Protocol methodology should be considered which decreases the potential for pain or distress. In addition to thorough searches of the literature, this can be done through the careful use of pilot studies to determine earlier endpoints or less invasive alternatives.

Pharmacologic treatment of pain or distress should be given as consistent with the type of pain/distress and the needs of the research question. The veterinarian must be consulted for all such protocols and should provide guidance to investigators and the IACUC. The responses of different species to different anesthetics, analgesics or tranquilizers vary and are not fully defined. Often the effects of a given drug have only been examined in a single species and definitive information, for example, on cardiovascular and respiratory function or on the ability to relieve the perception of noxious stimuli, is missing. As a result, dosages have been developed on the basis of the amount required to produce cessation of movement when the animal is confronted by what is assumed to be a painful manipulation, in conjunction with an adequate recovery. Because of the imprecise nature of the studies, dosage ranges are often quite wide, requiring a very conservative approach to their use. The use of drug mixtures further complicates the choice of an adequate dose. Numerous reference texts exist and IACUCs may request that the veterinarian prepare current charts of recommended doses as an institutional resource for investigators.

Non-pharmacologic treatments should also be employed. This may include special housing considerations, dietary and other environmental enrichments, adjustments and careful supportive care.



**C.2.d. Table C. Signs, Degree and Length of Surgically Produced Pain\***

<b>Surgical Site</b>	<b>Signs of Pain</b>	<b>Degree of Pain</b>	<b>Length of Pain</b>
Head, eye, ear, mouth	Attempts to rub or scratch, self-mutilation, shaking, reluctance to eat, drink, or swallow, reluctance to move	Moderate to high	Intermittent to continual
Rectal area	Rubbing, licking, biting, abnormal bowel movement or excretory behavior	Moderate to high	Intermittent to continual
Bones	Reluctance to move, lameness, abnormal posture, guarding, licking, self-mutilation	Moderate to high: upper part of axial skeleton (humerus, femur) especially painful	Intermittent
Abdomen	Abnormal posture (hunched), anorexia, guarding	Not obvious to moderate	Short
Thorax	Reluctance to move, respiratory changes (rapid, shallow), depression	Sternal approach, high; lateral approach, slight to moderate	Continual
Spine, cervical	Abnormal posture of head and neck, reluctance to move, abnormal gait—"walking on eggs"	Moderate to severe	Continual
Spine, thoracic or lumbar	Few signs, often moving immediately	Slight	Short

\*Based on observations of dogs.

*Reprinted with permission from Recognition and Alleviation of Pain and Distress in Laboratory Animals. Committee on Pain and Distress in Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council. National Academy Press, Washington, DC. 1992.*



A checklist of institutional requirements that need to be satisfied as a component of protocol review might include the following in addition to those above:

- completion of occupational health and safety risk assessment,
- demonstrated knowledge of relevant rules and regulations,
- enrollment in occupational health and safety program,
- attendance at compliance training session, and
- viewing of safety training video.

Classifications of employees whose qualifications and training may require assessment include:

- investigators,
- research technicians,
- animal husbandry personnel, and
- veterinarian and veterinary technicians.

An important decision to be made by the IACUC is the level of training required of an investigator not actually involved in the day-to-day manipulation and care of the animals. If the investigator is responsible for the research activity and the animals involved, should she or he demonstrate proficiency in the areas indicated above? Is the investigator responsible for training personnel in the lab? If yes, should she or he demonstrate proficiency in those areas? An IACUC policy on this issue will prevent conflict later.

### ***Evaluating Qualifications and Training***

To prevent problems related to assessment of qualifications and training during protocol review, it is helpful if the IACUC determines any training needs during the protocol development and veterinary consultation. Discussion of new techniques, procedures, or manipulations at this time can provide the impetus for a training opportunity for both the veterinary staff and the research staff with demonstrated proficiency completed prior to protocol review. This training experience should be so noted in the protocol or otherwise documented.

Maintaining a database of all participants in the facility's training program who use laboratory animals will facilitate assessment of qualifications and training. With such a database, preliminary evaluation of an individual's



and training. This should not be viewed as a confrontational event, but rather one with educational value for both the veterinarian and the research staff. Documentation of this training experience should be made in the IACUC files or database.

In summary, evaluation of personnel qualifications and training is an essential component of the review of animal use protocols to ensure the humane care and use of laboratory animals. The challenge to IACUCs is to perform this evaluation in an efficient, consistent and uniform manner.

### **C.2.f. Veterinary Review and Consultation**

Each IACUC is required by the AWRs and the *PHS Policy* to have as one of its members a Doctor of Veterinary Medicine with direct or delegated program authority and responsibility for animal activities at the institution.

The AWRs and the *PHS Policy* require that the veterinarian be trained or experienced in laboratory animal science and medicine for the species used at the institution; the *Guide* recommends the IACUC veterinarian be American College of Laboratory Animal Medicine (ACLAM) certified or have equivalent experience.

The Report of the American College of Laboratory Animal Medicine on Adequate Veterinary Care in Research, Testing and Teaching (1996) states:

The veterinarian must be involved in the review and approval of all animal care and use in the institutional program. This includes advising on the design and performance of experiments using animals as related to model selection, collection and analysis of samples and data from animals, and methods and techniques proposed or in use. This responsibility is usually shared with investigators, the IACUC, and external peer reviewers.



- that aseptic techniques are appropriate for the procedure; and
- that adequate post-operative care, to include post-operative analgesics where indicated, is provided.

### ***Reviewing Protocols To Ensure Humane Euthanasia of Animals***

The American Veterinary Medical Association (AVMA) provides guidance on the most humane methods to be used for euthanasia of animals, to include those used in research, testing and training. Their most recent recommendations are contained in the “2000 Report of the AVMA Panel on Euthanasia” (*JAVMA* Vol. 218, No. 5, pages 669–696). The veterinarian on the IACUC, using that publication or subsequent editions as the principal reference, can assess the investigator’s proposed method of euthanasia.

