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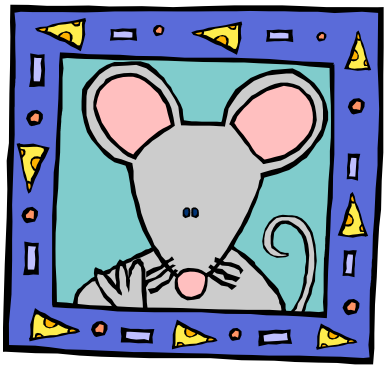

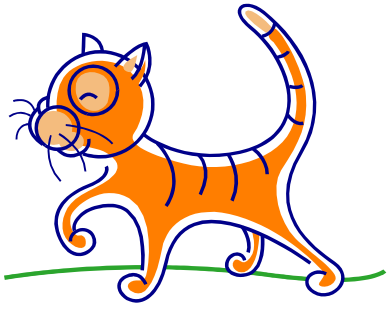

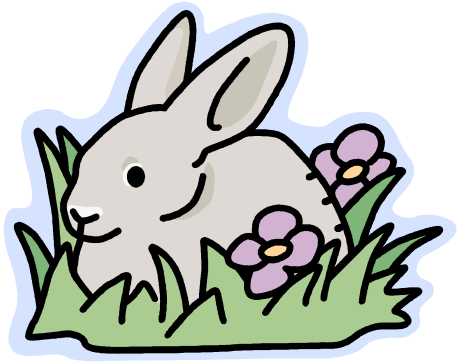

ANIMAL USERS TRAINING HANDBOOK

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Content Approved by UCHC ACC

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University of Connecticut Health Center

Animal Care and Use Program Personnel Training

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I. ANIMAL CARE AND USE PROGRAM OVERVIEW

1. Overview

Proper care, use, and humane treatment of animals used in research, testing, and education require scientific and professional judgment based on knowledge of the needs of the animals and the special requirements of the research, testing, and educational programs.

The University of Connecticut Health Center is required to ensure that animal use conforms to a multitude of state and federal regulations which include compliance with the Animal Welfare Act (AWA) in accordance with the Animal Welfare Regulations (9 CFR, 1985, 2005), the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (2002), and the recommendations promulgated by the *Guide for the Care and Use of Laboratory Animals* (1996).

Responsibility for directing the program lies with the Director of the Center for Laboratory Animal Care (CLAC). The institution is responsible for maintaining records of the activities of the Institutional Animal Care and Use Committee (IACUC) and for conducting an occupational health and safety program as well as a training program. Overall responsibility for the animal care program and the IACUC lies with the institutional official (IO).

2. Brief History of Animal Use and Literature Review

The use of animals in the life sciences dates back to ancient Greece and the earliest medical experiments. To learn about swallowing, ancient physicians cut open the throat of a living pig. To study the beating heart, they cut into its chest.

For centuries, physicians and researchers used animals to enhance their knowledge about how the various organs and systems of the body functioned, as well as to hone their surgical skills. As this knowledge grew, new scientific disciplines were born. First, physiology and pharmacology, and much later bacteriology and immunology, evolved as animal experimentation became more widespread.

As long as animals have been used in experiments, people have expressed concerns about such research. Questions about the morality, necessity, and scientific validity of animal experiments have arisen since those ancient physicians first began to study bodily functions.

The rise of modern biomedical science in the nineteenth century saw an increase in both the numbers of animals used in experiments and in the number of complaints about vivisection. Although opinion varied among scientists and the public about the degree of suffering experienced by animals, most scientists were united in the belief that animal experiments were necessary to expand their knowledge.

If you look in the literature, you see that, from the mid-1800s on, there is a steady increase in animal use in medical education, Harvard University and Johns Hopkins School of Medicine being early advocates of animal use. The use of rats and mice as research animals dramatically increased in the early 1900s with the Wistar Institute in Philadelphia and Jackson Labs being leaders in the use of these rodents.

