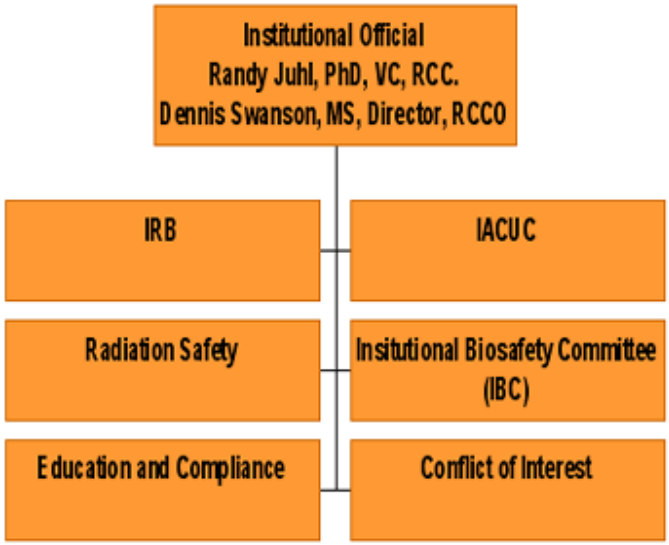
Institutional Animal Care and Use Committee (IACUC)

1 The Research Conduct and Compliance Office (RCCO)

Research Conduct and Compliance (RCCO) Organization

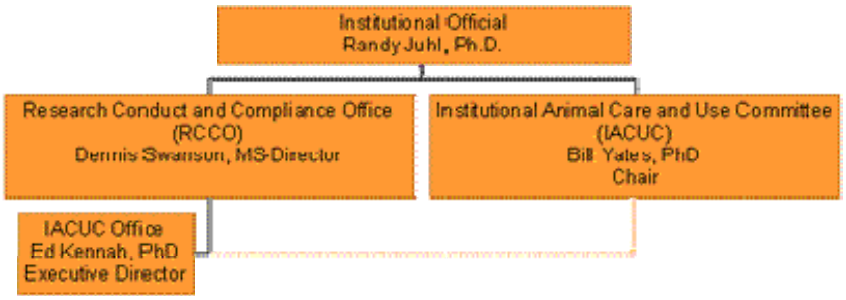


RCCO Functions

- Institutional Review Board (IRB) and IRB administration
- Institutional Animal Care and Use Committee (IACUC) and IACUC administration
- Radiation Safety Committee and office operations
- Education and Compliance audit, education, training and certification
- Institutional Biosafety Committee (IBC) rDNA registration and IBC administration
- Conflict of Interest Committee and office operations

2 IACUC Reporting, Contact Information, Office Staff

Institutional Animal Care and Use Committee Reporting



Click here to see a larger view of the reporting chart.

The IACUC Office

Location:

Suite 200, Hieber Building
3500 Fifth Avenue
Pittsburgh PA 15213
IACUC Email: iacuc@pitt.edu
Phone: 383-2008
IACUC Web site: www.iacuc.pitt.edu

Please call or email with any questions on the writing of, or status of, IACUC protocols, training requirements or personnel status, and issues of compliance or animal welfare

3 Education and Compliance, Organizational Chart, IACUC Membership

Animal Care and Use Program Education and Compliance

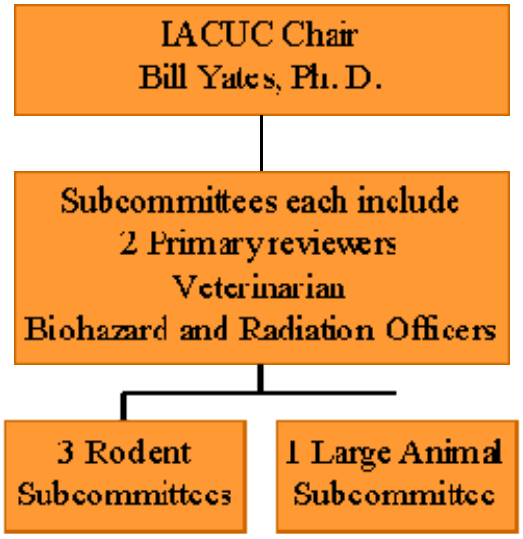
Training Coordinator: 412/383-1737

- Responsible for documentation and coordination of mandated training programs for all personnel involved in research protocols and animal care