### ***After Protocol Review and Approval***

Following IACUC approval of protocols, the veterinarian is in a position, through periodic visits to the animal facility and animal activity areas, to observe and evaluate animal well-being and decide whether the animal activities are being conducted in accordance with the conditions described or referenced in the protocol. The veterinarian, by virtue of training and experience, is able to serve in advocacy, oversight, and intervention roles that are distinct and unique among the IACUC members and research staff.

### ***Checklist***

#### ***Some Examples of the Veterinarian’s Responsibilities During Protocol Development and Review\****

- Choice and use of appropriate analgesics/anesthetics
- Verification of appropriate drug dosages, route of administration and choice of agent
- Assistance in selection of appropriate animal model
- Identification of refinement initiatives to ensure that manipulations have a minimal impact on animal welfare
- Oversight of aseptic surgery and peri-operative care
- Oversight of animal health and husbandry pertinent to the protocol and the entire colony



## **C.3. Other Protocol Review Considerations**

### **C.3.a. Agricultural Research**

Farm animals are used in a variety of research contexts, including:

- vaccine trials,
- studies of basic biological processes,
- studies of pharmacokinetics and organ transplantation, and
- studies of nutritional, breeding and management methods to increase the supply and quality of food and fiber.

Unlike typical laboratory animals, farm animals used for research and teaching may be housed in many different kinds of environments, ranging from traditional laboratory environments to enclosed or extensive farm settings. Because of these factors, as well as the regulatory complexity surrounding farm animal oversight, determining standards for the evaluation of research, teaching, and testing using farm animals is more complicated than for other laboratory animals.

#### ***Applicability of PHS Policy and the AWRs***

Farm animals used for improving animal nutrition, breeding, management, production efficiency, or the quality of food and fiber are specifically excluded from the definition of “animal” in the AWA. The *PHS Policy* applies to vertebrates used in research, research training and biological testing, funded by the PHS. Some Assurances extend coverage of the *PHS Policy* to all animal activities at an institution. Hence, farm animals used in research, teaching or testing may be covered by the *PHS Policy* and the AWRs. Farm animals used in agricultural research may not be covered by either.

OLAW advises institutions that uniform and consistent standards are an essential ingredient in a quality animal care and use program. Public perception of a potential double standard should also be considered.



AAALAC also uses both the *Guide* and *Ag Guide* as reference documents for the accreditation of farm animal facilities and programs. Thus, the use of a performance-based approach is desirable.

### ***Review of Protocols and Facilities***

Institutions employ a number of different approaches to reviewing activities involving animals used for agricultural research and teaching. Some have a single committee that reviews all protocols, while others have a sub-committee or even a separate committee that reviews agricultural animal research protocols. (As applicable, committees must comply with the membership and review procedures required by the *PHS Policy* and the *AWRs*.) There are benefits and limitations associated with each of these approaches. However, what is most important is that the institution ensures uniform and high-quality oversight of all research, teaching, and testing activities involving animals, regardless of the species or the type of research being conducted.

For thorough oversight of agricultural animal care and use, it is particularly important that there be agricultural expertise on the IACUC. The *Ag Guide* suggests that the IACUC include, among other members:

- a scientist from the institution with experience in agricultural research or teaching involving agricultural animals;
- an animal, dairy or poultry scientist who has training and experience in the management of agricultural animals; and
- a veterinarian who has training and experience in agricultural animal medicine and who is licensed or eligible to be licensed to practice veterinary medicine.

There are unusual aspects of agricultural research that deserve careful consideration by IACUCs. As mentioned previously, there are certain husbandry practices common on commercial farms that have the potential to cause pain or distress that would not ordinarily be permitted under the regulations governing research. The *Ag Guide* recommends that IACUCs review these procedures, as well as husbandry conditions that do not meet the standards outlined in the *Ag Guide*, even if they are considered normal practice. Another unusual aspect of agricultural research is that the animals may be killed and marketed for human food at the end of studies, which means that there are special considerations with respect to avoiding residues from therapeutics and other drugs.



Stricklin, W.R. and J.A. Mench. 1994. Oversight of the use of agricultural animals in university teaching and research. *ILAR News* 36:9-14.

Swanson, J.C. 1998. Oversight of farm animals in research. *Lab Animal* 27, 28-31.

Tillman, P. 1994. Integrating agricultural and biomedical research policies: conflicts and opportunities. *ILAR News* 36:29-35.

AAALAC International Position Statement on "Farm Animals".

### **C.3.b. Antibody Production**

Antibodies are important tools for research. Depending on research needs antibodies may be produced by polyclonal or monoclonal technique. Each technique requires that specific issues be addressed in animal protocols. IACUCs should ensure adequate training of personnel in the use of proper technique when any method of immunization is proposed. The advantages of a centralized service utilizing skilled technicians to meet multiple research groups' needs for polyclonal and monoclonal antibodies is another refinement which may enhance animal welfare in larger research programs. There are also many commercial sources of antibodies made to order.

A good resource is "Information Resources for Adjuvants and Antibody Production: Comparisons and Alternative Technologies." AWIC Resource Series, No. 3. August 1997. Call Number: aHV4701.A94no.3. ISBN 090076791X. The document includes over 500 bibliographic citations regarding adjuvants and antibody production methods compiled from scientific journals, proceedings and newsletters. A company/institute listing of suppliers of antibodies and antibody production products is included. Emphasis is placed on citing comparative studies and research into alternative methods.

#### ***Polyclonal Antibody Production***

Injection of an immunogen (e.g., protein, virus, bacterium) into an animal produces a humoral response, which induces the production of a population of heterogeneous antibodies, with varying specificities toward different molecular regions (epitopes) of the immunogen. Two types of lymphocytes (T cells, derived from the thymus, and B cells, derived from marrow) are responsible for the production of polyclonal antibodies. Polyclonal antibodies produced in response to infection can be effective in recognizing and eliminating foreign material, but the heterogeneity of the product limits its use in research and industry.



Because of the severity of the secondary immune response to mycobacterium in CFA, IFA must be used with booster antigen administrations in cases where CFA has been used in the initial injection.

For many years CFA was the only effective adjuvant, but this is no longer true. Other adjuvants are available as alternatives and may be suitable for use in an investigator's experiments.