The UK was the first country to establish any laws regarding animal welfare with the British Cruelty to Animals Act of 1876. However, the United States had some of the first organizations formed with the primary function of opposition to animal use in research and testing. These organizations included the Pennsylvania Society for the Prevention of Cruelty to Animals (1867), American Antivivisection Society (1883), and the California Antivivisection Society (1908).

The stage was set for the use of animals in research and testing in 1949 with the Nuremberg Military Tribunal's decision in the case of the United States v Karl Brandt et al. This decision includes what is now called the Nuremberg Code, a ten point statement delimiting permissible medical experimentation on human subjects. Point 3 of this Code states that the experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

The animal protection movement has broadened its scope and support base considerably during the post World War II period. There was a large economic boom in the US and a resultant large increase in scientific research. There was also a huge increase in the NIH budget which helped to increase scientific research.

Animal rights activists were not the only individuals to be involved in discussions of the use of animals in research— the scientists were now getting involved in what they perceived as their right to, and the necessity of, animal research. In 1950, the Animal Care Panel was founded by Drs. Nathan Brewer, Elihu Bond, Robert Flynn, Bennett Cohen, and Albert Schroeder all veterinarians and truly pioneers in laboratory animal medicine. Their mission was to ensure the humane treatment of animals used in research and testing. In 1951, they published their *Proceedings of the Animal Care Panel*— a document which was utilized by the US legislature as it wrote both the Animal Welfare Act and PHS policy approximately 15 years later. In 1957, British researchers W. Russell and R. Burch published their book *The Principles of Humane Experimental Technique*. It was in this publication that the authors advocated the "three Rs" of replacement, reduction, and refinement. These concepts are now considered standard concepts in reviewing applications of animal research.

In 1952, the Institute of Laboratory Animal Resources (ILAR) was founded. The Animal Facilities Certification Committee (Board) was formed which, in 1965, would change its name to the American Association for the Accreditation of Laboratory Animal Care (AAALAC). 1963 saw the first publication to promote standards in laboratory animal care with *Guide for Laboratory Animal Facilities and Care*, the first edition of what is now the 7th edition (1996) of the *Guide for the Care and Use of Laboratory Animals* (the *Guide*). In 1967, the Animal Care Panel formed in 1950 had changed its name to the American Association for Laboratory Animal Science (AALAS).

Not to be outdone by the scientists, the US government started to regulate animal research. In 1962 an NIH grant was used to generate the 1st edition of the *Guide* which was published in 1963. The Laboratory Animal Welfare Act was first passed in 1966 which changed to the Animal Welfare Act in 1970. 1971 saw the development of the NIH Policy which required institutions using NIH funds to have an NIH assurance and suggested accreditation through AAALAC, required annual inspections, and demanded compliance with the AWA and the *Guide*. The Public Health Service Policy was first passed in 1973 included animals for research, testing, education, and demonstration. 1985 saw the passing of the PHS Act (Health Research Extension Act of 1985) which further regulated laboratory animal care.

The public was not to be outdone, either. The 1962 publication of *Silent Spring* by Rachel Carson brought animal welfare to society as a whole, not just the activists, scientists, or government agencies. 1966 saw an article in LIFE magazine entitled "Concentration Camps for Dogs" which fired up animal activists and the general public. Greenpeace was founded in 1969. With the publication of Peter Singer's 1975 treatise, *Animal Liberation*, animal welfare issues continued to be a hot topic. When society became aware of what became known as "The Silver Spring Monkeys" case and the University of Pennsylvania Head Injury Studies (both of which used non-human primates and had some deplorable animal care problems), the debate regarding animal use sky-rocketed and continues to this day. Some of the "animal welfare" organizations have challenged, and continue to challenge, whether human beings have the right to "use" animals for any purpose. Others question the morality, necessity, and validity of animal tests, just as their counterparts did centuries ago.

