# IACUC MANUAL

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## About this Handbook

Maintaining humane animal care in research and teaching is a dynamic endeavor and requires conscientious interpretation of animal welfare regulations. This Handbook explains the regulations, guidelines and processes involved when doing animal-based research at the University of Pittsburgh. While this Handbook addresses a wide range of matters that warrant the concern, attention and thoughtful interpretation by the research community, it claims neither to be exhaustive nor definitive, nor can it possibly address all of the inevitable variations among actual cases that will arise.

If you have a question or concern that is not addressed in this handbook, please contact one of the officers named on the handbook's cover.

## Institutional Animal Care and Use Committees

Institutional Animal Care and Use Committees (IACUC's) are self-regulating entities that, according to U.S. federal law, must be established by institutions that use laboratory animals for research or instructional purposes. Such committees are mandated by law to oversee and evaluate all aspects of an institution's animal care and use program.

Two agencies of the US Government require the appointment of an IACUC: the United State Department of Agriculture (USDA) requires an IACUC at any institution that uses animals covered under the Animal Welfare Act, and the Public Health Service (PHS) requires an IACUC at any institution that conducts PHS-supported research involving live vertebrate animals.

Section IV.A.3.b. of the PHS Policy addresses the compositional requirements of an IACUC. The Policy states that the committee must consist of not less than five members, and include at least:

- One Doctor of Veterinary Medicine, with training or experience in laboratory animal science and medicine, who has direct or delegated program authority and responsibility for activities involving animals at the institution;
- one practicing scientist experienced in research involving animals;
- one member whose primary concerns are in a nonscientific area (for example, ethicist, lawyer, member of the clergy); and
- one individual who is not affiliated with the institution in any way other than as a member of the IACUC, and is not a member of the immediate family of a person who is affiliated with the institution

No more than three regular, voting members are allowed to represent the same department or administrative unit.

# The University of Pittsburgh IACUC

The University of Pittsburgh has established an IACUC, which is qualified through the experience and expertise of its members to oversee the institution's animal program, facilities, and policies. The Institutional Official, the Vice Chancellor for Research Conduct and Compliance, has been designated by the Chancellor to appoint its membership and endorse its authority.

The Pitt IACUC consists of over 35 voting members and several ad-hoc nonvoting members, representing 25 university departments. Ad hoc non-voting members provide consultation expertise to the committee, particularly in the areas of veterinary medicine and occupational health and safety. Faculty members serve for a period of three years.

IACUC consists of over thirty faculty researchers and veterinarians, as well as other University staff with expertise in many areas that impact animal research. These individuals have volunteered their time to serve on the committee. University of Pittsburgh personnel interested in being members of the IACUC should contact the IACUC Office. The IACUC Chair recommends the appointment of new members to the Institutional Official, who appoints new members to the IACUC by issuing an appointment letter.

## Subcommittees

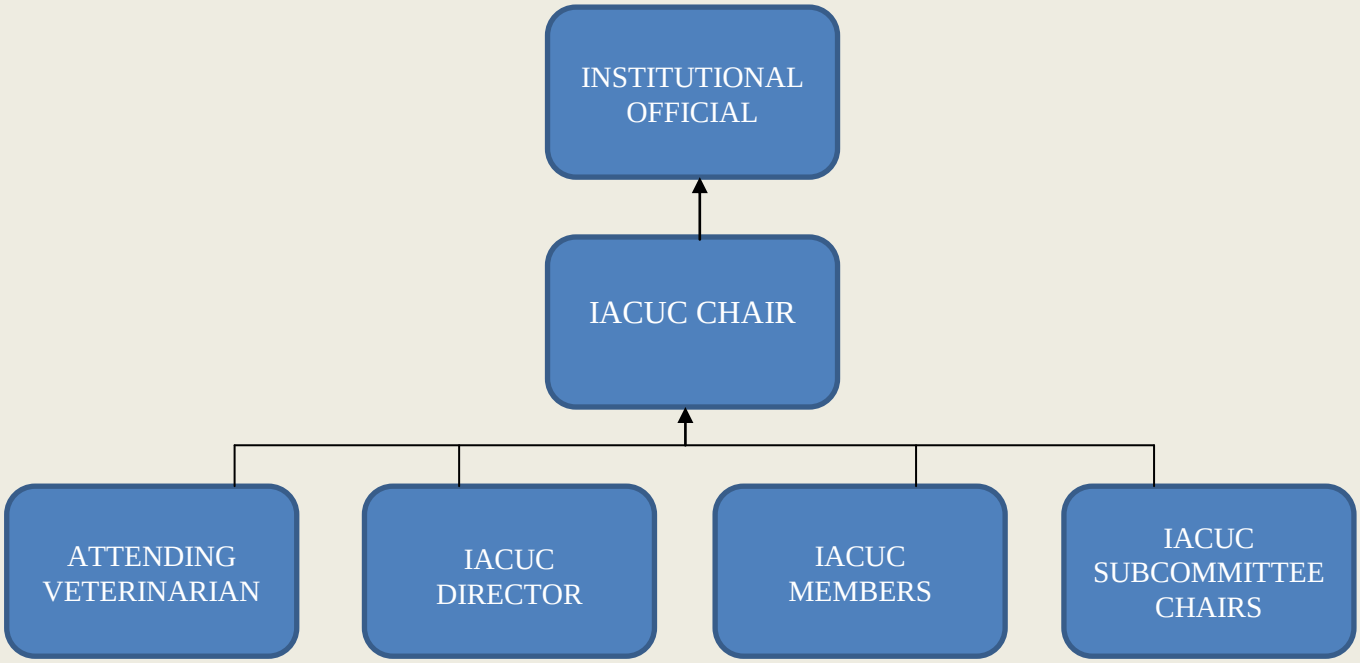
For the purpose of protocol review, the IACUC is divided into four subcommittees: three for the review of rodent protocols, and one for the review of large animals and nonhuman primates. The large volume of rodent work at the university necessitates three rodent-specific subcommittees. Each subcommittee consists of several faculty members and veterinarians that are assigned to the subcommittee by the IACUC Chair. The IACUC Chair also appoints a subcommittee chair. The subcommittee chairs function to educate new IACUC members placed on their subcommittee as to the process of protocol review and to assist in prompting reviewers delinquent on a specific protocol.

An Executive Committee exists for the purpose of reviewing IACUC issues, such as incidents of noncompliance, and for making recommendation to the IACUC on how to respond to such incidents. The Executive Committee is composed of the IACUC Chair, Vice-Chairs, the Attending Veterinarian, the IACUC Director and Compliance Officer, the IACUC Director of Regulatory Affairs, the subcommittee chairs, and legal counsel.

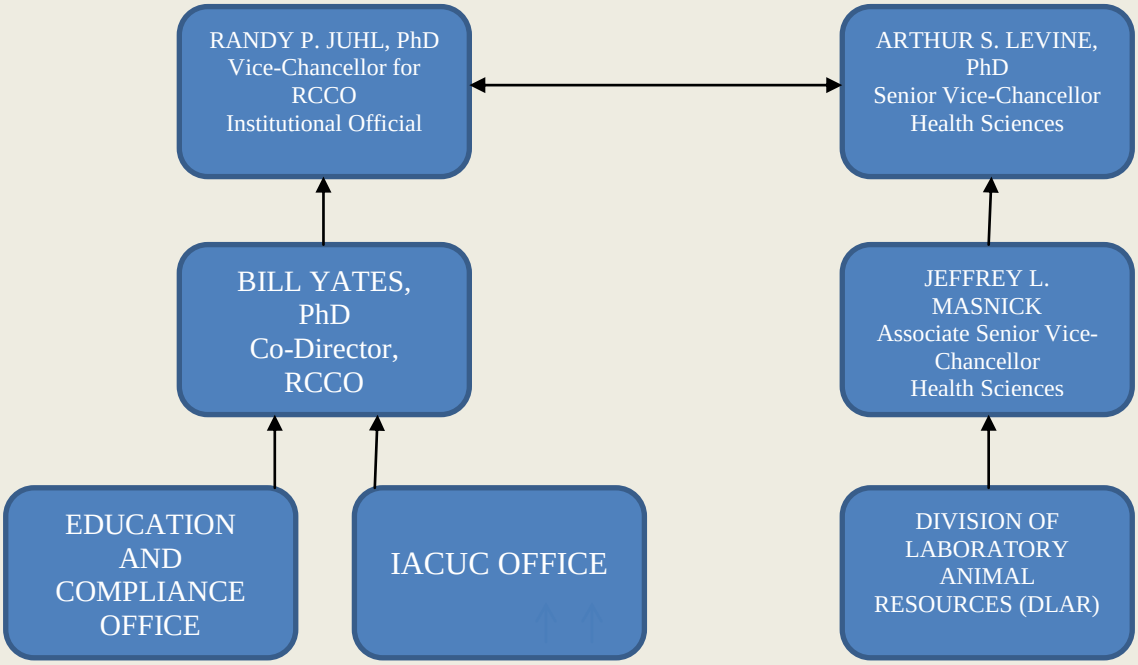
Specialty subcommittees are formed by the IACUC when the need arises.

## IACUC Reporting Structure

Functionally, the IACUC reports directly to the Institutional Official, Dr. Randy Juhl, Vice Chancellor for Research Conduct and Compliance, by the following scheme:




Administratively, as the following scheme illustrates, the IACUC Office staff report through the Research Conduct and Compliance Office (RCCO) to the Vice Chancellor for Research Conduct and Compliance. The veterinary/animal care staff of the Division of Laboratory Animal Resources (DLAR) report to the Sr. Vice Chancellor, Health Sciences.