### ***Route of Injection***

The range of recommendations for routes and sites of administration of antigen-adjuvants preparations, volumes per site and number of sites per animal for different species vary in the literature and institutional guidelines. Particularly with the use of CFA, it is important to note that the severity of potentially painful inflammatory reactions may be minimized by injection of a small volume of inoculum per site and the use of multiple injection sites when appropriate. Injection sites must be sufficiently separated to prohibit coalescing of the inflammatory lesions.

Using multiple sites for immunization also provides more foci for antigen presentation and the involvement of more lymph nodes. Intradermal and subcutaneous routes are commonly used to take advantage of antigen-processing dendritic cells present within the dermis. Hair should be clipped from intradermal and subcutaneous injection sites, and the site should be aseptically prepared with betadine or nolvasan scrub followed by alcohol or other appropriate antiseptics. The following recommendations apply primarily to antigen solutions in CFA or IFA. Volumes ranging from 0.05 ml to 0.10 ml per site have been recommended for intradermal injections in rabbits. A total of five intradermal sites has been recommended. Because intradermal sites ulcerate with FCA, sterile inocula must be used and the site must be properly disinfected to prevent secondary bacterial infection. Subcutaneous injection volumes in the rabbit vary from recommendations of 0.10 ml to 0.25 ml to 0.40 ml per site. Number of sites recommended varies from 4 to 10.

Footpad injections in rabbits are prohibited. Where scientific justification is provided, footpad injections may be permitted in rodents, but only in one hind foot, and with the animals housed on soft bedding. Suggested maximum injection volumes can range from 0.01 to 0.05 for mice and 0.10 ml for rats. The need for footpad injections must be critically evaluated by the IACUC before approval.



The ascites method has been one of the most popular means for producing large quantities of highly concentrated monoclonal antibodies since its inception in 1972. However, improved techniques and culture media have demonstrated that mAbs can be produced by *in vitro* techniques at a quality and concentration that are similar to that of ascites. The National Research Council's report on Monoclonal Antibody Production specifically states "*in vitro* methods for the production of monoclonal antibodies should be adopted as a routine method unless there is a clear reason why they cannot be used...". In accordance with the *PHS Policy* and the *Guide*, alternatives to the use of animals (*in vitro* techniques) for the production of mAbs must be considered in place of the ascites method. (See the [Office of Extramural Research Guidance concerning the Production of Monoclonal Antibodies in Animals, NIH Guide for Grants and Contracts, Notice OD-00-019, 2/3/2000](#), and the [11/17/97 OPRR Dear Colleague letter on Production of mAbs Using Mouse Ascites Method](#)).

The ascites method should only be used after *in vitro* failure of each cell line has been demonstrated, or other adequate justification is provided. Analysis of individual cell lines is necessary because the production performance of each hybridoma cell line grown *in vitro* is highly variable. Despite this variability, work performed by Petrie indicates that at least 90% of all hybridomas that are placed on *in vitro* production protocols will yield adequate amounts of high quality mAbs.

Several resources for the *in vitro* production of mAb are available. Some institutions have core facilities that may provide an *in vitro* mAb production service. The NIH also sponsors a national cell culture core facility (National Cell Culture Center, Minneapolis, MN; <http://www.nccc.com>).

## **References**

### ***In Vitro* mAb Production References**

Jackson, L.R., B.A. Trudel, and N.S. Lipman. 1999, Small Scale Monoclonal Antibody Production *in Vitro*; Methods and Resources. *Lab Animal* 28(3):38-50.

Alternatives in Monoclonal Antibody Production, 1998, The Johns Hopkins Center for Alternatives to Animal Testing (CAAT) and National Center for Research Resources (NCRR) Workshop.

Schulhof, J. (ed). 1999. Small-Scale Monoclonal Antibody Production, special edition *Lab Animal* Autumn 1999.



Investigators developing a new spontaneous or induced mutant animal model need to maintain their own breeding colony because there is no alternative source for this mutant. While trying to establish a breeding colony for a new mutant model, the investigator is also simultaneously working to determine phenotype, to identify affected physiological system(s), and define inheritance pattern.

To review standard operating procedures for breeding colonies, the IACUC will need information about colony management. Examples of necessary information include:

- number of breeders and number of young per cage,
- breeding system including number of females per male or continuous versus interrupted mating,
- weaning age,
- separation of animals at weaning, and
- methods for identification of individual animals.

Large numbers of animals may be required to maintain a breeding colony. The exact number of animals can only be approximated because it is impossible to predict in advance the exact number and sex of offspring. The estimated number of animals should clearly distinguish between:

- breeders,
- young that cannot be used in experiments because they are of the wrong genotype or sex, and
- animals that will be subject to experimental manipulations.

Colony management practices should be briefly described in the investigator's animal protocol, and justification provided for departure from standard institutional practices.

Determining which animals to include in the estimated number of animals on an animal protocol can be challenging to the investigator and the IACUC in the absence of IACUC-developed guidelines. The estimated number of animals that are kept for breeding purposes and not subject to any experimental manipulations should be part of the animal protocol.

Studies involving genetic analysis are animal intensive. Genetic analysis can involve determining if a single gene has dominant or recessive inheritance, identifying different genes involved in a quantitative (polygenic) trait,



be included in the number of animals used. If suckling animals will be euthanized at or prior to weaning because they are the wrong genotype or sex for the experiment, then they may be included as animals held or euthanized but not subject to experimental manipulations.

One option is for the IACUC to request estimated animal numbers as follows:

Estimated number of weaned and adult animals to be subject to experimental manipulations	_____ *
Estimated number of suckling animals to be subject to experimental manipulations	_____ *
TOTAL	_____

\*Estimated numbers should be further subdivided based on invasiveness of procedures using institutional criteria:

Estimated number of breeders held but not subject to experimental manipulations	_____
Estimated number of suckling animals to be euthanized at or prior to weaning, and not subject to experimental manipulation	_____

In summary, the IACUC's role for oversight regarding breeding colonies includes ensuring that the need for a breeding colony has been established based on scientific or animal welfare concerns, that the procedures used in the breeding colony are evaluated and approved by the IACUC on a regular basis (e.g., as part of the semiannual program review), that there is a mechanism for tracking animals, and that the standards of care and animal well-being for the animals in the breeding colony are consistent with the *Guide*.