It has been due, in large part, to the tension between researchers who view laboratory animals as essential to their work and individuals who oppose animal tests that the modern alternatives movement has evolved. In the 1980's and 1990's, humane animal care philosophy has enabled researchers and

animal welfare advocates to come together with a common goal: to find scientifically valid alternatives to animal tests.

In March, 1997 NASA promulgated the document "NASA Principles for the Ethical Care and Use of Animals". It was intended to guide careful and considered discussion of the ethical challenges that arise in the course of animal research under NASA's auspices, but is helpful to animal use in general. Briefly stated, the document states that a strong allegiance to the principles of bioethics is vital to responsible research practices and that vertebrate animals warrant moral concern. The use of animals in research involves responsibility— not only for the stewardship of the animals, but to the scientific community and society as well. The three basic principles of the document include:

1. Respect for life— this principle requires that animals used in research should be of an appropriate species and health status and should involve the minimum number required to obtain valid scientific results. It also recognizes that the use of different species may raise different ethical concerns.
2. Societal Benefit— This principle entails that where animals are used, the assessment of the overall ethical value of such use should include consideration of the full range of potential societal good, the populations affected, and the burdens that are expected to be borne by the subjects of the research.
3. Non-malficence— this principle entails that the minimization of distress, pain, and suffering is a moral imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in humans may cause pain or distress in other sentient animals.

Humane care and use of laboratory animals is a topic which is world-wide. OneVoice, an animal rights organization based in France, recently commissioned an opinion poll of 1000+ French citizens aged 15 and older. The results were as follows:

1. 64% of the respondents somewhat or completely disagreed with the use of animals in research and testing,
2. 87% believed that research which causes animals to suffer should be prohibited,
3. 85% support potential animal use alternatives such as computer technology, cell cultures, and statistical models,
4. 60% agree that animal testing for cosmetics should be banned,
5. 72% support a total ban on the use of dogs and cats in research and testing, and
6. 70% feel that governmental regulations are insufficient to curb animal experimentation.

Similar polls have been performed in the US and UK with similar results. It is reasonable to assume that the issue of humane animal care will continue to be in the public consciousness for the foreseeable future. It would be reasonable to conclude that humane laboratory animal care and use is assured only by a close working relationship between society, governmental agencies, scientists who use laboratory animals, and the institutions (through their IACUCs) which perform animal experimentation.

3. Protocol Review

Adequate review of your protocol depends on the Animal Care Committee (ACC), which is our institutional IACUC, receiving a thorough, well-written document that conforms to USDA and PHS policies as well as recommendations set forth by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and the *Guide*.

There are many federal agencies which govern protocol requirements: the PHS Policy (Health Research Extension Act of 1985 with revisions in 1986 and 2002); NRC Guide on OHS (1977), Animal Welfare Act (9 CFR) and USDA animal care policies (19997-2002). In addition, AAALAC requires institutions to follow all recommendations in the *Guide* to maintain accreditation with that organization.

Animal research in the United States is considered by many experts to be more highly regulated than human research.

The copy of the current protocol form (version 7/1/06) is located on the ACC website (http://clacc.uchc.edu/ACC/Animal_Care_Committee.htm). All new applications must be filled out on this form. You can obtain an on-line version of this form from the ACC website (http://clacc.uchc.edu/ACC/SubmittingProtocols.htm). This form has been devised to conform to key information required by AAALAC, PHS, and the USDA. The mandated information includes: selection and justification of species; living conditions of the animals; justification for the use of animals; applications of the principles of replacement, reduction, and refinement; ethical cost-benefit relationship; treatment of pain and discomfort; post-procedure monitoring; restraint; euthanasia; qualification of research personnel; and occupational health and safety.