## IACUC ROLES AND RESPONSIBILITIES

The IACUC, as an agent of the Unviersity of Pittsburgh,it charged with several responsibilities that this handbook explain in the pages that follow. In brief, they are:

- **Program Evaluation.** The review of the University's animal program every six months, using the *Guide for the Care and Use of Laboratory Animals* (*Guide*), 8th Ed. (2011), as a basis for evaluation.
- **Facilities Inspection.** The inspection of the university's animal facilities (including satellite facilities and investigator-managed housing facilities and use-sites) every six months, using the *Guide* as a basis for evaluation.
- **Animal Welfare Concerns.** The review of concerns involving the care and use of animals at the university.
- **Program Improvement.** The formulation of recommendations to the Institutional Official regarding the university's animal program, facilities, or personnel.
- **Protocol Review and Approval.** The review and approval of activities related to the care and use of animals and proposed significant changes to ongoing approved activities at the University. Likewise, the IACUC is authorized to require modifications to proposed activities and, in consultation with the Institutional Official, to suspend ongoing activities involving animals and report the action to the NIH Office of Laboratory Animal Welfare (OLAW).
- **Personnel Training.** The IACUC ensures that all personnel involved with animal care, treatment or use are provided with training on applicable University policies concerning research integrity, occupational health and safety, IACUC function, species-specific animal use, humane practices and the concept, availability and use of research, teaching or testing methods that replace, reduce, or refine the use of animals or animal distress.
- **Reporting.** The submission of reports of IACUC activities to the Institutional Official, OLAW and accreditation agencies.

## The IACUC Office

The main function of the IACUC Office is to facilitate the interaction between the IACUC and the research community at the University, to maintain accurate records of research protocols, and to verify compliance with applicable animal welfare regulations. In addition, the IACUC Office personnel are a resource to faculty seeking advice on regulatory and animal welfare issues. They are available to assist investigators in maintaining compliance with federal, granting agency, and university animal welfare regulations.

The IACUC Office staff is comprised of three IACUC Coordinators, one Protocol Manager, one Regulatory Coordinator and one Office Coordinator. The staff reports to the Director of Regulatory Affairs, who in turn reports to the IACUC Director and the IACUC Chair.

The IACUC Office is responsible for maintaining the following records: The IACUC is responsible for maintaining these records:

- OLAW Assurance documentation
- Minutes of IACUC meetings
- Records of IACUC activities and deliberations
- Minority IACUC views
- Documentation of protocols reviewed by the IACUC, and proposed significant changes to protocols
- IACUC semiannual program evaluations and facility inspections, including deficiencies identified and plans for correction
- Accrediting body and USDA determinations.

All records are kept for a minimum of three years, with the exception of records that relate directly to protocols which must be kept for the duration of the activity and for an additional three years after completion of the activity. Records documenting such activities as the provision of adequate veterinary care, training, and occupational safety, are expected to conform with the recommendations of the *Guide* and with commonly accepted professional standards.

## Meetings

The IACUC meets on the third Monday of each month unless precluded by a holiday. A schedule of meeting is available on the IACUC website, www.iacuc.pitt.edu. IACUC business may only proceed with the attendance of a quorum consists of one more than half of the regular IACUC voting members. The meeting is divided into two segments. The first segment is the IACUC Protocol review meeting where issues concerning protocols being considered for full committee review (see Protocol Review Process below) are discussed. This is a closed meeting with attendance limited to only members of the IACUC, investigators whose protocols are being reviewed, and other persons adding expertise on the issues of concern. The second segment is the General IACUC meeting where issues relating to animal care and use at the University are discussed. This meeting is open to the public. Contact the IACUC Office for the location and time of the General Meeting if you would like to attend.

The Executive IACUC meets monthly on the first Monday of the month unless precluded by a holiday. This is a closed meeting.

Minutes of the IACUC and Executive meetings are kept by the IACUC Office and are made available for review to the pertinent regulatory agencies, as required.

# Program Evaluation

PHS Policy and USDA Regulations require that the IACUC conduct a semi-annual evaluation of the animal care and use program. Key aspects of this evaluation include IACUC functions and procedures, protocol review practices, provisions for dealing with reports of non-compliance or other concerns regarding animal care and use, and the procedures employed to meet reporting requirements. In addition, the institution's occupational health program, veterinary care procedures and personnel qualification review process are evaluated.

Program evaluation deals principally with administrative aspects of the animal care and use program. Ongoing review of established practices allows the opportunity for the IACUC to detect changes in operating procedures from those published (such as in this manual), thereby allowing revisions to one or the other, as appropriate. The program review is assigned to the IACUC Chair and Vice Chairs or their designees. The Semiannual Program and Facility Review Checklist is used for guidance.

The IACUC will review and approve a draft report prepared for by the IACUC Director from the program review comments. The deficiencies are categorized as minor or significant. Copies of the draft report are sent to the supervisors responsible for the areas cited and a timetable and corrective action plans are requested for all deficiencies.

## Facilities Inspection

PHS Policy and USDA Regulations require the IACUC to inspect all University of Pittsburgh animal facilities every six months. This includes all DLAR animal facilities, animal facilities managed by other University departments and all locations outside the DLAR where animals are housed or taken. These inspections provide an ongoing mechanism for ensuring that the university maintains compliance with applicable animal care and use policies, guidelines and laws. The inspections also benefit the program for animal care by serving as an educational opportunity for animal care personnel, research staff and IACUC members. The interaction of the IACUC and the animal care personnel at the University of Pittsburgh is to be constructive, and not adversarial, as both ultimately share the same goals of responsible animal care.

Before the inspections commence, IACUC members receive a listing of all facilities to be inspected on specific dates and are asked to sign up for inspections. At least two IACUC members inspect each facility, as required by USDA Regulations. No IACUC members wish to attend a particular inspection are excluded, and additional ad hoc consultants may be requested, if necessary. The inspection team must have a working knowledge of the *Guide* and USDA Regulations in order to perform effective evaluations. In addition, each IACUC member can avail themselves to the Semiannual Program and Facility Review Checklist.

USDA Regulations also require inspection of all other animal containment facilities in which animals are kept for more than twelve hours, while PHS Policy requires inspection of all surgical facilities and areas in which animals are maintained longer than

24 hours. The Compliance Officer maintains list of all such facilities. The Compliance Officer and at least one other IACUC member inspect these facilities outside the DLAR every six months. The inspection criteria are the same as used in DLAR facilities.

The Compliance Officer notifies the supervisory personnel of housing facilities and animal-use sites to be inspected of the date and time of an inspection. Advance notification allows individuals to be available to answer questions. If the appropriate personnel are not available on the scheduled date, the Compliance Officer and other IACUC members may return at their own discretion, without advance notice. The Compliance Officer takes notes throughout the inspection to assist in preparation of the final report. Apparent deficiencies are discussed with the person in charge of the facility to ensure the accuracy of the team's findings.

The Compliance Officer prepares a draft report after the visit, noting any deficiencies, which are categorized as minor or significant. USDA Regulations and PHS Policy define a significant deficiency as one of significant threat to animal health or safety. Copies of the draft report are sent to the supervisors responsible for the areas cited and the DLAR Executive Director. The Compliance Officer requests a corrective action plan all deficiencies found during the inspection. Deficiencies noted as corrected are immediately verified by the Compliance Officer. Remaining deficiencies and corrective action plans are presented to the IACUC during one of the monthly IACUC meetings. The following tabular format is used:

**SITE**
**DATE OF VISIT**
**VISITORS COMMENTS/MINOR**
**DEFICIENCIES**
**CORRECTIONS**

The IACUC reviews the report to verify that all comments have been reported and that the corrective actions planned are adequate. The IACUC Chair and Director then use this information to prepare the semi annual report to the Institutional Official on the status of the animal care and use facilities at the University of Pittsburgh. If the institution is unable to meet the corrective action plans proposed in the semi-annual report, the IACUC, through the Institutional Official, must inform Animal and Plant Health Inspection Service (APHIS) officials within fifteen working days of the lapsed deadline. If the activity is federally funded, the relevant agency also must be informed.

# Animal Welfare Concerns

The Animal Care and Use Committee (IACUC) at the University of Pittsburgh investigates all concerns regarding the care, treatment, and use of animals for research or teaching at the university. To report a concern, please contact any or all of the following:

| | | |
|---|---|---|
| **Dr. Frank Jenkins, Chair, IACUC** | **fjenkins@pitt.edu** | **412-623-3233** |
| **Dr. Denise Capozzi, Director, IACUC** | **dcapozzi@pitt.edu** | **412-383-2009** |
| **Dr. David Schabdach, Senior Executive Director, DLAR and Attending Veterinarian** | **dschab@pitt.edu** | **412-648-8166** |
| **DLAR Emergency On-Call Veterinarian** | | **412-917-2340** |
| **University of Pittsburgh Confidential AlertLine** | | **1-866-858-4456** |

Anonymous reports are acceptable, and all are investigated. The identity of anyone making an anonymous report will be held in confidence to the extent possible. The University AlertLine permits complete anonymity in reporting. In addition, federal laws prohibit discrimination or reprisal for reporting violations of standards and regulations promulgated under the Animal Welfare Act.

## Receiving and Handling Allegations

Reports of concerns involving the care and use of animals submitted to one of the above listed individuals will be sent to the IACUC Office and immediately distributed to the IACUC Chair, University Veterinarian, IACUC Director, and the Compliance Officer. The University Veterinarian, a designee, or the Compliance Officer will investigate the allegation as soon as possible to ensure that the health and well-being of the involved animals are not compromised. The IACUC Director will refer allegations related to biological, chemical, or radiological safety of University personnel to the appropriate University office.