Compliance Officer: 412/383-2009

- Responsible for auditing components of the animal research program and assuring compliance with existing regulations and policies

IACUC Organizational Chart



IACUC Membership

The IACUC currently consists of 36 members representing 21 different University departments. If you would like to serve on the IACUC or wish to know the name of your department's representative, contact the IACUC office.

Per federal law, the IACUC must include (in addition to scientists):

- a veterinarian
- a non-scientist
- a non-institutional or lay representative

To maintain a committee that represents the broad interests of the University, the Animal Welfare Act states that no more than three individuals serving on the IACUC can come from the same administrative unit.

4 Duties and Responsibilities

The major function of the IACUC is to establish and maintain measures to ensure the appropriate care and use of all animals involved in research, teaching, and testing.

Duties assigned to the IACUC by the Federal Government include:

- Semi-annually review the University Animal Care and Use program to ensure that humane care and use of animals are being maintained;
- Semi-annually inspect all animal facilities and animal use areas to ensure conformity with federal guidelines;

- Report to the Institutional Official on the status of the animal research program, and submit an annual report to NIH on the status of the program;
- Review and approve all research and teaching procedures using live animals through protocol review;
- Provide a training program for all personnel involved in using or handling laboratory animals;
- Develop policies that reflect local concerns regarding the use of animals.

5 Protocol Review Process

5.1 Types of Protocol Applications

- **New submissions** After an initial protocol application is submitted, protocols must be re-submitted every three years for as long as the project is active.
- **Renewals** All IACUC protocols must be renewed annually by completing an abbreviated form.
- **Modifications**

o Researchers may request relatively minor changes on an approved protocol (e.g., title, type of euthanasia or anesthesia, <25% increase in the number of animals, etc.) on the modification form;
o Because any individual coming in contact with animals for research purposes MUST be listed on the relevant protocol, the modification form may be used to add or delete personnel from protocols.

5.2 Protocol Review Process

- Application forms for protocols should be downloaded from the IACUC web site: www.iacuc.pitt.edu.

  A workbook, available from the Environmental Health and Safety (EHS) Office Website, should be downloaded and completed at the same time. This workbook will be reviewed by EHS according to procedures described in the Occupational Health and Safety section of this training module.
- To assist researchers with the completion of their applications, sample protocols are available on the IACUC website (Protocol Writing Assistance section).
- Once completed, the form should be emailed to the IACUC office (iacuc@pitt.edu), and the EHS Workbook should be submitted to EHS (biosafe@pitt.edu). The IACUC protocol application will not be processed unless the EHS Workbook is completed.
- IACUC protocol applications will be assigned to a subcommittee for review, and the Principal Investigator (PI) will be notified that the application was received. If

such notification is not received within two days after submission, the PI should contact the IACUC Office.

- Two primary reviewers from the Subcommittee, along with a veterinarian and hazard specialists, will review the application. Applications must also be made available to other IACUC members who may wish to review them.

- After all five Subcommittee reviewers have made comments (within 1-2 weeks), any questions will be emailed to the PI from the IACUC office.

- After the PI's responses are reviewed by the Subcommittee members and found acceptable, the application is approved. ('designated' reviewer system).

- A letter approving the protocol is signed by the IACUC Chair and delivered to the PI.

- The IACUC's goal for protocol review turn-around time is 30 days.
- Any IACUC member may request a full committee review of any protocol. The entire committee meets monthly.

- Any PI may request to address the full committee regarding protocol issues. This request should be made directly to the IACUC Chair.