There are differing requirements of how long a protocol is "valid"; PHS policy and USDA policy are similar yet different in this regard. PHS Policy requires the ACC to perform a **complete re-review** of the project **at least** once every three years. USDA requires the ACC to conduct continuing review **no less** often than annually. In order to satisfy both requirements, the ACC uses the following criteria for review: A protocol is valid for 3 years providing that a yearly review form is submitted after years one and two. If a protocol will be continuing after 3 years, a new protocol must be written and submitted.

Protocol Review Methods

There are only two protocol review methods (for initial review, modifications, and continuing review) which fulfill PHS and USDA requirements: Designated Member Review (DMR) and Full Committee Review (FCR). We use both protocol review methods at the Health Center. In FCR, a primary, veterinary, and safety reviewer is assigned for each protocol by the ACC Administrator. At a convened meeting of a quorum of the ACC, each protocol is presented by the primary reviewer and then the protocol is discussed by all ACC members to approve, modify, or disapprove the protocol by a simple majority vote. In DMR, a primary, veterinary, and safety reviewer is assigned to each protocol to represent the full committee. Every member of the ACC is notified of the review for an opportunity for review and call for a full committee review if any member wants it. If no one calls for a full committee review, then it is up to the dedicated reviewers to review the document, request changes, and approve the protocol. DMR cannot disapprove protocols- only a full committee review may do that.

Approval Criteria for each section of a protocol review

Section I: Selection and Justification of Species

- The animal model selected should be the most appropriate species for the project based upon anatomical, physiological, or other characteristics in consideration of the scientific objectives and the need to obtain valid results.

Section II: Living Conditions of Animals

- The living conditions of animals must be appropriate for their species and contribute to their health and comfort. Any deviation from standards set forth by the *Guide* and the USDA regulations must be scientifically justified and approved by the ACC.

Section III: Justification for the Use of Animals

- Procedures involving animals should be designed and performed with due consideration given to their relevance to human or animal health, the advancement of knowledge, or the good of society.
- Protocols involving animals should have a sound research design and the animals selected should yield valid results.

● Projects involving animals must not unnecessarily duplicate previous experiments. While duplication is often a scientific necessity, it should be justified.

Section IV: Application of the Principles of Replacement, Reduction, and Refinement

● Replacement: When an objective(s) can be achieved using reasonably available non-animal models or *in vitro* models, the alternative should be used, thus avoiding the need for live animals.
● Reduction: The number of animals to be used should be minimized to the greatest extent possible consistent with sound scientific and statistical standards.
● Refinement: Procedures should be used that have the least amount of potential pain, discomfort, distress, or morbidity (PDDM) in consideration of any limitations imposed by the objectives of the project. PDDM should be minimized through pharmacological and other means.
● The investigator must provide a written narrative describing the methods and sources used to determine that alternatives to painful/distressful procedures were not available. The written narrative must include: databases searched (must be greater than one), or other sources consulted (i.e., named expert), the date of the search, the years covered by the search, and the key words and/or search strategy. All three Rs must be addressed.

Section V: Ethical Cost-Benefit Relationship

● The ethical cost of the research must be outweighed or balanced by the potential value of research to human or animal health, the advancement of knowledge, or the good of society.

Section VI: Treatment of Pain and Discomfort

● Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in animals.
● Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with state of the art sedation, analgesic, or anesthesia unless withholding is justified for scientific reasons.
● Pain alleviating agents should be administered as part of a continuum when appropriate in accordance with established veterinary practices. Where pain is concerned, the animal should always be given the benefit of the doubt.

Section VII: Post-Procedure Monitoring

● All animals must be monitored at appropriate intervals which are dictated by the species, the nature of the intervention(s), the degree of potential post procedure pain, discomfort, or distress, the likely duration, and the possible complications.
● During monitoring, animal should be evaluated for the presence of pain, discomfort, or distress. In assessing animal welfare, the monitor should use criteria based upon the normal behavioral pattern of the species. Simple observation by a skilled monitor can reveal a great deal of information.