The University Veterinarian, or designee, or Compliance Officer shall remedy immediately any identified problems that negatively impact the health or welfare of animals. Deficiencies compromising the immediate health and well-being of humans involved in the incident will be remedied immediately by the appropriate University official.

Based on a report of noncompliance, the Institutional Official may suspend a protocol immediately if the circumstances so warrant. This action will be reviewed at the next convened meeting of the IACUC at which a quorum is present.

The University Veterinarian, the Institutional Official, and, as designated by the Institutional Official, the Compliance Officer, are authorized to suspend further conduct of all or any portion of animal subject research upon the identification of significant animal welfare concerns and/or significant noncompliance with the respective IACUC-approved protocol or institutional policies. This suspension shall remain in effect until such time that the convened IACUC has formally addressed the matter.

Following resolution of any immediate animal welfare concerns, the Compliance Officer will thoroughly investigate all aspects of the allegation and prepare a written incident report. A copy of the incident report will be sent to the involved principal investigator (PI) with the request that the PI submit his/her response regarding the identified problems to the IACUC. The IACUC Executive Committee will review the report at its next regularly scheduled meeting and will ascertain the completeness of the investigation and will develop recommendations for corrective actions and, if warranted, sanctions for subsequent presentation at the next convened meeting of the IACUC.

At its convened meeting, the IACUC shall:

- Review the incident report and discuss the allegations with the investigator(s) involved.
- Substantiate the validity of the allegation by a majority opinion of the IACUC.
- Record a listing of noncompliance issues.
- Decide on the response to the originator of the allegation.
- Decide on reporting the noncompliance issues to relevant regulatory agencies.
- Determine appropriate sanctions and/or additional corrective actions for the investigator.

The minutes of the IACUC meeting will record these actions.

The IACUC Chair will send a letter to the Institutional Official (IO) delineating the noncompliance issues and the recommended corrective actions/sanctions. The Institutional Official, in consultation with the IACUC, may impose further corrective actions/sanctions for the investigator or support the IACUC's recommended corrective actions/sanctions.

The IACUC Chair will send a letter to the investigator describing the noncompliance issues and the required corrective actions/sanctions, with related deadlines, prescribed by the IACUC. The letter will also inform the investigator of his/her option to appeal the decision by writing the IACUC Chair, within 10 days of receipt of this letter, detailing the basis of the appeal and requesting a second meeting with the IACUC.

The IACUC Chair will also inform the originator of the allegation of the IACUC's disposition of the allegation.

## Determination of Corrective Actions and Sanctions

All issues reported to the University of Pittsburgh IACUC involving known or suspected noncompliance with federal regulations and /or IACUC requirements or determinations governing animal research is submitted for review by the IACUC as described above. If the IACUC, by majority vote, finds the allegations have merit and represent noncompliance the following guidelines will be used to determine corrective actions/sanctions:

**For Serious or Continuous Noncompliance Issues**

Acts of noncompliance are deemed serious if they impact, or have the potential to impact, the health, safety or well-being of animals or personnel. If the IACUC determines that the reported problem represents serious or continuing noncompliance with federal regulations and/or IACUC requirements or determinations it may institute one or more of the following sanctions:

- Termination of the IACUC approval of the respective research protocol.
- Suspension of the IACUC approval of the respective research protocol.
- Suspension of an animal research-related activity.
- Suspension of further animal orders for the research study.
- Suspension of animal-use privileges of the investigator or any listed co-investigator for a duration and under conditions determined by the IACUC.
- Institution of an IACUC-mandated corrective action plan.
- Levy a monetary fine.
- Take such other action as the IACUC deems appropriate.

**Termination and Suspension**
Serious or repeat noncompliances may result in the termination of the applicable protocol or the suspension of the protocol or an animal research-related activity described in the protocol. A previously-approved research protocol may be Terminated or Suspended by:

- a vote by a quorum of voting IACUC members;
- the Institutional Official, in consultation with the IACUC.

Animal research-related activities may be suspended if the activity if found to produce harm or potential harm to animals or research personnel, if the activity may result in pain or distress, or if the activity otherwise threatens the welfare of research animals. Any animal research-related activity described in an investigator's IACUC protocol may be suspended by:

- a vote by a quorum of voting IACUC members;
- the Institutional Official;
- The IACUC Chair, in consultation with the Institutional Official;
- The University Veterinarian, in consultation with the Institutional Official and the IACUC Chair;
- The Compliance Officer, in consultation with the Institutional Official and the IACUC Chair.

Upon the termination or suspension of a protocol, all animal-based research described in the protocol must cease immediately, and the animals may not be accessed or manipulated except by animal facility personnel for the purpose of providing food, water, and standard enrichment for the species. If an animal research-related activity is suspended, only the suspended activity must immediately cease. Failure to comply with a termination or suspension constitutes work not approved by the IACUC and will be considered a further instance of noncompliance.

More serious noncompliance circumstances may necessitate revoking an investigator's animal-use privileges at the University. This action may be taken against a single

investigator or an entire research group, at the IACUC's discretion. This requires a vote by a quorum of voting IACUC members. The length of suspension may be a set length of time or until a set of conditions is met, also at the IACUC's discretion, as the circumstances dictate.

Terminated protocols may not be resumed. Suspended protocols or research-related activities may be re-activated only via a vote by a quorum of voting IACUC members, though the IACUC may stipulate the conditions under which the suspension will be lifted during the initial vote to suspend.

The decision to terminate or suspend a research protocol or animal research-related activity and the reason(s) for the decision will be reported, within one week of the decision, to the Institutional Official, the NIH/OLAW and, if applicable the USDA Animal and Plant Health Inspection Service and any Federal agency funding the study.

**Reporting Noncompliance to PHS/OLAW**
The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy), Section IV.F, paragraph 3, identifies three areas that require prompt reporting to the Office of Laboratory Animal Welfare (OLAW):

- any serious or continuing noncompliance with the PHS Policy;
- any serious deviation from the provisions of the *Guide for the Care and Use of Laboratory Animals*; and
- any suspension of an activity by the IACUC. The determination that a problem falls within the meaning of either a) or b) requires a degree of judgment by the IACUC.

The language used in the Policy was chosen purposely to permit the judicious application of professional judgment by the IACUC in determining what incidents should be considered serious and reportable to OLAW. In an effort to assist IACUCs in making such judgments, OLAW offers the following examples of occurrences that they have determined meet these reporting criteria:

a) Serious or continuing noncompliance with the PHS Policy, such as:

   - Failure to correct situations identified in previous semiannual evaluations as significant deficiencies.
   - Conducting animal-related activities without appropriate IACUC review and approval.
   - Failure of animal care and use personnel to adhere to IACUC-reviewed and approved institutional policies and procedures.

b) Serious deviation from the provisions of the *Guide*, such as:

   - Conditions that jeopardize the health or well-being of animals, including accidents, natural disasters and mechanical failures resulting in actual harm or death to animals.

- Shortcomings in programs of veterinary care, occupational health or training, identified during semiannual program review and not corrected within institutionally determined time frame.

c) Suspension of an activity by the IACUC, the Institutional Official, IACUC Chair, or University Veterinarian:

- Any IACUC intervention that results in the temporary or permanent interruption of an activity involving animals.

NOTE: SERIOUS NONCOMPLIANCE WITH THE PHS POLICY AND DEVIATIONS FROM THE GUIDE MUST BE REPORTED TO OLAW, EVEN IF IDENTIFIED INITIALLY BY OTHER AGENCIES, SITE VISITORS OR CONSULTANTS.

**Reporting Noncompliance to USDA/APHIS**
The Animal Welfare Act Regulations (AWAR) requires prompt reporting to APHIS when the IACUC suspends (or terminates) all or part of an investigator's protocol, even if the suspension is temporary (2.31,d,7). This regulation is applicable to all AWAR-covered species, which are warm-blooded vertebrate animals. Purpose bred mice and rats and wild-caught birds used for research purposes are exempted from this requirement, as the use of these animals is not regulated by the AWAR.

The IACUC will also report to the USDA any noncompliance involving AWAR-covered species that is also reported to PHS/OLAW.

**For Minor Noncompliance Issues**
Acts of noncompliance are deemed minor if they do not impact the health, safety or well being of animals or personnel. If the IACUC determines that the reported problem represents a minor noncompliance with federal regulations and/or IACUC requirements it may take one or more of the following actions:

- Elect to make corrective action only.
- Provide a verbal and/or written listing of the issue of noncompliance to the investigator and require a corrective action plan at a regular meeting of the IACUC and recording this incident in the IACUC minutes.
- Provide a written listing of the issue of noncompliance to the investigator and require a corrective action plan within a specified time period. The letter may or may not be copied to the investigator's department chair depending on the IACUC's decision on the sanction.

## Requests for Reconsideration

A principal investigator may request that the IACUC reconsider its findings and any sanctions if there is evidence that was not was not considered during the committee's deliberation. The procedure for request for reconsideration of any IACUC decision is as follows:

- The investigator must submit an appeal in writing to the IACUC Office. The appeal must include the details and rationale of the request and must be submitted within ten (10) days of being notified of the IACUC's decision.