### **References**

Beamer, W.G., Senior Staff Scientist, The Jackson Laboratory. Bar Harbor, ME. Personal communication.

Festing, M.F.W. 1987. Animal production and breeding methods. In: *The UFAW Handbook on the Care and Management of Laboratory Animals*. 6th ed., pp. 18-34. T B Poole (ed). Churchill Livingstone Inc., New York.

Fox, R.R. and B.A. Witham (eds). 1997. *Handbook on Genetically Standardized JX mice*. 5th edition, pp. 43-44, 120-125. The Jackson Laboratory. Bar Harbor, ME.



### ***Species Selection***

The investigator should provide information on the population to be studied and a rationale for choosing that particular population. The U.S. Fish and Wildlife Service (USFWS) issues many of the necessary permits. In issuing permits the USFWS assesses the risk to the animal population and the IACUC may rely on that assessment rather than attempt to determine the potential impact on the population.

With regard to small or declining populations, many state wildlife or natural resource agencies also issue research permits. In the event that a state research permit is required and has been issued, the IACUC may assume that the state agency has assessed the risk to the population and found it to be acceptable.

An IACUC that has additional questions about the selection of species or the impact on the population to be studied may require the investigator to provide additional information or the Committee may consult with biologists with relevant expertise.

### ***Site Selection***

The selection of the study site for the research should maximize the opportunity for data collection and minimize the disruption caused by the investigator. The selection process should also take into consideration other activities in the area, such as agricultural practices, tourism, and hunting, which may interfere with the research protocol.

Permission to utilize the site may be necessary and the investigator must be able to assure the IACUC that necessary permits or permission have or will be obtained. Appendix E describes various site-specific permits required for field investigations.

### ***Methodologies Employed***

The potential short- and long-term effects of procedures on individual animals should be evaluated in all protocols. If animals are to be captured, the methods used and the numbers involved should be detailed in the protocol submitted to the IACUC. There should be a description of measures taken to prevent potential injuries and alleviate potential distress, and of the possible impact of capture on subsequent behavior and survival of the animals.

If animals are to be monitored individually, the investigator must indicate whether they will be identified by natural markings or will be artificially



Euthanasia of wildlife in the field can raise unique and challenging issues. The Report of the AVMA Panel on Euthanasia includes considerations and techniques for euthanasia of wildlife and should be used by the IACUC as a resource.

### **Conclusion**

Many of these issues are difficult to address definitively, but their consideration will help the IACUC judge the potential impact and value of the study proposed, and can be expected to assist the investigator in obtaining maximum information from the study with minimum negative impact on the animals studied or their environment. The IACUC should ensure that the investigator complies with applicable regulations and policies and obtains any required permits; the IACUC may wish to obtain copies. Many of the issues arising from proposals to conduct field research on vertebrate animals will require the judgment of experienced professionals in the field and the IACUC should feel free to seek advice or consultation if necessary.

### **References**

Acceptable field methods in mammalogy: Preliminary guidelines approved by the American Society of Mammalogists. 1987. *J Mammalogy* 68(4, Suppl.): 1-18.

Bowman, P. 1989. Institutional animal care and use committee review of wildlife field research. *Lab Animal* 18 (3): 28-30.

Burghardt, Z.M. and H.A. Herzog, Jr. 1980. Beyond conspecifics: Is Brer Rabbit our brother? *Bioscience* 30: 763-768.

Guidelines for the Capture, Handling, and Care of Mammals. Undated. American Society of Mammalogists. (<http://www.mammalsociety.org/committees/commanimalcareuse/98acucguidelines.PDF>)

Guidelines for the treatment of animals in behavioural research and teaching. 2000. *Animal Behavior* 59:253-257.

Guidelines for the use of fish in field research. 1987. American Society of Ichthyologists and Herpetologists (SIH), American Fisheries Society (AFS), and the American Institute of Fisheries Research Biologists (AIFRB). *Copeia* (Suppl.) 1-12. Also: *Fisheries* 13(2):16-23.

Guidelines for the Use of Live Amphibians and Reptiles in Field Research. 1987. American Society of Ichthyologists and Herpetologists (ASIH), The Herpetologists' League (HL), and the Society for the Study of Amphibians and Reptiles (SSAR). *J Herpetology* 4 (Suppl.): 1-14.

*Guidelines to the use of wild birds in research*. 2d Edition, 1999. The Ornithological Council.



### ***Radioactive Materials***

The U.S. Nuclear Regulatory Commission (USNRC) directly, or by its state designee, issues licenses permitting institutions to procure, use and dispose of specified radioactive materials. These licenses do not cover:

- X-ray machines;
- high voltage accelerators;
- electron microscopes; and
- radioactive materials from sources other than reactor by-products, although these are all sources of ionizing radiation.

RSCs have oversight for the procurement, use and disposal of radioactive materials; therefore, their approval should be coordinated with IACUC review of any proposal that involves radioactivity. General information on potential health risks from exposure to ionizing radiation can be found in the USNRC Regulatory Guide.

### ***Biohazardous Materials***

Infectious diseases may be a factor in many animal studies due to natural infections as well as those specifically induced as part of research. Consensus biosafety guidelines have been established for the use of animals in research involving infectious agents (*Biosafety in Microbiological and Biomedical Laboratories*). These guidelines provide a concept for assessing risks and selecting appropriate safeguards. Four biosafety levels, which consist of combinations of practices, safety equipment and facilities, are described in this CDC/NIH document.

Certain human pathogens as listed in the Select Agent List (Appendix A, 42 CFR 72.6) must be registered and approved by the Centers for Disease Control (CDC) prior to transfer from one registered facility to another. Similar requirements are in place with the USDA for the transfer of foreign animal disease agents.

The NIH publication, *Guidelines for Research Involving Recombinant DNA Molecules*, promulgated by the NIH Office of Biotechnology Activities, also includes four biosafety levels and represents a key reference for work involving recombinant microorganisms. Recombinant DNA experiments involving animals also require approval from the IBC.