Section VIII: Restraint

● Mechanical restraint must be justified. It is unacceptable to use mechanical restraint procedures on conscious animals if non-mechanical forms of restraint can be used.
● The restraint device must provide the animal with the opportunity to assume its normal postural adjustments. The animal should be conditioned to the device, the duration of restraint must be minimized, and the animal observed at appropriate intervals.

Section IX: Euthanasia

● The method of euthanasia should be based upon the species, size of the animal, the scientific objectives of the experiment, and its ability to quickly and painlessly produce a loss of consciousness and death. Euthanasia must comply with current AVMA guidelines.

Section X: Qualification of Research Personnel

● Personnel who perform procedures involving live animals must be knowledgeable about the biology of the species under study and must be fully qualified by training and experience to carry out their assigned surgical and non-surgical procedures and responsibilities related to the care of the animals. Any individual who lacks the prerequisite qualifications must be trained before they interact with the animals.

Section XI: Occupational Health and Safety

● The ACC must be satisfied there is an effective occupational health and safety program which ensures that the risks associated with the experimental use of animals are reduced to acceptable levels and that personnel are appropriately trained.

4. The Three Rs: Replacement, Reduction, and Refinement

The growth of medical and veterinary research and of the pharmaceutical and biotechnology industries has brought about a vast increase in the numbers of non-human animals employed as the subjects of experiment. We owe to animal experimentation many, if not most, of the benefits of modern medicine and countless advances in fundamental scientific knowledge. With the increase of the use of animals, it has been recognized that the most humane treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiments.

The treatment of experimental animals may be broadly divided into two categories: their treatment when not actually under experiment (husbandry) and their treatment in the course of the experiments themselves. We look toward providing humane treatment in both categories.

Replacement is the substitution for conscious living higher animals of insentient material. **Reduction** is a decrease in numbers of animals used to obtain information of a given amount and precision. **Refinement** is any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used.

There is clearly overlap between these categories; however, despite the overlap, this threefold division is useful as a means of bringing some order to the subject of humane use of laboratory animals.

“Replacement technique” is a term commonly used to describe any scientific method employing non-sentient material which may replace methods which use conscious living vertebrates. This would include higher plants, microorganisms, and metazoan endoparasites.

Replacement techniques may be relative and absolute. In relative replacement, animals are still required. In absolute replacement, animals are not required at all. Absolute replacement may be seen as the ideal, but having relative replacement combined with reduction is seen as a viable alternative.

Reduction is desirable in any procedure, however directly humane, which employs large numbers of animals. Reduction is of great importance and, of all modes of progress on the three Rs, it is the one most obviously, immediately, and universally advantageous in terms of efficiency. One general way in which great reduction may occur is by the right choice of strategies in the planning and performance of whole lines of research. Many investigators settle early in their research career on some strategy that appears to suit them and are liable never to change from that strategy.

In a research project by Hume (1957), he showed that every time any particle of statistical method is properly used, fewer animals are employed than would otherwise have been necessary. Failure to make some of the planned observations is a common mistake in many experimental procedures.

Refinement choices change as our knowledge of science increases. We have much more effective pain relieving alternatives today than we did even 10 years ago. Refinement techniques include the basic experimental design being used in the protocol- using those techniques which have been shown to give the best results- the choice between procedures for a given objective. The research design should avoid elaborate and roundabout methods. Careful formulation of research questions is another refinement technique: it is a useful guiding principle in experimentation to ask the question and then draw up, at least mentally, a list of procedures by which is could be answered.

The choice of species is among the most important variables in the determination of procedures. The species you choose for your experimentation should be the species which best matches the requirements of the investigation. It is preferable to use lower vertebrates when given a choice of species.