- A representative from the IACUC Office will acknowledge receipt of the appeal and forward a copy to the IACUC Chair and the IACUC Director.
- The IACUC Chair will decide if the issue requires full committee review or if it can be addressed by a subcommittee.
- The investigator will be informed of the decision and may be asked to appear before either the full committee or the subcommittee to discuss the request.
- Following any discussion of concerns with the investigator, the IACUC or subcommittee will reconsider the issue.
- A written record of the discussion and reconsideration will be made.
- A summary of the written record along with the IACUC's reconsideration decision will be sent to the investigator and the Institutional Official.
- If the investigator is dissatisfied with the result, further reconsideration of the matter may be requested by appealing to the Institutional Official in writing. Such written requests must be filed with the IACUC Office within ten (10) days of the IACUC reconsideration decision being rendered.
- The Institutional Official will meet with the IACUC or subcommittee for further discussion, if warranted.
- A written record will be made of the meeting between the IACUC and the Institutional Official and a summary provided to the investigator along with the final decision on the issue.

# Protocol Review and Approval

The IACUC is responsible for assuring that the research, husbandry, teaching and testing programs involving animals at the University of Pittsburgh comply with all applicable regulations and policies and responsibly address concerns regarding animal welfare. To fulfill this responsibility, the IACUC reviews all animal research and testing procedures. **No animal experimentation or use is permitted at the University of Pittsburgh without written approval by the IACUC.** This requires all animal users at the University to complete a protocol application using the Institution's online protocol management system. This system manages the review process from beginning to end, and allows the research team access to the protocol and its state in the review and approval process at all times. The system stores all protocol information in an online database so that the IACUC may accommodate requests for information from the Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC), Office of Laboratory Animal Welfare (OLAW), and the US Department of Agriculture (USDA) and any other regulatory or internal requests.

## Protocol Application Process:

Investigators must submit all new IACUC protocol applications via Animal Research Online (ARO), the IACUC's online protocol management system. A guide for completing online applications can be found Applications are processed in the order that they are received at the IACUC Office. There are no expedited reviews.

The IACUC Chair oversees the protocol review process. The Chair assigns Designated Member Reviewers to one or more Subcommittees formed to review protocols of certain species. There are three rodent sucommittees and one Large Animal and Primate subcommittee. Each subcommittee contains scientific members, nonscientific members, veterinarians, environmental health and safety (EH&S) reviewers, administrative reviewers and other individuals, such as radiation safety reviewer, necessary for the review of any protocol so assigned.

An IACUC Coordinator responsible for guiding the protocol through the review process is assigned to each protocol. The Coordinator reviews all applications for accuracy and completeness. Incomplete applications or applications with administrative errors must be returned to the Investigator for revision before being sent to reviewers. The assigned Coordinator also ensures that all required training for the protocol has been completed by each member of personnel listed on the protocol and will notify the Investigator of any pending requirements.

Based on the species of the protocol, the Coordinator, using the online protocol management system, sends each protocol application to the five assigned Subcommittee's Designated Member Reviewers (two scientific members, one veterinarian, one administrative reviewer and one EH&S analyst). Initial reviews are expected to be completed in two weeks. Reviewers may approve the application, request revisions to or ask questions about the application, or refer the protocol to the full IACUC for review.

Once all IACUC Designated Member Reviewers have returned their reviews of the application, the Coordinator sends any questions to the Investigator. The Investigator must answer all questions and revise their application accordingly.

If the investigator does not respond to the reviewers' questions after four weeks, a reminder will be sent. If six weeks passes with no response, the IACUC Office may withdraw the protocol from review.

After the Investigator sends responses (completed review form and rappropriately revised protocol) the Coordinator sends the materials back to the IACUC Designated Member Reviewers for approval. This process will continue until all IACUC reviewers have approved the application, at which time the protocol will be approved by the IACUC Chair or Vice-Chair by electronically signing a letter of approval.

All personnel listed on a protocol must satisfy all IACUC and EH&S mandated training and safety requirements prior to approval.

The entire IACUC receives a weekly listing of new protocols submitted to the IACUC Office. The listing provides the name(s) of the Investigator(s), the project title, the funding agency, a project description narrative, the species of experimental animal, and the number of animals to be used in the study. Any IACUC member with an interest in a protocol on the list, may request to be assigned as a reviewer and submit a review of the protocol and/or refer it to the full committee for review.

No IACUC member can participate in the IACUC review of a protocol or activity in which that member has a conflicting interest except to provide information requested by the IACUC.

## Full Committee Review

If a protocol is referred to the full IACUC, a vote of approval at a convened meeting with quorum present is required for the application to be approved, unless the IACUC votes to refer the application back to the original subcommittee. If the full committee has questions, the decision regarding approval will be tabled until the next convened meeting.

Applications may be referred to the full IACUC for any reason by any IACUC member. Typical reasons for referral to the full committee include:

- Applications including death as an endpoint
- Studies including animal pain or distress that is not scientifically justified
- Requests for >12 housing outside of a university-managed facility (such as a laboratory)
- Questions regarding the required harm/benefit analysis

The results of the IACUC's deliberations are sent to the Investigator along with any questions or requirements that must be satisfactorily addressed to grant approval of the application by the next scheduled committee meeting.

The Investigator will be notified of the committee's decision following the full committee meeting. If ithe committee decides not to approve the application, the Investigator will be informedof the reason for the action.

## Committee Decisions

**Approval**
If the IACUC considers that all significant points have been addressed by the Investigator and that all questions that have been raised during review have been satisfactorily addressed. Once a protocol has been approved, the Investigator has permission to conduct the experiments described in the proposal on the number of animals justified.

At the time of approval, the IACUC Office will generate and approval letter and the IACUC Chair will be informed of the results of the review. The IACUC Chair then verifies that the review was conducted in accordance with all regulations and IACUC policies. If the review is deemed appropriate, the IACUC Chair signs the approval letter electronically. The application is not approved until the IACUC chair has issued an approval.

Approval letters are addressed to the Investigator for submission and verification to granting agencies to verify IACUC review and approval. They are available for download any time thereafter. A copy of the approved protocol and Risk Assessment, which delineates the hazards associated with the application and the training/medical surveillance requirements, is always available online to all personnel listed on the protocol.

Once the application is approved by either the subcommittee reviewers or the full committee, the IACUC assigns an eight-digit protocol number to the protocol. The first two digits of the protocol number designate the year of approval, the third and fourth digits designate the month of approval and the last four digits identify the application. For example, 12020033, indicates the application was approved in February of 2012 and assigned number 0033.

IACUC protocol approval is provided for a time period of three years, as specified by PHS Policy IV C 5. This policy requires *de novo* review of the protocol after three years. Protocols that have not significantly changed in the three years since their original submission can be easily resubmitted for review.

**Disapproval**
If an Investigator refuses to modify a proposal in accordance with the full IACUC's directions, or fails to supply information showing that their laboratory has appropriate facilities and staff for the proposed research, the full IACUC may, at a convened meeting with a quorum present, decide not to approve the protocol. The specific reasons for disapproval will be presented to the investigator in writing.

Appeals of a decision not to approve an application may be submitted to the IACUC Chair. Appeals must include additional evidence that was not previously made available or the solicitation of experts able to assist the IACUC in their deliberations.

Disapproved proposals cannot be administratively approved by a higher authority. However, an IACUC approved protocol can be administratively disapproved due to financial, facility-related or other considerations.

**Termination**
The IACUC may terminate an approved protocol due to the following reasons:

- Non-compliance issues (see **Receiving and Handling Allegations**)
- Failure to renew annually
- Failure to complete required training

For failure to renew annually and failure to complete required training, the Investigator is given a 30 day notice prior to termination. The investigator will be notified of protocol termination by email. The DLAR is notified of all IACUC terminated protocols and will decide the disposition of study animals.

Investigators with protocols that have been terminated due to failure to annually renew must submit an annual renewal application immediately and address any training and/or medical surveillance issues right away. **The IACUC Office will not approve annual renewal applications thirty days after termination**. If an annual renewal application is not approved in this time frame, a new protocol application must be submitted, reviewed and approved before research may continue.

**Withdrawal**
The IACUC may withdraw any pending protocol from the review process if the PI does not respond in a timely fashion during the review process. This occurs when questions are sent to the PI and the PI takes longer than 2 months to respond. The IACUC will send notice to the PI that the protocol will be withdrawn from the review process if a response is not forthcoming. The IACUC may also withdraw applications for review if any training requirements are not satisfied in a timely manner.

## Other Committees

Some protocols may require the approval of other committees within the Research Conduct and Compliance Office (RCCO) before the IACUC will issue a final approval or before animals may be obtained, even if all of the reviewers and/or the full IACUC has approved it. The following conditions always hold:

- If the Investigator identifies a conflict of interest in the protocol, the Conflict of Interest Office must issue its approval before the IACUC protocol will be approved.
- If the application describes the use of human stem cells, the Human Stem Cell Research Oversight Committee (hSCRO) must issue its approval before the IACUC protocol will be approved.

- If the application describes the use of genetic engineering, including rDNA use or the breeding of transgenic animals, approval from the Institutional Biosafety Committee must be secured before animals may be obtained.
- Applications making use of the Regional Biosafety Laboratory must submit an RBL Pre-Project form prior to IACUC Submission. To obtain this form, contact the Center for Vaccine Research, info@cvr.pitt.edu.

## Protocol Modifications

Both the AWA and PHS Policy require that the IACUC review and approve, prior to initiation, proposed modifications to ongoing activities using animals. Modifications are submitted to the IACUC through the online protocol management system. Modifications to older protocols that have not been approved via the online system are submitted using a Word-based Modificiation Request Form. All requests are reviewed using the same process and have the same requirements. The following modifications cannot be requested using this process:

- Changing the species used
- Adding procedures that do not logically relate to the specific aims of the original protocol
- An unrelated change in the scientific aims of the original protocol application
- Switching from non-survival to survival surgery
- Switching from single to multiple survival surgeries.