Another class of hazardous chemical routinely encountered in the laboratory environment is aldehydes. Specific OSHA guidelines are available for handling aldehydes and other chemicals. *Material Safety Data Sheets*, which provide useful information on specific hazardous chemicals, must be accessible on site for each hazardous agent present.

### ***Hazardous Waste***

Animal wastes contaminated with radioactive materials, recombinant organisms, infectious agents or other hazardous chemical agents must be carefully managed to avoid human exposure or damage to the environment. Special efforts should be made in experimental design to minimize the generation of wastes containing hazardous chemicals. Those containing radioactivity in addition to hazardous chemicals are particularly difficult to deal with. Wastes containing infectious agents should be decontaminated, preferably in a steam autoclave, before disposal. Incineration is the recommended treatment for contaminated feed and bedding. The professional health and safety staff, who have responsibility for hazardous waste management at the institution, should review institutional policies when animal care proposals involving hazardous materials are received.

### ***References***

*Biosafety in Microbiological and Biomedical Laboratories*, 4th Edition, May 1999. U.S. Department of Health and Human Services Publication (CDC) 93-8395.

NIH Guidelines for Research Involving Recombinant DNA Molecules. NIH Office of Biotechnology Activities.

Occupational Exposure to Hazardous Chemicals in Laboratories. January 31, 1990. *Federal Register* Vol. 55:3327-3335 29CFR1910.1450.

U.S. Nuclear Regulatory Commission Regulatory Guide. 1996. Regulatory Guide 8.29, Instruction concerning risks from occupational radiation exposure.

*Occupational Health and Safety in the Care and Use of Animals*. 1997. National Research Council, National Academy Press, Washington, DC.



For other behavioral studies using non-aversive stimuli, such as running mazes, it may be necessary to maintain animals at a reduced body weight to enable food treats to be used as an effective reward. Experiments involving food and water restriction for teaching purposes must be rigorously justified and carefully monitored.

- Some behavioral studies produce potentially high levels of distress, including those using aversive stimuli, such as unavoidable noxious electric shock and surgical ablations or drug-induced lesions designed to affect the animal's behavior or performance. The educational benefits of such procedures should be carefully reviewed and clearly justified, bearing in mind that studies involving unrelieved pain or distress are generally inappropriate when employed solely for instructional purposes (U.S. Government Principle IX).
- Laboratory studies in physiology, neurophysiology, biology, and pharmacology often involve observations and experiments using animals. For all procedures, including those in which animals are euthanized to obtain tissues (e.g., in the teaching of anatomy or tissue harvest for *in vitro* procedures), the procedures and method of euthanasia, if any, must be reviewed by the IACUC. The number of animals used should always be the minimum necessary to accomplish the objectives of the proposed educational activity.

### ***Animal Use in Veterinary Teaching***

Many North American veterinary schools use live animals to teach anesthesia, animal handling, surgical procedures, recovery from anesthesia, post-operative management and postmortem examinations following terminal procedures. Animals designated for teaching may be kept long term and participate in many classes over the course of a year or more.

All instructional use of animals in non-survival as well as survival instructional procedures should be reviewed by the IACUC. Repeated procedures on designated teaching animals should be limited and reviewed by the IACUC. Federal limitations on multiple survival surgeries must be observed. Cost savings alone is not an adequate reason for performing multiple survival surgical procedures.

Some schools make alternatives available for those students who do not wish to participate in animal laboratories. Alternatives to the use of animals acquired specifically for instruction include the use of client-owned animals, or dogs and cats from animal control facilities that are made



### **C.3.g. Surgery**

Surgical procedures are a common component of animal research activities, and IACUCs are often called upon to assess the details of these procedures. Further, the IACUC is responsible for determining that personnel are qualified and trained in the procedures to be performed.

#### ***Definitions***

*Major surgery:* Penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions.

*Minor surgery:* Does not expose a body cavity and causes little or no physical impairment.

*Survival surgery:* The animal awakes from surgical anesthesia.

*Non-survival surgery:* The animal is euthanized before recovery from anesthesia.

#### ***Reviewing Protocols for Surgical Procedures***

Some of the aspects of a surgical procedure that the IACUC reviews are:

- details of the procedure (e.g., the actual procedure itself, pre- and post-operative care, aseptic technique, sequence of multiple procedures);
- appropriateness of the species for the procedure proposed;
- qualifications of the personnel performing the surgical procedures;
- species-specific and procedure-specific facility requirements;
- patient monitoring practices in the surgical and post-surgical periods; and
- personnel occupational health and safety issues.

The veterinarian should always be one of the IACUC's primary sources of information on surgery and post-operative issues. Other sources include the AWRs (9 CFR 2.31(d)(1) (ix) and (x)), the *PHS Policy*, the *Guide*, and other publications referenced at the end of this section. While the numerous references available provide background and a basis for reviewing surgical protocols, the IACUC relies on professional judgment to review the unique situations surrounding surgery in an experimental setting. Surgical procedures performed in a research setting have review requirements that may be different from those in a routine veterinary clinical setting.



If a procedure may cause more than momentary or slight pain or distress, the AWRs prohibit the use of paralytics without concurrent anesthesia.

Some procedures may require specialized facilities to ensure their success. For example, major survival surgery in non-rodents requires dedicated surgical facilities. Details of such physical requirements can be found in the *Guide*. The IACUC should assess the availability of necessary facilities during the protocol review process.

### ***Patient Monitoring***

The sophistication of patient monitoring required varies with the species and the procedure, but during protocol review, the IACUC should expect evidence of the following:

- a pre-surgical assessment;
- adequate monitoring of depth of anesthesia and animal homeostasis during the surgical procedure;
- support such as fluid supplementation, external heat or ventilation;
- monitoring and support during anesthetic recovery; and
- post-surgical monitoring details, (e.g., what will be done and how often, who will be responsible, and the name and phone number of the individual to contact in the case of post-surgical complications).

### ***Recordkeeping***

Recordkeeping is an essential component of peri-operative care. For major surgical procedures on non-rodent mammals, an intra-operative anesthetic monitoring record should be kept and included with the surgeon's report as part of the animal's records. This record should be available to the personnel providing post-operative care. Post-operative records, at a minimum, should reflect that the animal was observed until it was extubated and had recovered the ability to stand. These should be supplemented by records evaluating the animal's recovery, administration of analgesics and antibiotics, basic vital signs, monitoring for infection, wound care, and other medical observations.