Methods to Reduce Animal Numbers

1. Statistics and Power Analysis

The term ***Reduction Alternatives*** describes methods for obtaining comparable levels of scientific procedures or for obtaining more information from a given number of animals. Proper statistical design is essential. There is evidence that poor experimental design and inappropriate statistical analysis has lead to the inefficient use of animals. This may be due to a low level of statistical expertise in the investigators so that they are unaware of the potential value of obtaining statistical advice. Alternatively, they may be unable to do so because of a lack of qualified biometricians with experience in their field of interest. In a research project by Hume (1957), he showed that every time any particle of statistical method is properly used, fewer animals are employed than would otherwise have been necessary.

Statistical significance and biological significance are not the same; however, statistical and biological significance can be linked through the use of statistical power analysis. The statistical power of a test is the probability of getting a statistically significant result, given that the null hypothesis is false. Power is proportional to the sample size, significance criterion, and effect size, and is inversely proportional to the variance in the population. Effect size is a measure of biological significance: it is the difference between the results predicted by the null hypothesis and the actual state of the population being tested. Power analysis can be used to determine whether the experiment has a good chance of producing a statistically significant result if a biologically significant difference exists in the population or, in other words, determining if the experiment has a high power given a biologically significant effect size. What constitutes "high power" is best left to the researcher, but conventions of 0.8 and 0.95 have been suggested in the literature.

It is beyond the scope of this general introduction to teach statistics to the researchers, but there are methods that are out there that are available. Consultation with a biostatistician can yield benefits to the PI and the experimental animals. For a good general article on selecting appropriate numbers of animals for research, as well as web sites for statistical education, please refer to the following ACC website: http://clacc.uchc.edu/ACC/Methods%20to%20reduce%20animal%20numbers/WaystoReduceAnimalNumbers.htm.

2. Pilot Studies

Pilot studies are a good way to reduce the number of animal used; the ACC may even require a pilot study when reviewing a protocol. Pilot studies can be used to estimate variability and evaluate procedures and effects.

3. Appropriate Use of Endpoints

The precision of an experiment depends mainly on the sample size and error variance. Careful attention must be given to the type of endpoint used. Qualitative endpoints (e.g., dead/alive) often involve severe

pain and distress and generally provide less information than quantitative measurements. More information can generally be found using quantitative endpoints and can, in some instances, lead to a reduction in the number of animals used during an experiment.

4. Sharing Animals
In some instances, it is possible to share research animals. For instance, animals euthanized by one investigator can provide tissue for use by another investigator. There are instances in which this should never be attempted (e.g., animals have been exposed to biological hazards or recombinant DNA), but it is a method to reduce animal numbers that should be explored by researchers.

5. Use Quality Animals and Veterinary Care
When PIs use the correct choice of an animal model- one that uses healthy, genetically similar animals- it generally decreases variability and, hence, animal numbers. You can minimize the loss of animals by providing good post-operative care, avoiding unintended breeding, and planning ahead so that the appropriate number of animals needed for the studies are ordered and/or bred.

6. Computer Simulations
Though not always possible, there are cases in which there are computer simulations available which can mimic functions of physiology. These are typically most helpful in the case of training protocols.

7. Use of Cell Culture
When possible, consider the use of cell cultures rather than animals. For example, there are *in vitro* systems which use cell culture to generate monoclonal antibodies rather than using laboratory animals.

8. Auto Controls
It would be helpful, whenever possible, to design experiments in which animals serve as their own control. For example, if a procedure were to be performed on a limb, instead of doing the procedure on both limbs of an animal- and having separate control animals- do a unilateral procedure with the control being the opposite limb. Though this is not always possible, it is a well-established method for reducing animal numbers.

9. New Instrumentation and Techniques
Using new instrumentation or innovative techniques that can improve precision can reduce the number of animals needed for a study. This has the added benefit of also being a refinement technique for the protocol.

5. Evaluating Pain and Distress in Laboratory Animals

Government agencies and the *Guide* state that, unless determined to be otherwise, anything that would be considered painful or distressful to humans should be considered to be painful or distressful in animals. The USDA, under the AWA, states that for any procedures which are determined to cause pain / distress in laboratory animals, a veterinarian must be consulted in the planning stages of the procedure(s).