- ***Protocol approval is not an assurance that space is available in the animal facilities. It is recommended that PIs contact the Division of Laboratory Animal Resources (DLAR) for information prior to ordering animals.***

- Any protocol using biohazards submitted to the IACUC must have approval from the Biosafety Committee.

o All animal protocols are reviewed by the Environmental Health and Safety Office to assure that occupational health and safety are maintained. This review process is discussed further in the Occupational Health and Safety section of this training module.

o A Workbook must be completed (available from http://www.ehs.pitt.edu) and submitted at the same time as the protocol to facilitate this review. This workbook should list all chemical and biological agents used in the study.

o The Institutional Biosafety Committee (IBC) is responsible for reviewing and approving all work involving recombinant DNA (rDNA) at the University of Pittsburgh. Institutions that perform recombinant DNA research are required by Federal guidelines to have an expert committee in place to review safety procedures for such research. The University of Pittsburgh's Institutional Biosafety Committee (IBC) is made up of faculty members, as well as two members from the community.

Contact information:

University of Pittsburgh Biosafety Committee
Biosafety Officer 412/624-9505
Director 412/624-9505
Email biosafe@ehs.pitt.edu

Institutional Biosafety Committee
Director 412/383-1768
Email rdna@pitt.edu

5.2.1 Causes for Delay in Protocol Processing

- Application is incomplete.
- The PI has not responded to questions posed by the IACUC Committee.
- A Subcommittee member has requested a Full Committee review.

5.2.2 Issues that Often Delay Approval

- Project Personnel
  All personnel listed as participants on a project MUST have completed the appropriate training. See the IACUC website for information on training requirements.
- Rationale For Numbers of Animals Requested
  The number of animals requested must be in agreement with the proposed number of groups and the numbers per group. The number of animals per group must be based on statistical power analysis, where possible.
- Assignment to Pain and Distress Categories
  The percentage of animals listed in various pain and distress categories must equal 100%.
- Experimental Manipulation
  Procedures should be described so that reviewers know what will happen to the animal from the time it arrives at the University until euthanized.
- Experimental manipulations must be detailed clearly and in lay terms.
- Tables and flow charts are useful in expediting review. (PIs should not insert the Methods section of a grant into the application.)
- The experimental endpoint (dependent variable) must be specified.
- Search For Alternatives
  The Animal Welfare Act and USDA Policy 12 require that a search for alternatives to potentially painful/distressful procedures, performed on animal

species other than rats and mice, be included for protocols employing such procedures. This search must be documented by a description of computer databases used, as well as inclusive dates and keywords employed. The search can include consultation with experts or attendance at meetings at which alternatives were discussed. Narratives must be provided that are clearly based on the results of the literature search or expert consultation must be provided. Although a reference librarian is available for assistance in performing searches (Alice Kuller, Falk Library, 412/648-1971), it is the responsibility of the PI to review the literature uncovered in the search.

- Responses to Reviewers' Concerns
  Direct and thorough responses to concerns raised during the review process will greatly reduce protocol turnaround time.

5.2.3 "Red Flag Issues" (that require greater scrutiny by the IACUC)

- "High profile" studies i.e., use of nonhuman primates or biohazardous agents
- Death as an endpoint
- Mouse ascites production
- Multiple survival surgical procedures
- Stress/trauma paradigms, such as prolonged restraint, cold exposure, etc.
- Long-term restraint
- Use of hazardous agents
- Food and/or water deprivation

5.2.4 Protocol Numbering Process

The following protocol numbering system is employed by the IACUC Office:

- Protocols are assigned a 7-digit number according to the date of approval (first four digits), and a unique place-holder (last three digits):

  - Year__/month__/Place holder___;
  - -A or -B following the protocol number indicates a first or second annual renewal;
  - -1,-2,….-x at the end indicates the number of minor modifications.

5.2.5 Protocol Renewal

- A renewal application must be submitted annually, and a new protocol application must be submitted every three years in order to continue work under a given protocol.