*Transgenic* refers to insertion of exogenous DNA (deoxyribonucleic acid) into cells. Typically, cDNA (complimentary deoxyribonucleic acid) made from specific mRNA (messenger ribonucleic acid) is inserted into cells using microinjection, electroporation or certain nonpathogenic viruses. (Electroporation is the brief application of an electric field to a cell to increase permeability of the cell membrane for purposes of introducing drugs or genes into the cell.) Each of these methods has been used to insert new DNA into the pronucleus of a fertilized mouse egg and to create transgenic mice. The manipulated fertilized eggs may or may not be cultured *in vitro* for one to three days before they are surgically implanted into the oviducts or uterus of pseudopregnant female mice. The inserted DNA incorporates in chromosomes of a percentage of embryos developing from the micro-injected eggs. The DNA incorporates at different genetic locations and a different number of copies of the DNA may incorporate in different embryos. Thus, each embryo has the potential to become a unique transgenic mouse even though the same quantity and type of DNA was injected into genetically identical fertilized eggs. All manipulated, fertilized eggs do not become live born transgenic mice. Losses occur at every step from injection through gestation and delivery.

Mice can carry transgenes, but unless the cDNA is incorporated into germ cells, the mouse is unable to transmit the transgene to its offspring. A mouse that passes the transgene to the descendants is called a ‘founder’. Thus, many fertilized eggs have to be injected to obtain a few transgenic mice, and only a few of these transgenic mice will be ‘founders’ of this transgenic line.

*Targeted mutation* refers to a process whereby a specific gene is made nonfunctional (‘knocked-out’) or less frequently made functional (‘knocked-in’). Creation of a targeted mutation requires several steps in the laboratory. The specific gene is identified, cloned and manipulated to make it nonfunctional (‘knocked-out’). The manipulated gene is attached to another DNA sequence called a promoter and introduced into embryonic stem (ES) cells by electrical or chemical methods. These ES cells are cultured in special media that permits identification of ES cells incorporating the manipulated gene. ES cells incorporating the manipulated gene are injected into an early embryo (blastocyst). The ES cell injected blastocysts are surgically implanted into the uterus of pseudopregnant female mice. Some injected blastocysts develop into viable embryos and gene deficient ‘knock-out’ mice are born.



that produce no observable, clinical impact on the well-being of the mouse. If the mutant phenotype has minimal impact on the well-being of the animal, the standard of 'normal' can be similar for mutant and non-mutant animal. Hypogonadal (Gnhr<hpg>) and 'little' (Ghrhr<lit>) are examples of spontaneous mutations with minimal impact on well being of the mouse. Homozygous hypogonadal mice are normal in all ways except for small, non-functional gonads. Homozygous 'little' mice are smaller than non-mutant littermates. Growth hormone transgenic mice tend to have larger body size than normal, but are otherwise clinically normal with the exception of reduced fertility.

In the case of mutants where phenotype involves clinical abnormalities, the standard for 'normal' may have to be modified to encompass the expected phenotype. For example, 4 to 5 week old homozygous dystrophic mice (Lama<dy-2J>) have difficulty abducting hindlegs and have an abnormal gait. As these mice age, muscular weakness progresses in hindlegs and eventually extends to involve all skeletal muscles. The standard for 'normal' for homozygous dystrophic mice must include difficulty abducting hindlegs and an abnormal gait. Adenopolyposis coli 'knock-out' mutant mice (Apc<Min>) are clinically normal until the intestinal polyps develop, after which time the mice become anemic and lose weight. Experimental end-points for these latter and similar mutant models should focus on (1) ability of the mutant to access feed and water, (2) response of the mutant to stimuli, and (3) general condition of the mutant (i.e., is the mutant excessively thin, showing progressive weight loss or hunched posture?).

Many institutions have a centralized induced mutant facility that receives the genetic material from investigators and performs the manipulations to develop 'founder' transgenic or 'knock-out' mice. The 'founder' mice are returned to the investigator who undertakes breeding to expand the line. Review of the centralized induced mutant facility should focus on personnel qualifications, animal related practices such as aseptic surgery, and average number of mice required to produce 'founders' for a single DNA construct, recognizing, however, that the number of mice required is a very rough estimate because of differences in responses of different strains or stocks of mice, variations in success rate for different DNA constructs, and subtle or less subtle uncontrollable environmental changes.



## **C.4. Monitoring of Approved Protocols**

After the IACUC has approved a protocol, it has a responsibility to ensure that procedures are carried out in the laboratory or classroom as described in the protocol. This section will briefly review ways that the IACUC can monitor the conduct of approved protocols.

### **Acquisition and Tracking**

Animals should be obtained only from licensed dealers or other legal sources, and it is incumbent upon an institution to establish mechanisms to monitor and document the number of animals acquired and used in approved activities. This is best accomplished if animal purchases may be made only through the institution's animal resource facility or other appropriately designated office. Once animals have been acquired, they should be included in a tracking system. Many institutions have automated systems that will alert an appropriate individual when an investigator has reached a preset percentage (e.g., 80 to 90%) of the number of animals approved for a specific project, and can prevent ordering animals in excess of the number approved. Institutions with small programs using limited numbers of animals may choose to maintain a manual log of IACUC approved activities and numbers of animals acquired.

Tracking animal use becomes more complicated when investigators maintain breeding colonies. Keeping track of animal usage may be accomplished by requiring that investigators with breeding colonies maintain accurate records. Investigators can be required to report to the designated office, at regular intervals, the number of animals born, weaned, or used in studies. This report can be tallied against the numbers in the approved protocol.

### **Compliance Specialist**

Some IACUCs have a full or part-time compliance specialist who monitors procedures in vivaria, laboratories, and classrooms, and reports his or her observations to the IACUC. This individual should have laboratory animal training and experience, and be authorized to conduct announced or unannounced laboratory inspections on behalf of the IACUC. In addition to this role, the compliance specialist may periodically survey individual



## **Review of Publications**

In academic institutions and many companies, much research is eventually published. Some IACUCs choose to review some published descriptions of animal use to verify that work was done according to the approved protocol.