A new protocol application must be submitted to incorporate any of the above changes, because the IACUC is required to review new issues arising related to animal welfare. Any changes to an IACUC protocol that present animal welfare issues not addressed in the original protocol will require the submission of a new protocol. The new protocol submission is required to address how all animal welfare issues will be mediated.

Two types of modifications are recognized. An Administrative Modification is an addition or deletion of personnel, protocol title change or additional protocol titles, a change in the funding source, a change in the animal source or vendor, a request for animal housing or use outside the Institution that meets established IACUC requirements or a request for additional animal strains that do not require additional husbandry or housing considerations beyond those in the approved protocol. Administrative modification requests are reviewed by IACUC Office personnel, and if appropriate changes have been made to the protocol and records, they grant approval usually within two to three business days. Requests for additional personnel require that the new personnel satisfy all IACUC and EH&S mandated training and safety requirements prior to approval.

Other acceptable modifications to an IACUC-approved protocol include: changes in anesthetic or the analgesic agents, changes in euthanasia method(s), changes in any surgical procedures or addition of a surgical procedure, requests for additional animals, changes in nonsurgical procedures involving animals, changes in the animal strain, any changes that will affect the previously approved USDA Pain/Distress Category, requests to use additional test agent(s), and other changes that logically relate to the specific aims of the original protocol application.

The Investigator must clearly explain why the modification is being requested and how it relates to the original specific aims of the previously approved protocol.

Modifications are reviewed using nearly the same process as new protocols. The modification request is assigned to the species-appropriate Subcommittee and is

reviewed by at least four Designated Member Reviewers: 1 scientific member, 1 veterinarian, an EH&S analyst and an administrative reviewer. Questions and answers circulate between the reviewers and PI. After all issues have been resolved, and all reviewers have issued an approval, the request is approved and, after review by the IACUC Chair, an approval letter is issued. The approved protocol, with all approved changes integrated, is then available through the online protocol managaement system.

Certain modifications are administratively flagged for full committee review: requests for more than 25% of the originally-approved number of animals justified for the study/experiments, modifications involving death as an endpoint, and requests for new >12 hour housing sites outside of DLAR space all must be approved by the full IACUC.

## Annual Renewal

Although PHS Policy grants protocol approval for a three-year period, the AWA requires continuing reviews of activities involving animals at appropriate intervals as determined by the IACUC, but not less than annually. To satisfy this AWA requirement, the University of Pittsburgh's IACUC requires each active protocol to go through an annual renewal process. The IACUC protocol number can be used to determine the month in which the protocol is due for renewal. The IACUC assigns an eight-digit protocol number to the protocol (older protocols have only seven digits, but the principle is the same for both). The first two digits of the protocol number designate the year of approval, the third and fourth digits designate the month of approval, and the last four digits identify the protocol. For example, protocol number 12020033 indicates the protocol was approved in February of 2012 and assigned number 0033. In this example the protocol must go through the Annual Renewal process before the end of February.

The online protocol management system sends Investigators and certain members of their staff reminders to renew their protocols 90, 60, and 30 days before protocols will expire. The Principal Investigator must log in and submit an annual renewal application online. An IACUC Coordinator reviews all applications received for their completeness and accuracy. The IACUC Office will return the renewal application to the Investigator if the application is incomplete or inaccurate. The Investigator is informed of receipt and entry into the review process by e-mail.

Prior to approval of an annual renewal, the entire IACUC receives a weekly listing of annual renewal applicatioins received by the IACUC Office. The listing provides the name(s) of the Investigator(s), the project title, the funding agency, a project description narrative, the species of experimental animal, and the number of animals to be used in the study. Any IACUC member, including the unaffiliated and nonscientific representatives, with interest in an annual renewal on the list, may request a copy and submit a review of the annual renewal and/or call the annual renewal to full committee review.

Following the administrative review of the annual renewal application by the IACUC Coordinator, if no problems are identified the annual renewal is approved by the IACUC Chair or Vice-Chair. No annual renewal application is approved unless all training and medical surveillance requirements have been met. Investigators who do not submit

renewal applications will have their IACUC approval terminated. The termination process is as follows:

- The Investigator receives, 90, 60, and 30 days before required renewal notices of the need to renew by e-mail.
- The month of the required renewal, the Investigator will be contacted by the IACUC Office, either by letter or phone call, and made aware of the deadline to renew. The 30-day renewal reminder letter is copied to the Investigator's Department Chair.
- If no response is received by the expiration deadline, the IACUC will terminate the approval of the protocol in a letter to the Investigator, with copies going to the Investigator's Department Chair and the Institutional Official.
- A protocol termination notification will be sent to the DLAR and any animals assigned to the protocol will be confiscated. The DLAR veterinarians will decide the fate of the confiscated animals.

## Post-Approval Monitoring

As part of the IACUC's responsibility to oversee and evaluate the institution's animal program, the Compliance Office conducts protocol audits. These audits provide an ongoing mechanism for ensuring that the University maintains compliance with the applicable animal care and use policies, guidelines and laws. The audits also benefit the program for animal care by serving as an educational opportunity for the animal care personnel, research staff and IACUC members. The audit procedure is conducted with an IACUC member using the following procedures:

**Study Selection**
Semi-annually the Compliance Officer (CO) will submit a list of studies selected for audit to the Executive IACUC for review and approval. Once a lists of protocols to be audited has been identified, a time is set, in consultation with the Investigator and IACUC member, for the audit to take place.

**Protocol Review**
The protocol, including all approved modifications annual renewals, as well as the questions asked during the review process, is reviewed by the audit team. The protocol review serves to compare animal care and use issues described in the protocol with actual procedures performed in the laboratory and described in research logs. In addition, the protocol review audits the workings of the IACUC protocol approval process.

**Study Audit**
The study audit serves as a direct observation of study procedures and comparison of the observations with the protocol and the *Guide*. All personnel involved in the study must have knowledge of the IACUC approved protocol, particularly the specific procedures in which they are involved. The audits are to verify that the study meets the following requirements:

- Procedures with animals avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.
- Procedures that may cause more than momentary or slight pain or distress to the animals are performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.
- Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved are painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- The living conditions of animals are appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied.
- Medical care for animals is available and provided as necessary by a qualified veterinarian.
- Personnel conducting procedures on the species being maintained or studied are appropriately qualified and trained in those procedures.
- Methods of euthanasia used are consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.

**Audit Report**

Following the audit, the CO collects all issues and comments from the inspectors for preparation of any corrective actions, which may include a request to modify the protocol or sanction by the IACUC. Audit reports will be incorporated into the Semi-Annual Report.

# Approval of Work Performed Outside the University

There are many circumstances that involve partnerships between collaborating institutions or relationships between institutional animal care programs. There are also many instances of work contracted from an institution with a company involving the use of live animals.

## Collaborations with Other Institutions

OLAW and APHIS agree that, in cases of collaborations between institutions, individual research projects need not be reviewed and approved by more than one IACUC. It is, however, imperative that institutions define their respective responsibilities. If both institutions have full PHS Assurances, they may exercise discretion in determining which IACUC reviews research protocols and under which institutional program the research will be performed. It is recommended that if an IACUC defers protocol review to another IACUC, then documentation of the review should be maintained by both committees.

The IACUC requires that the Pitt Investigator notify the IACUC Office before work commences. The requirements below represent the IACUC's responsibilities and policies.

For animal work performed at a collaborating institution, the Pitt IACUC requires:

- The performing institution must have a PHS Assurance.
- The performing institution must be AAALAC-Accredited (or, for Canadian institutions, certified by the Canadian Council on Animal Care (CCAC)).
- If the species used is regulated by the Animal Welfare Act, the performing institution must have a USDA registration.
- The Pitt IACUC must receive a copy of the approved protocol and approval letter from the performing institution.
- The Pitt IACUC must receive annual approval letters and any approved modifications to the protocol.
- The Pitt IACUC Office must receive either a copy of the performing institution's semi-annual report(s) for the period of the study *or* any information about significant questions or issues (such as compliance issues) raised during the semi-annual inspection.

After adherence to the requirements has been verified and all required materials received, a letter will be written and sent to the Investigator.

## Animal Work Contracted with a Company

The University of Pittsburgh may have contractual arrangements for certain aspects of the animal care and use program with other animal care agencies or facilities. Such offsite locations may include contract laboratories, collaborating universities, and other types of research facilities. If the university owns these animals, then the Pitt IACUC

has the responsibility of insuring the health and well-being of the animals while they are housed at the offsite location.

For animal work contracted with a company, the Pitt IACUC requires:

- The company must have a PHS Assurance.
- The company must be AAALAC-Accredited.
- If the species used is regulated by the Animal Welfare Act, the company must have a USDA registration.
- The Pitt IACUC Office must receive a copy of the approved protocol and approval letter from the performing institution. If the protocol cannot be obtained for proprietary reasons, a statement of work from the company is acceptable.

If these conditions are met, the IACUC will issue a letter granting permission to use the company for the work.

A listing of all organizations with a PHS Animal Welfare Assurance is available at the following web site: http://grants1.nih.gov/grants/olaw/assurance/300index.htm. Note that some companies are subsidiaries of a larger organization that has filed an Animal Welfare Assurance for all of its components. If the company is not listed on the web site indicated above, the Investigator should contact the company to ascertain whether its animal welfare assurance was filed through a different business name. The Investigator must also have a Pitt IACUC-approved protocol in place prior to shipment of animals to the University.