- The Principal Investigator will receive a reminder at 90 days, 60 days, and 30 days prior to annual or 3-year protocol expiration dates.

- The Principal Investigator must submit the renewal or new application no less than 30 days before expiration, and respond to all reviewer queries in a timely manner to assure that work can be continued without interruption.

- If a lapse in protocol approval does occur, no further animal ordering will be permitted, and any animals currently on hand will be confiscated. No further experimentation on those animals will be allowed until the protocol has been approved.

5.3 Institutional Animal Care and Use Committee (IACUC)

- PIs are asked to volunteer for a three-year term of IACUC service in order to help them understand the process, and convey that understanding to their colleagues.
- Prompt response to Committee questions leads to timely protocol approval.
- PIs should submit a completed protocol questionnaire at least one to two months before approval is needed.
- For help in completing their application, PIs should consider a consultation with an IACUC coordinator, faculty IACUC representative, or DLAR veterinary staff member prior to protocol submission.

6 Grant Review

- Grants submitted to the National Institutes of Health (after October 1, 2002) are required to comply with the Public Health Service "Just in Time"
- This policy prohibits the release of grant funding to investigators until the IACUC has reviewed the grant application and has ensured that all proposed methods are described in an approved IACUC protocol.
- To comply with this policy, the PI should download the "Grant Application Review Form" from the IACUC website. The completed form should be submitted to the IACUC office, along with the Methods section of the grant application.
- To assure that grant monies are released in a timely manner, the grant review process should be initiated as soon as the PI learns that a fundable score was received.
- The IACUC will review the grant application; if all procedures are appropriately described in the IACUC protocol, the Office of Research will be informed that grant funding can be released.
- For procedures not described in active protocols, the PI will be informed so that new protocols or protocol modifications can be submitted.
- The Office of Research will not release any grant monies to investigators until the IACUC grant review process is complete.
- This policy policy applies only to grants submitted to the National Institutes of Health.

7 Training

7.1 Defining the Training Program

- All persons using animals in teaching or research must complete Use of Laboratory Animals in Research and Education (Module 3) on the Education and

Certification Program in Research & Practice Fundamentals website (http://rpf.health.pitt.edu/rpf/).

- In addition, investigators/personnel using animals for research must complete the Research Integrity Module (Module 1) on the Research & Practice Fundamentals website (http://rpf.health.pitt.edu/rpf/).
- Furthermore, investigators must complete specialized training relevant to the species they employ in their research. Watching a videotape and completing a test that is submitted to the IACUC training coordinator usually accomplish such training.
- The three video training modules are:
  Small Animal (rodents)
  Large Animal (mammals other than rodents or nonhuman primates)
  Nonhuman Primates

  To arrange for this video training, PIs and other research personnel should contact the Training Coordinator.

7.2 Compliance with Training Requirements

- All individuals (PIs, Graduate Students, Postdoctoral Associates, Research Technicians, Undergraduate Students, Volunteers) coming into contact with animals for research purposes MUST complete the required training program prior to being added to the relevant protocol.
- Animal care staff must also complete training relevant to the species they will have contact with, and may be required to complete training for all animal species
- The training required for a protocol is listed on the Risk Assessment document provided to the Principal Investigator when the protocol is approved.
- PIs have the responsibility of ensuring that all individuals coming into contact with animals under their protocols have received all mandated training and are listed on the protocols.

8 Investigator Responsibility

Principal Investigators must also ensure that all individuals conducting experimentation on animals are listed on the relevant IACUC protocol. Individuals must be added to the protocol prior to beginning research using animals.

PIs must also make a copy of the protocol readily available to any individual listed on the protocol. It is advised that a binder containing all active protocols for the laboratory be located in a place that is readily accessible to all staff and students.

The issue of pain and/or distress is a critical one. It is the investigator's responsibility to address this issue in depth during the protocol approval process by indicating what procedures will be used to eliminate pain/distress as much as possible during the study.