## **Conclusion**

Although no IACUC has the staff or time to observe all animal use in an institution, the IACUC can help establish a climate of compliance. To ensure that animal use conforms to local policy and federal regulations, it is prudent for the IACUC to confirm that animals are used according to protocol.

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## **D. Evaluation of Animal Care and Use Concerns**

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## **Evaluation of Animal Care and Use Concerns**

To help ensure that laboratory animals receive humane care and use or treatment in accordance with the highest ethical standards, laws, regulations and policies governing animal research, the IACUC must review and, if warranted, address any animal-related concerns raised by the public or institutional employees. Procedures must be established to ensure that concerns are communicated to the IACUC. The Committee must review each concern in a timely and systematic manner and, when necessary, take prompt, appropriate corrective actions.

## **PHS Policy, Animal Welfare Act, and USDA AWR requirements**

The *PHS Policy* requires the IACUC to “review concerns involving the care and use of animals at the institution”, and the *Guide* states that the IACUC is responsible for “establishment of a mechanism for receipt and review of concerns involving the care and use of animals.” The Animal Welfare Act (AWA) (7 U.S.C. 2142; Section 13) requires training of personnel who are involved in animal care or treatment, including “methods whereby deficiencies in animal care and treatment should be reported.” The AWRs (9 CFR Part 2, Subpart C, 2.32 (c)(4)) require each research facility to provide the methods whereby any employee of the facility can report deficiencies in animal care and treatment. In addition, the AWRs, Section 2.31(c)(4) require the IACUC to “review and, if warranted, investigate concerns involving the care and use of animals at the facility resulting from public complaints received and from reports of noncompliance received from laboratory or research facility personnel or employees.”

In addition, the AWRs (9 CFR Part 2, Subpart C, Section 2.32(c)(4)) state that “no facility employee, Committee member, or laboratory personnel shall be discriminated against or be subject to any reprisal for reporting violations of any regulation or standards under the [Animal Welfare] Act.”

## **Compliance**

To ensure compliance with federal law, regulations, and policies, it is strongly recommended that each IACUC develop and implement policies and procedures to ensure that all animal care and use concerns are brought to its attention for consideration. Some of the elements that should be included



Although written concerns are more convenient to deal with, complainants may not be willing to submit them in this manner. In such cases, the individuals who receive concerns should document them fully to ensure that the issues are clear and to prevent misunderstandings. Requests for anonymity should be honored to the extent possible.

## **IACUC Responses to Complaints**

While specific methods for evaluating concerns about animal care and use may vary from institution to institution, all methods should contain these elements:

- There should be a procedure for verifying stated concerns.
- Verified concerns should be related to the AWRs, the *PHS Policy* or institutional policies.
- There should be guidelines for effecting appropriate corrective measures, when necessary.

One of the roles of the IACUC is to review all concerns about the animal care and use program, regardless of origin, and investigate them if warranted. The IACUC Chair is normally responsible for ensuring that concerns are addressed, but may delegate investigation to a subcommittee. If the Chair has, or is perceived to have, a conflict of interest, the Institutional Official (IO) should delegate the responsibility for assuring that the concern is addressed to another non-conflicted member of the IACUC.

Concerns may include situations or activities ranging from those in which animals are reported to be in immediate, actual or perceived jeopardy to those in which violations of the AWRs or institutional Animal Welfare Assurances are alleged to be occurring but animals are not in apparent danger. They may focus on allegations of past policy and procedure violations.

The course of action taken by the IACUC should be driven by the potential significance of the alleged situation. For example, conditions that reportedly jeopardize the health or well-being of animals should be evaluated immediately. To cope promptly with such situations, some institutions have policies whereby a veterinarian or other designated person is authorized to halt procedures which they believe do not comply with institutional policies until the IACUC can be convened and consider the matter formally. Similarly, situations that may involve potential criminal activity or human safety should be reported promptly to the institution's law enforcement or



## **Suggested IACUC Procedures for the Investigation of Animal Care and Use Concerns\***

### ***Initial Evaluation and Actions***

Upon receipt of a concern the IACUC Chair should convene a meeting of the IACUC. After initial review of the complaint the IACUC should determine whether it requires further investigation and immediate action, further investigation but no immediate action, or no action. Once this decision has been made, the IACUC should determine which individuals or other institutional or noninstitutional offices may require notification at this time.

If immediate action appears warranted because animal or human welfare may be compromised, the IACUC should notify the IO and proceed accordingly. Veterinary medical intervention, suspension of a research activity, and/or notification of appropriate safety, occupational health, or other officials, are examples of actions that may be taken immediately to protect animal or human welfare. In accordance with the AWRs (9 CFR Part 2, Subpart C, Section 2.31[d][7]), if an activity is suspended, the IO shall report that action to APHIS and any federal agency funding that activity. If the activity is supported in any way by the PHS, the IACUC, through the IO, must promptly notify OLAW (PHS Policy, IV.F.3.) (OPRR Reports 94-02, 1/12/94).

### ***Investigation***

Should the IACUC determine that further investigation is required, the Chair, or another individual or subcommittee appointed by the Chair, should conduct the investigation and report back to the IACUC. It is important to avoid actual or perceived conflicts of interest in this process.

The IACUC should charge the designated person or group with its requirements for information gathering and impose a completion date. The assigned completion date will depend on the IACUC's determination of whether immediate remedial action may be required.

### **\*DISCLAIMER**

*Neither the AWRs nor the PHS Policy provide specific guidance regarding the consideration of concerns or the institutional conduct of investigations. Owing to the considerable diversity of concerns that may arise and the contexts in which they may be voiced, no one set of procedures will be suitable for investigating all potential situations that involve violations of or deviations from animal care and use practices required by the PHS Policy, AWRs, the Guide and other federal statutes and regulations regarding animals. Consequently, the following suggestions are broad, intended for general use, and not intended for application in all situations.*



Subsequent actions of the IACUC may include:

- implementing measures to prevent recurrence (such measures often include changes in administrative, management or IACUC policies and procedures, and may include sanctions\*);
- notifying the IO and the AV of its actions;
- notifying funding or regulatory agencies, as required; and
- notifying the complainant, any persons against whom allegations were directed, and pertinent program officials (appropriate supervisory and management staff, the public affairs office, institutional attorneys, etc.).