Acute pain and/or distress in animals is generally rapid in onset and more intense than chronic pain. The following are signs that may be exhibited by an animal in acute pain and/or distress:

- Guarding: animal protects painful area by moving away or biting the handler
- Vocalization: animal may vocalize on movement or on palpation of painful area
- Self-mutilation: animal may repeatedly lick, bite, scratch, or shake the painful area
- Restlessness: pacing, constant shifting of weight, repeated standing up or lying down
- Abnormal ambulation: reluctance of difficulty in moving or rising from a lying to a standing position
- Abnormal postures: hunched posture, head hanging down, stiff-legged, tucked abdomen

Chronic pain/distress may be more intermittent or less intense than acute pain/distress and is often more difficult to assess. The following are signs that may be exhibited by an animal in chronic pain/distress:

- Clinically evident body weight loss and/or dehydration
- Change in temperament or behavior towards handler
- Lack of self-grooming, as evidenced by ruffled or soiled hair coat
- Reluctance to move or ambulate

Criteria for establishing endpoints:
The following parameters should be considered when establishing humane endpoints:

1. Body weight of animals as compared to age-matched, untreated cohorts or to a defined baseline
2. General physical appearance of the animal
3. Behavior of the animal
4. Response of the animal to external stimuli
5. Measurable clinical signs (e.g., body temperature, blood cell counts)
6. Ability of an animal to gain access to food and water and normal eating/drinking habits
7. Ability of an animal to ambulate

The following are endpoints that would require notification of the Attending Veterinarian and initiation of treatment, removal of animals from study, and/or euthanasia of animals:

1. Rapid body weight loss (>10% in 48 hours or >20% over course of experiment)
2. Debilitating diarrhea (>48 hours in duration)
3. Self-induced trauma
4. Bleeding from any orifice
5. Neurological signs incompatible with maintenance of normal life functions (e.g., inabilities to eat, drink, or ambulate)
6. Excessive or prolonged (greater than 24 hours) hyper- or hypothermia
7. Respiratory difficulties (e.g., labored breathing, nasal discharge, coughing)
8. Ambulatory difficulties: any animal unable to ambulate or maintain a normal body position
9. Jaundice or anemia
10. Change in behavior (e.g., lethargy, hunched posture)
11. Inability to gain access to food or water and eat/drink normally
12. Non-responsive to external stimuli
13. Moribund condition

Any animal found moribund should be euthanized immediately or the Attending Veterinarian should be notified for consultation on immediate medical intervention plans. For group-housed animals, consideration should be given to moving animals to individual cages when their condition deteriorates to the point that injury from other animals is likely.

Monitoring

Any animal experiencing adverse clinical signs should be monitored a minimum of twice each day. Monitoring and clinical care should be provided and documented similarly on weekends and holidays.

Written records of all monitoring and treatments must be maintained in order to assure adequate care is being provided. Checklists/score sheets may be helpful in ensuring appropriate observations are made, consistently interpreted, and properly documented. Personnel should be identified who are responsible for the evaluation, record keeping, and notification of the investigator and/or Attending Veterinarian.

The plan for the parameters to be monitored, the frequency of monitoring, the qualified personnel who will perform evaluations, and the criteria for euthanasia must be described in the approved animal care and use protocol.

The *Guide* and the federal Animal Welfare Act require that the criteria and process for timely intervention and removal of animals from study be specified in animal care and use protocols. In addition, the methods used to eliminate or ameliorate pain or distress in animals on study must be described in the protocol(s) that are reviewed and approved by the Animal Care Committee.

Appropriate endpoints must be chosen based on consideration of the scientific requirements of the study, the expected and possible adverse effects animals may experience, the expected time course and progression of adverse effects, and the earliest predictive indicators of adverse effects.