To this end, in their book *Principles of Humane Experimental Technique* (1959) Russell and Birch described the "three Rs" of reduction, refinement, and replacement, to improve animal welfare and "advocate alternatives to live animal use in research."

8.1 The 3 R's

- Reduction: reducing the number of animals used in a study without jeopardizing statistical validity;
- Refinement: decreasing in the incidence or severity of painful/distressful procedures, i.e., the use of genetic models in place of surgically or chemically-induced models; the use of Specific Pathogen Free (SPF) and bred-for-research animals;
- Replacement: substituting insentient materials, i.e., in vitro methodologies and computer models, for conscious, living, higher animals.

9 Mistreatment of Animals and Noncompliance

It is the IACUC's responsibility to investigate all allegations of mistreatment of animals or noncompliance in a thorough and timely manner.

- Good faith reporting of such violations ("whistle blowing") will not be detrimental to an individual's standing within the institution, and discrimination or reprisal for reporting of violations is prohibited by Federal Law. The University of Pittsburgh's Animal Care and Use Committee investigates all concerns regarding the care and treatment of animals. To report a concern, contact one of the following:
    - IACUC Chair 412/647-9614
    - IACUC Director 412/383-2014
    - Compliance Officer 412/383-2009
    - DLAR Director 412/648-8950
    - Any IACUC member or DLAR veterinarian (DLAR on call emergency pager: 412/917-2340)
- Sanctions for noncompliance with University policies regarding animal research may include:
    - Letter of reprimand
    - Monetary fine to be paid by PI
    - Frequent, unannounced inspections
    - Suspension/termination of the IACUC approval of the respective research study
    - Suspension of further animal orders for the respective study
    - Permanent revocation of animal use privileges at the University of Pittsburgh
    - Notification of funding agency of IACUC actions.

10 Summary

The Research Conduct and Compliance Office (RCCO)

The RCCO Office was formed to bring together some of the regulatory compliance units at the University that oversee biomedical and psychosocial research and teaching. With time, additional regulatory units may join this Office. The responsibility for the Research Conduct and Compliance Office and its constituent regulatory units rests with the Vice Chancellor for Research Conduct and Compliance.

Organizational Charts, and IACUC Staff

In 1985, two government agencies, the United States Department of Agriculture and the National Institutes of Health, implemented regulations that require each research institution that is involved in animal-based research to organize an Institutional Animal Care and Use Committee (IACUC). The two agencies outlined similar requirements for committee functions. The Committee is responsible for the institution-wide animal research program, including review of all proposed research and teaching protocols involving animals. The Committee is responsible to an Institutional Official, who is, in turn, responsible for submitting annual reports on the status of the program to Federal agencies.

Duties and Responsibilities

It is the responsibility of the IACUC to establish and maintain measures that ensure the appropriate care and use of all animals involved in research, teaching, and testing at the University of Pittsburgh.

Protocol Review

A major component of mandated IACUC oversight is the review of all research, teaching and testing protocols involving animals. To accomplish this function the Committee is subdivided into four Subcommittees: three Rodent Subcommittees and one Large Animal subcommittee. The Subcommittees review protocols, and only after all questions and queries made by the Subcommittee have been answered satisfactorily is the protocol given final approval.

Grant Review

Grants submitted to the National Institutes of Health (after October 1, 2002) are required to comply with the National Institutes of Health "Just in Time" IACUC review policy.

Training

Federal law mandates that research facilities provide training for personnel participating in animal protocols involving research, teaching and testing.

Investigator Responsibility

Principal Investigators must ensure that all individuals conducting experimentation on animals are listed on the relevant IACUC protocol. Individuals must be added to the protocol prior to beginning research using animals. Furthermore, all individuals must be adequately trained in performing procedures on animals before such procedures are attempted.

Mistreatment and Non Disadvantages

It is the IACUC's responsibility and function to investigate all allegations of mistreatment or noncompliance in a thorough and timely manner.