*\*Note on Sanctions:* Aside from empowering the IACUC to suspend a previously approved activity, the AWRs and the *PHS* Policy are silent regarding IACUC- or institutionally imposed sanctions.

Some institutions, as part of their programs, have developed policies and procedures that authorize the IACUC to impose sanctions on behalf of the institution. In other institutions, IACUCs recommend actions to the IO for implementation, and in still others, there exists a combination of these approaches. Some of the institutional sanctions that have been devised include:

- counseling;
- issuing letters of reprimand;
- mandating specific training aimed at preventing future incidents;
- monitoring by the IACUC or IACUC-appointed individuals of research, testing, or training involving animals;
- temporary revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals, pending compliance with specific, IACUC-mandated conditions;
- permanent revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals; and
- recommending to the IO that institutional (e.g., reassignment, termination of employment) sanctions be imposed.



# **E. Recordkeeping and Communications**

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## E.1. Recordkeeping and Reporting

### Introduction

The *PHS Policy* and AWRs include recordkeeping and reporting requirements. The responsibility for these functions should be clearly delegated. Usually the IACUC office is assigned this task. The individuals responsible should understand federal animal use requirements and the institution's program, and should also be aware of the Freedom of Information Act (FOIA) and any state open records laws. Many of the reports written may be accessible under such laws, and care should be taken to use language that is clear and precise to ensure accurate interpretation.

### Recordkeeping

#### *Minutes*

The *PHS Policy* and the AWRs require that the institution maintain “minutes of IACUC meetings, including records of attendance, activities of the Committee, and Committee deliberations” (PHS Policy IV. E; 9 CFR Part 2 Subpart C 2.35 (a)(1)). The IACUC has some latitude in the degree of detail in these minutes.

*Records of attendance:* Although members may arrive late or leave during a meeting, generally a member is marked as either present or absent. An exception would be when the IACUC member leaves the meeting room during discussion of a protocol on which that member is a participant. If the temporary absence of a member drops the number of members present below the quorum, this should be noted in the minutes. Certain official IACUC actions require a quorum (see [Section A.2. Quorum Requirements](#)).

*Activities* of the Committee include corrections or approval of previous minutes; presentation of program, policy, facility and compliance reports; and decisions on policies, protocols, and amendments.

*Deliberations* refers to the discussion and reasons leading to particular IACUC decisions. Although some IACUCs maintain a verbatim record (e.g., audio or videotapes), minutes should include as a minimum a summary of the key points discussed prior to a committee decision.



It is important that the approved Assurance document is distributed appropriately within the institution and that members of the IACUC are familiar with this document, as compliance with the Assurance is required to be eligible for PHS funding.

### ***USDA Registration***

Institutions that use species of animals covered by the AWRs for research, testing, experiments, or teaching on its premises as specified in the AWA are required to be registered with the Animal Care division of the Animal and Plant Health Inspection Service (APHIS), using APHIS form 7011. The form is submitted to APHIS via the Regional Director of Animal Care (AC) for the state in which the facility has its principal place of business. At academic institutions, the submission is usually made by the institution, not the individual departments or schools, and signed by the IO. An approved USDA registration is given a number in the format ##-X-####, where X is a letter (R for research institution) and # is usually a digit. The registration may be renewed every three years. The institution is required to notify the AC Regional Director within ten (10) days of any change in the name, address, ownership or operations affecting its status as a research facility. The Regional Director may place a facility that has not housed animals for two years in inactive status. The registration can be cancelled by written request if a facility no longer uses, or intends to use, animals (see [Table B](#)).

### ***Semiannual Facility Inspections and Program Evaluations***

The *PHS Policy* and the AWRs require that the IACUC evaluate the institution's animal program at least once every six months, including an inspection of facilities, and submit a report to the IO. The *PHS Policy* allows the IACUC discretion in how it evaluates its facilities and program. The report format is not mandated, but OLAW offers models for both facility inspections and program reviews on its Web site.

The report must contain a description of the nature and extent of the institution's compliance with the *PHS Policy* and *Guide*; any departures must be identified and modifications proposed, with a plan and timetable for correction. Any minority views of IACUC members must be included.



### ***Annual Report***

The IACUC at an institution with an approved PHS Assurance must submit an annual report to OLAW through the IO. This report details changes in the animal care and use program, IACUC membership, and AAALAC accreditation status. Minority reports from IACUC members must be included. It also includes the dates of semiannual review and reports submitted to the IO. The PHS and AAALAC annual reporting dates may be synchronized with the USDA reports.

A sample annual report format is provided on OLAW's Web site and may be utilized, but is not required.

On or before December 1, each facility registered with the USDA must submit an annual report to the APHIS, AC Regional Director, for the state in which the facility is registered. Form 7023 is usually prepared by the IACUC and signed by the CEO or IO. It lists the number of each covered species used, by pain categories. The report includes assurances that animal care and use are at professionally accepted standards, that alternatives to painful procedures have been considered (see [Section C.2.a. Alternatives](#)) and that AWRs are followed.

When an IACUC-approved deviation from USDA standards and regulations is required for scientific or other reasons, the report must address the reasons for the deviation, and the number and species of animals affected.

### ***Suspension and Noncompliance***

At an institution with an approved PHS Assurance, the IACUC must report promptly, through the IO, the circumstances and actions taken in the following instances:

- any serious or continuing non-compliance with the *PHS Policy*,
- any serious deviation from the provisions of the *Guide*, and
- any suspension of any activity by the IACUC.

It is recommended that the institution contact OLAW immediately following the event, and send a formal report, describing the circumstances and any actions taken, to OLAW after IACUC and IO review. Similarly, accredited institutions must report promptly to AAALAC serious issues relating to the animal care and use program, such as investigations by the USDA or OLAW, or other serious incidents or concerns that negatively affect animal well-being.











































