Please note that PHS prohibits the use of NIH funds to pay for animal work performed by a company that has not filed an animal welfare assurance with PHS.

**Custom Animal Production**
Most animals used in research are ordered from a catalog of already available strains from University-approved vendors. The purchase of these animals requires an IACUC-approved protocol onto which the animals are placed upon receipt and orders for such animals must be processed through the DLAR Anorder system. However, if an investigator make a contractual arrangement with a company to construct a unique gene-modified or surgically manipulated animal, specifically for your federally-funded research (i.e., the animal would not have been generated without your order and the animal is made to your specifications), then you must obtain IACUC approval, via the adherence to the requirements above, for this unique animal production prior to initiation of the project.

## Appropriate Modification of Protocol

If a study includes work performed at another institution or company, the relevant protocol(s) must be modified appropriately. To do this, submit a modification request to the IACUC Office. If all requirements have been met, the request will be handled administratively.

**Rederivation or Cryopreservation with Jackson Laboratories or Taconic**
Because the Universtiy has negotiated master agreements with Jackson Laboratories (JAX) and Taconic, Inc., rederivation and cryopreservation work done at these companies, under said agreements, can be quickly approved without protocol modification, following the process below:

- The Investigator must submit a statement of work from the company that includes a project number.
- The Investigator must send the appropriate protocol number.

Please note that the Investigator must ensure that the protocol given is approved for the strain and number of animals to be shipped. If the protocol is not approved for the specific number and strain, the Investigator must submit a modification request, which must be approved before animals can be shipped to the University.

## Requests for Exemption to AAALAC-Accreditation Requirement

Requests for an exemption to the requirement for AAALAC Accreditation may be considered by submitting a request to the IACUC Office if the following conditions are met:

- The University of Pittsburgh does not own the animals.
- The University of Pittsburgh IACUC receives a letter from the University of Pittsburgh faculty member sponsor formally requesting an exemption from this policy. This letter must explain in detail why work must be done specifically at the performing institution.
- The Universtiy of Pittsburgh IACUC receives a description of the country's animal welfare laws and regulations as they pertain to animal research (links to government websites are acceptable if in English) and a description of the official certifications and accreditations the performing institutions has attained (with appropriate documentation of each).

The request is forwarded to the IACUC Chair and is brought to the Executive Committee for deliberation. If the request is deemed satisfactory, it will be presented at the next IACUC meeting for vote.

# Personnel Training

The University of Pittsburgh provides training to all personnel who use or care for animals.

**All individuals listed on IACUC protocols must complete the necessary training modules. This includes:**

- Principal Investigators
- Research Fellows, Technicians/Assistants
- Animal Care Technicians
- Any individual involved in the design and implementation of research studies using laboratory animals.

All listed individuals are required to complete the Research Integrity module, which covers laws and regulations, and the Use of Laboratory Animals in Research and Teaching module. Certification for the latter module is required every three years.

In addition, everyone involved in the use of animals is required to complete the appropriate online species-specific training modules, corresponding to the species listed on the protocol. These sessions include Small Animal (rodents), Large Animal (rabbit, ferret, cat, dog, pig, sheep, goat, and calves, etc.), and Primates. Species-specific animal training modules require certification every three years. They can be found on HSConnect's Animal-Based Research Modules page.

Other Training, offered by the Environmental Health and Safety Department such as Chemical Hygiene, Bloodborne Pathogens, Formaldehyde training etc. may be required.

For more information regarding the IACUC's training requirements, please contact the RCCO training coordinator at 412-383-1737.

# External Program Review

## National Institutes of Health
## Office of Laboratory Animal Welfare (OLAW)

**Annual Report to OLAW**
Each year, the University of Pittsburgh must submit a report to OLAW that includes:

- Changes in the institution's program of animal care and use
- Changes in the membership of the IACUC
- Dates that the IACUC conducted its semiannual program evaluations and facility inspections; and
- Minority IACUC views (e.g., minority opinions expressed during a semiannual evaluation or inspection, in the course of a protocol review or IACUC evaluation of animal welfare concerns, or in recommendations to the Institutional Official).

The Institutional Official and the IACUC Chairperson must sign this report. The report is submitted on December 1 each year, coinciding with the Annual Report to the Institutional Official.

**Reporting Noncompliance, *Guide* Deviations, and Suspensions To OLAW**
The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy), Section IV.F, paragraph 3, identifies three areas that require prompt reporting to the Office of Laboratory Animal Welfare (OLAW): (a) any serious or continuing noncompliance with the PHS Policy; (b) any serious deviation from the provisions of the *Guide for the Care and Use of Laboratory Animals*; and (c) any suspension of an activity by the IACUC. The determination that a problem falls within the meaning of either (a) or (b) requires a degree of judgment by the IACUC. The language used in the Policy was deliberately chosen to permit the judicious application of professional judgment by the IACUC in determining what incidents should be considered serious and reportable to OLAW. In an effort to assist IACUCs in making such judgments, OLAW offers the following examples of occurrences that they have determined meet these reporting criteria:

- Serious or continuing noncompliance with the PHS Policy, such as:
    - Failure to correct situations identified in previous semiannual evaluations as significant deficiencies
    - Conducting animal-related activities without appropriate IACUC review and approval
    - Failure of animal care and use personnel to adhere to IACUC - reviewed and approved institutional policies and procedures
- Serious deviation from the provisions of the Guide, such as: conditions that jeopardize the health or well being of animals, including accidents, natural disasters and mechanical failures resulting in actual harm or death to animals

- Suspension of an activity by the IACUC, which is any IACUC intervention that results in the temporary or permanent interruption of an activity involving animals

The IACUC usually fulfills the requirement that such information be reported promptly by calling the Office of Laboratory Animal Welfare, Compliance Division, at 301-402-4371, and orally apprising OLAW of the situation. OLAW will usually ask for a follow up with a written letter upon resolution of the matter.

**NOTE:** Serious noncompliance with the PHS policy and deviations from the guide must be reported to OLAW, even if identified initially by other agencies, site visitors or consultants.

## United States Department of Agriculture (USDA)

### USDA Annual Report

As required by Section 13 of the AWA and further explained in 9 CFR, Part 2, Section 2.36, the University of Pittsburgh must submit an annual report (APHIS Forms 7023 and 7023-A) to the Animal Care Regional Office located Raleigh, NC. This report is due in the Regional office on or before **December 1** of each year. These forms must be signed and certified as correct by the Chief Executive Officer (CEO) or legally responsible Institutional Official (IO), and must include all species covered by the AWA used in research, tests, experiments, or for teaching and those on hand at the end of the U.S. Department of Agriculture's (USDA) fiscal year (FY) (October 1 through September 30). By signing the report, the CEO or IO is also certifying that the institution has adhered to the assurance statements at the bottom of the APHIS Form 7023. Reporting of animals used is based on the USDA FY (October 1 through September 30). Animals are to be counted only once, regardless of the number of proposals in which they were used. If an animal was used in more than one proposal, it must be counted in the most painful category. Animals used in multi-year studies will be counted once each fiscal year. Animals counted and listed in USDA Pain Category E must have a detailed statement explaining the procedure(s) and the basis for withholding pain-relieving medications. Entries in Category "E" must be explained in detail and attached to APHIS Form 7023. At a minimum, these statements should address the following:

- A complete description of the procedure(s) producing pain and/or distress in the animal(s). This explanation should include, as appropriate, the name of the test, the reference from the Code of Federal Regulations if the test is mandated by federal regulations, or other relevant guidelines.
- A complete explanation for withholding drugs for relieving pain and/or distress. For example, provide scientific justification that such drugs would adversely affect the test/study results, or cite all regulation(s) and/or Federal Agency policies that prohibit the use of these drugs.

A summary of IACUC-approved exceptions to the regulations or standards must also be attached to APHIS Form 7023. At a minimum, this summary should include the following:

- Identify IACUC-approved exception(s) to the regulations or standards, including exceptions to the dog exercise plan and/or the nonhuman primate plan for environmental enhancement.
- Describe IACUC-approved exemption(s).
- Identify the species and number of animals used.

It is not necessary to report birds, amphibians, rats of the genus **Rattus,** mice of the genus **Mus** specifically bred for use in research, or any other animals not defined as animal by 9 CFR, Part 1- Definitions of Terms, Section 1.1. Wild rats and mice *are* covered and must be reported.

**Reporting Non-compliance to USDA**
If the IACUC suspends an activity involving animals, the Institutional Official, in consultation with the IACUC, shall review the reasons for suspension, take appropriate corrective action, and report that action with full explanation to APHIS and any Federal agency funding that activity.

## AAALAC International

The Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC) is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. The University of Pittsburgh maintains an Accredited status, the conditions of which, as set by the AAALAC International Board of Trustees, are as follows:

- The care and management of laboratory animals should be directed by qualified persons.
- All animal care personnel should be suitably qualified by training and experience in the care of laboratory animals.
- Physical facilities and the methods of care and use for animals should permit their maintenance in a state of well-being and comfort.
- The *Guide for the Care and Use of Laboratory Animals* shall serve as a basic guide to the establishment of specific standards for accreditation. For programs outside the U.S., AAALAC International may establish standards based on prevailing directives and conventions of the country in which the accreditable unit is located.
- The accreditable unit shall observe any and all statutes and governmental regulations which bear upon animal care and use including, but not limited to, the prevailing standards of sanitation, health, labor and safety of the jurisdiction(s) in which it is located.
- The accredited unit shall submit an annual report which describes elements of the animal care and use program as specified by AAALAC International. In addition, the accredited unit shall promptly notify AAALAC International (e.g., through copies of correspondence) of adverse events relating to the animal care and use program. Examples include investigations by the USDA or OLAW, as well as other serious incidents or concerns that negatively impact animal well-being.
- All qualified applicant units are initially site visited. Accredited units and those on provisional status are routinely revisited at 3 year intervals. Additional interim or

follow-up visits may be required to confirm correction of deficiencies or if there are major changes in programs or facilities.

- If an accredited unit fails to meet the criteria of an active animal care and use program, as defined above, the unit must notify the AAALAC International Executive Office at 5283 Corporate Drive, Suite 203, Frederick, MD 21703, tel: 301-696-9626, fax: 301-696-9627. AAALAC International will inform the unit that in order to maintain accreditation, an active animal care and use program must be resumed within twelve months. After failing to meet the criteria of an active animal care and use program for twelve consecutive months after notification by AAALAC International, accreditation of the unit will be revoked. If the unit resumes an active animal care and use program after revocation, a new application for accreditation must be submitted.

# Regulations and AAALAC Accreditation

The University of Pittsburgh follows the regulations and guidelines of the Animal Welfare Act, the Public Health Service Policy, AAALAC and those outlined specifically for the University. University specific guidelines are delineated in this manual.

## Animal Welfare Act (ACT)

***Animal Welfare Act as Amended*** **(7 USC, 2131-2156)**
The complete Animal Welfare Act includes all amendments (1970, 1976, 1985, 1990) following the 1966 enactment. This version is current through 1996 and can be found in *United States Code*, Title 7, Sections 2131 to 2156.

**Public Law 89-544** ***Act of August 24, 1966***
Enacted August 24, 1966, Public Law 89-544 is what commonly is referred to as The Animal Welfare Act although that title is not mentioned within the law. It authorizes the Secretary of Agriculture to regulate transport, sale and handling of dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits intended to be used in research or "for other purposes." It requires licensing and inspection of dog and cat dealers and humane handling at auction sales. The complete amended act can be found in *United States Code,* Title 7, Sections 2131-2156.

**Public Law 91-579** ***Animal Welfare Act of 1970***
Enacted December 24, 1970, Public Law 91-579 expands the list of animals covered by the Act to include all warm-blooded animals determined by the Secretary of Agriculture as being used or intended for use in experimentation or exhibition, excepting horses not used in research and farm animals used in food and fiber research. Exhibitors are incorporated into the act and research facilities are defined. Retail pet stores, state and county fairs, rodeos, purebred dog and cat shows, and agricultural exhibitions are exempt from the Act. The Secretary is directed to develop regulations regarding recordkeeping and humane care and treatment of animals in or during commerce, exhibition, experimentation, and transport. There is also mention of inspections, and appropriate anesthetics, analgesics, and tranquilizers. There are further regulations on dog and cat commerce.

**Public Law 94-279** ***Animal Welfare Act Amendments of 1976***
Enacted April 22, 1976, Public Law 94-279 is primarily refining previous regulations on animal transport and commerce. "Carrier" and "Intermediate Handler" are defined. Health certification prior to transport of sale is required and must be performed by a veterinarian. Licenses, method of payment, and penalties for violations are discussed. This amendment also introduces and defines "animal fighting ventures" to the Act. Animals used for hunting waterfowl, foxes, etc. are exempt. It is illegal to exhibit or transport via interstate or foreign commerce animals used in fighting ventures such as dogs or roosters.

**Public Law 99-198** ***Food Security Act of 1985, Subtitle F - Animal Welfare***
Also called "The Improved Standards for Laboratory Animals Act" and enacted December 23, 1985, this section clarifies what is meant by "humane care" by

mentioning specifics such as sanitation, housing, and ventilation. It directs the Secretary of Agriculture to establish regulations to provide exercise for dogs and an adequate physical environment to promote the psychological well-being of nonhuman primates. It specifies that pain and distress must be minimized in experimental procedures and that alternatives to such procedures be considered by the principle investigator. It also defines practices that are considered to be painful. No animal can be used in more than one major operative experiment with recovery (exceptions are listed). The establishment of the Institutional Animal Care and Use Committee (IACUC) is introduced with a description of its roles, composition, and responsibilities to the Animal and Plant Health Inspection Service (APHIS). Also included is the formation of an information service at the National Agricultural Library to assist those regulated by the act in prevention of unintended duplication of research, employee training, searching for ways to reduce or replace animal use, and to provide information on how to decrease pain and distress. The final section explains the penalties for release of trade secrets by regulators and the regulated community.

**Public Law 101-624** ***Food, Agriculture, Conservation, and Trade Act of 1990, Section 2503 -Protection of Pets***
Enacted November 28, 1990, and establishes a holding period for dogs and cats at shelters and other holding facilities before sale to dealers. It requires dealers to provide written certification regarding each animal's background to the recipient. Specific items included on the certificate are mechanisms of enforcement, injunctions, and penalties for violation.

***Code of Federal Regulations, Title 9*** ***- Animal Welfare***
The current version of the regulations developed by the U. S. Department of Agriculture specify how to comply with the Animal Welfare Act and its amendments. The section is divided into 4 sub-sections: Definitions, Regulations, Standards, and Rules of Practice Governing Proceedings Under the Animal Welfare Act. The Definitions section describes exactly what is meant by terms used in the legislation. "Animal", for example, specifically excludes rats of the genus *Rattus* and mice of the genus Mus as well as birds used in research. The Regulations section includes subparts for licensing, registration, research facilities, attending veterinarians and adequate veterinary care, stolen animals, records, compliance with standards and holding periods, and miscellaneous topics such as confiscation and destruction of animals and access and inspection of records and property. The bulk of the subchapter is the third section, which provides standards for specific species or groups of species. Included are sections for cats and dogs, guinea pigs
and hamsters, rabbits, nonhuman primates, marine mammals, and the general category of "other warm-blooded animals". Standards include those for facilities and operations, health and husbandry systems, and transportation. The final section sets forth the Rules of Practice applicable to adjudicating administrative proceedings under Section 19 of the Animal Welfare Act.

***Federal Register*, Vol. 54, No. 168, August 31, 1989, P. 36112-36163.** ***Animal Welfare; Final Rules; 9 CFR Parts 1 and 2***
Often referred to as the "Preamble" to the Animal Welfare Act amendments of 1985, the explanations of the regulations are used to identify the intent of the regulations published in *Title 9, Code of Federal Regulations*. This issue contains final regulations

developed to enact the 1985 amendments to the Animal Welfare Act covering the Definitions and Regulations sections. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Comments and final regulations are provided in many areas including the structure and functions of the Institutional Animal Care and Use Committee; the principal investigator's consideration of alternatives that reduce, refine, or replace animal use; records; licensing; registration; stolen animals; and research facilities.

***Federal Register*, Vol. 55, No. 32, February 15, 1991, P. 6426-6505. *Final Rule: Animal Welfare; Standards; Part 3***
This issue contains final regulations developed to enact the 1985 amendments to the Animal Welfare Act covering the Standards section. Extensive commentary is provided to respond to public comments about each of the proposed regulations. Comments and final regulations are provided concerning exercise in dogs and psychological well-being in nonhuman primates.

***Federal Register*, Vol. 58, No. 139, July 22, 1993, P. 39124. *Final Rule: Random Source Dogs and Cats***
The final rules implementing the 1990 amendment to the Animal Welfare Act and amending the animal welfare regulations by requiring pounds and shelters to hold and care for dogs and cats for at least 5 days (including one weekend day) before providing them to a dealer. Dealers must provide valid certification to anyone acquiring random source dogs and cats from them. Public comments and rationale for the regulatory decisions are discussed. This information updates *Title 9, Code of Federal Regulations , Subpart A, Parts 1 and 2*.

***Federal Register*, Vol. 58, No. 164, August 26, 1993, P. 45040. *Final Rule: Correction, Random Source Dogs and Cats***
Revises several sentences in the original final rule.

***Animal Care Policies***
The policy manual gives policies issued by APHIS/Animal Care that clarify the Animal Welfare Act regulations. Among the topics covered are "Written Narrative for Alternatives to Painful Procedures", "Space and Exercise Requirements for Traveling Exhibitors", and "Annual Report for Research Facilities". Originally issued in April 1997, new policies may be added at any time and included in the manual.

## PUBLIC HEALTH SERVICE (PHS) POLICY

**The Health Research Extension Act of 1985, Public Law 99-158, "Animals In Research."**
Passed by the U.S. Congress on November 20, 1985, this law provides the statutory mandate for the PHS Policy. It allows the Secretary, acting through the Director of NIH, to establish guidelines for the following:

i. The proper care of animals to be used in biomedical and behavioral research
ii. The proper treatment of animals while being used in such research

iii. The organization and operation of animal care committees

The Office of Laboratory Animal Welfare (OLAW, formerly Office for Protection from Research Risks, Division of Animal Welfare) at the National Institutes of Health, has responsibility for the general administration and coordination of the Policy on behalf of the PHS.

**U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training**

The U.S. Principles were promulgated in 1985 by the Interagency Research Animal Committee and adopted by U.S. Government agencies that either develop requirements for or sponsor procedures involving the use of vertebrate animals. The Principles were incorporated into the 1986 PHS Policy and provide a framework for research conducted in accordance with the Policy.

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

- The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et. seq.) and other applicable Federal laws, guidelines, and policies*
- Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society
- The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.
- Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. 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.
- Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.
- Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
- The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of

the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

- Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.
- 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.

  * The reader is referred to the *Guide for the Care and Use of Laboratory Animals*, prepared by the Institute of Laboratory Animal Resources, National Academy of Sciences.

**The Public Health Service Policy on Humane Care and Use of Laboratory Animals**

The Public Health Service Policy on Humane Care and Use of Laboratory Animals can be found in Chapter 54206 of the NIH Manual and Chapter 1-43 of the PHS Manual. The NIH originally initiated the Policy in 1971. It was extended to all PHS activities January 1, 1979, and was revised in the spring of 1985 with implementation to be effective January 1, 1986. With the passage of the Health Research Extension Act of 1985 (PL-99- 158), the policy was further revised and the Director of the NIH was required by law to establish specific guidelines. An additional revision was released in September 1986 reflecting the changes required by this Act.

Under the PHS policy, each institution using animals in PHS-sponsored projects must provide acceptable written assurance of its compliance with the Policy. In this Letter of Assurance the institutions must describe:

- **The Institutional Program** must include a list of every branch and major component of the institution to be covered under the assurance, the lines of authority for administering the program; the qualifications, authority and responsibility of the veterinarian(s), the membership of the IACUC and the procedures which they follow must be stated. The Occupational Health and Safety Program must be described for all those who have animal contact. A training or instruction program in the humane practices of animal care and use must be available to scientists, animal technicians and other personnel involved in animal care, treatment and use. The gross square footage, average daily census and annual usage of each animal facility must be listed.

- **The Institutional Status** must be stated as either:

  - Category 1 - American Association for Accreditation of Laboratory Animal Care (AAALAC) accredited or

  - Category 2 – Evaluated by the Institution's IACUC

- **The IACUC** must be appointed by the Chief Executive Officer and consist of at least five members; including a veterinarian with program responsibility, a practicing scientist, an individual whose expertise is in a non-scientific area and an individual who is not affiliated with the institution. This Committee must use the Guide to review the animal facilities and the institutional program for humane care and use of animals at least once every six months and prepare reports of these evaluations for the responsible institutional official. The Committee must review and approve animal-related components of proposals and significant modifications made in ongoing activities involving the care and use of animals. The Committee is responsible for reviewing concerns involving the care and use of animals and making recommendations to the Institutional Official regarding any aspect of the animal program, the facilities, or the personnel training. The Committee is also authorized to suspend activity involving the care and use of animals as set forth in the PHS Policy.

    - In reviewing the animal care and use component of a proposal, the IACUC must confirm that the project will be conducted in accordance with the AWA and consistent with the recommendations in the Guide. In addition, all procedures are reviewed to assure that pain or distress will be minimized and that (when necessary) appropriate anesthetics, analgesics and tranquilizers will be used. The living conditions and medical care available must be appropriate for the species used, and personnel conducting the procedures must be appropriately trained and qualified. Methods of euthanasia should be consistent with the recommendations of the American Veterinary Medical Association Panel on Euthanasia.

- **The investigator** is responsible for completing a proposal in accordance with the recommendations in the PHS Policy and the instructions contained in the PHS 938 application packet. As of October 1988, the instructions for completing 398 can be found in two locations within the application package. On page 6, the research investigator's responsibilities for assuring the humane care and use of animals are clearly addressed. Detailed instructions for completing Section F of the Research Plan which describes the use of vertebrate animals can be found on page 21.

- **The institution** is responsible for maintaining all the necessary records to document compliance with the PHS Policy and for filing annual reports which detail any changes in the program and indicate the dates of the semi-annual inspections and programmatic reviews.

- **The PHS Policy** described above is intended to implement and supplement the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals in Testing, Research and Training."

## ASSOCIATION FOR ASSESSMENT AND ACCREDITATION OF LABORATORY ANIMAL CARE (AAALAC)

AAALAC International uses the revised *Guide for the Care and Use of Laboratory Animals* (*Guide*), NRC, 1996, as the basis for assessing and accrediting animal care and use programs. AAALAC has modified its position statements to reflect changes in the *Guide*. The following positions will be used by the Council on Accreditation to evaluate and accredit animal care and use programs.

Some statements are paraphrased or excerpted directly from the *Guide*; others are AAALAC International interpretations of the *Guide's* intent. The principles of the *Guide* are outcome-based and include professional judgment and performance standards. If a program deviates from the standards of the *Guide,* there must be compelling reasons with strong rationales for it to be acceptable.

**Laboratory animals**
All vertebrate animals used or to be used in research, teaching or testing at accreditable units are to be included and evaluated in relation to the principles set forth in the *Guide* (NRC, 1996). This includes traditional laboratory animals, farm animals, wildlife, and aquatic animals.

**Adequate veterinary care**
Veterinary care is an essential part of an animal care program. Veterinary care is the responsibility of a veterinarian who is certified or has training or experience in laboratory animal science and medicine in the species being held and used.

Some aspects of the veterinary care program can be conducted by qualified personnel other than a veterinarian; however, a mechanism of direct and frequent communication should be adopted so that timely and accurate information on problems in animal health, behavior, and well-being is conveyed to the attending veterinarian.

The veterinarian should also contribute to the establishment of appropriate policies and procedures for ancillary aspects of veterinary care, such as providing advice on humane animal use in light of scientific requirements; reviewing protocols and proposals with respect to veterinary care, animal husbandry, and animal welfare; monitoring occupational health, hazard containment, and zoonosis control programs; and oversight of animal nutrition, husbandry, and sanitation.

The veterinarian must provide guidance to investigators and all personnel involved in the care and use of animals to ensure appropriate handling, immobilization, sedation, analgesia, anesthesia, and euthanasia. The attending veterinarian must provide direction in the management of protocol-associated disease, disability, or other sequelae; as well as oversight of surgery and postsurgical care.

**Occupational health & safety program**
An occupational health and safety program must be part of the overall animal care and use program. The basic elements of a program include hazard identification and risk assessment, personnel training and protection, written procedures and policies regarding hazard use and monitoring, and medical evaluation and preventive medicine.

The extent and level of participation of personnel in the program should be based on the hazards posed by the animals and materials used; on the exposure intensity, duration, and frequency; on the susceptibility of the personnel; and on the history of occupational illness and injury in the particular workplace. A health history evaluation is advisable before work assignment to assess potential risks for individual employees. Periodic medical evaluations and appropriate immunization schedules are advisable for some risk categories. Immunization of animal care personnel against tetanus is important. In accordance with the *Guide* (NRC, 1996), assurance must be provided by an organization that all personnel at risk are appropriately considered under the occupational health and safety program.

**Multiple major surgical procedures**
Multiple major survival surgical procedures on a single animal are strongly discouraged. However, under certain circumstances they may be permitted when they are scientifically justified by the user and with the approval of the Animal Care and Use Committee. Multiple survival surgical procedures may be justified when they are related components of a research project and are deemed essential. Cost savings alone is not an adequate reason for performing multiple survival surgical procedures.

**Survival surgery facilities**
The AAALAC International position statement pertaining to survival surgical facilities has been withdrawn due to the detailed information provided in the *Guide* (NRC, 1996).

**Farm Animals**
AAALAC International uses the current edition of the *Guide for the Care and Use of Laboratory Animals* (NRC 1996) as its primary standard for evaluating animal care facilities and programs. The full range of programmatic criteria outlined in Sections I-III of the *Guide* are entirely applicable to farm animals, and in accredited facilities, the use of farm animals in research should be subject to the same general ethical considerations as the use of other animals in research.

However, uses of farm animals are often separated into biomedical uses and agricultural uses, and different criteria for evaluating standards of housing and care for animals of the same species may be appropriate. Decisions on categorizing research uses of farm animals and defining standards for their care and use should be based on user goals, protocols, and concern for animal well-being and should be made by the Institutional Animal Care and Use Committee.

For animals in an agricultural setting, AAALAC International takes the position that, in accredited facilities, the housing and care for farm animals should meet the standards that prevail on a high-quality, well-managed farm. *The Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching* (FASS 1999) is recognized by AAALAC International as a reference resource for individual farm animal species. Regardless of an investigator's research objectives or funding source, institutions are expected to provide oversight of all research animals and ensure that their pain and distress is minimized.

**Cercopithecine herpesvirus 1, CHV1 (Herpesvirus-B)**
In addition to using the revised *Guide for the Care and Use of Laboratory Animals*, NRC 1996, as its primary document, AAALAC International also uses *Occupational Health and Safety in the Care and Use of Research Animals*, NRC 1997, "Guidelines for the Prevention and Treatment of B-Virus Infections in Exposed Persons," Holmes, et al., *Clinical Infectious Diseases* 20:421-39, 1995, and the *CDC/NIH Biosafety in Microbiological and Biomedical Laboratories*, 4th Ed., 1999, as resources for assessing the appropriateness of measures to protect personnel and prevent transmission of CHV1.

Each AAALAC International accredited institution housing macaques must have a protection and prevention program for CHV1 as a part of its occupational health and safety program. All macaques should be presumed to be harboring CHV1 and handled accordingly.

The basic elements of the program include standard operating procedures and training for handling macaques and their tissues and dealing with potential exposures; risk assessment and education of all personnel having potential contact with macaques; the presence of supplies for immediate and appropriate patient first aid and animal specimen collection; maintenance of a bite, scratch, and incident log; the required use of appropriate protective equipment, including that necessary for hand and arm as well as for eyes and mucous membrane protection; and access to occupational health and safety staff and medical care staff knowledgeable of both exposures and acute disease.