It is essential that properly qualified personnel monitor the animals at appropriate intervals to ensure adequate observation and care of the animals. Optimally, studies should be terminated when animals begin to exhibit adverse clinical signs **IF** this endpoint is compatible with meeting research objectives, since such endpoints minimize pain or distress. It is preferable to use the earliest endpoints compatible with the scientific requirements of studies; however, if the study requires moribundity or mortality as an endpoint, this must be specifically described and approved in the animal care and use protocol approved by the ACC.

6. Death as an Endpoint

The use of death as an endpoint has been regarded as essential in some investigations, but rapid developments are being made in this field, and it is an area where both investigators and the IACUC should make particular efforts to keep abreast of the current literature. The usual reason for selecting death as an endpoint is the difficulty of reliably differentiating animals that will die from those which will recover, despite them showing severe clinical signs of illness or toxicity. When clinical signs include subjectively distressing changes such as convulsions or severe dyspnea, then there is particular pressure to euthanize an animal rather than allow further deterioration of its condition.

Several constructive suggestions have been put forward to reduce the need for death as an endpoint in studies. In some circumstances, simple clinical indices such as the development of profound hypothermia can be used to reliably predict death. The use of death as an endpoint must be scientifically justified and approved by the IACUC during protocol review. In these circumstances, the IACUC must carefully assess whether criteria can be developed during the progress of the project under consideration. In many instances, failure to develop criteria may be due to insufficiently frequent observation of the animals, or critical events may occur at times of the day when personnel are not usually available, thereby precluding detailed observation. Animal care and use protocols that propose the use of moribundity or death as an endpoint must include the following information:

1. The scientific rationale for death or moribundity as an endpoint
2. Considerations of alternative endpoints
3. Why pain/distress relieving medications and/or treatments cannot be utilized
4. Number of animals to be used and why this is the minimum number of animals required
5. Plan that details the parameters to be monitored, the timetable and frequency of monitoring, and the personnel responsible for making recorded observations
6. Whether animals will be euthanized when moribund and, if not, what information is to be gained in the interval between moribundity and death.

There seems no doubt that progress in refining endpoints has only occurred as a result of investigators carefully evaluating their own particular models. It may be that even after careful assessment, no progress is made and animals must be allowed to die if the aims of the study are not to be compromised. **Under no circumstances** may the use of death as an endpoint be applied simply because it is an unambiguous and easy criterion to apply.

7. Personnel Qualifications and Training

Qualified and well-trained personnel assures humane care and use of laboratory animals, supports good science, supports efficient management of the animal care and use program, fosters high self-esteem among employees, and assures legal and regulatory compliance.

The University of Connecticut Health Center is ultimately responsible for assuring that personnel are adequately trained. The ACC has delegated responsibility from the IO to assess the effectiveness of training. Employees and their supervisors (including the principal investigator) are also accountable.

It is federally mandated that anyone who is responsible for laboratory animal care, treatment or use is adequately trained: including scientists, research technicians, students, animal care staff, and ACC members. It is optional for peripheral individuals to be trained (e.g., vendors, contractors, maintenance personnel).

Again, PHS policy and USDA policy differ on their minimum training requirements. USDA regulations: people must be trained in humane methods of animal care and use, methods that limit animal use or minimize animal distress, use of pain-relieving agents, and how to report deficiencies. PHS policy regulations: people must be trained in humane methods of animal care and use, methods that minimize the number of animals required, and methods that minimize animal distress.

The *Guide* states that the institution should provide formal or on-the-job training for animal care and use personnel and suitable orientation, background materials, access to appropriate resources, and specific training to assist ACC members.

Training should include: Information on applicable laws, regulations, and policies; ethical and scientific issues; alternatives to animal use, responsibilities of the institution, ACC, and research and veterinary staff; information regarding pain and distress, information regarding the use of anesthetics, analgesics, tranquilizers, and neuromuscular blocking agents; survival surgery and post-surgical care; and euthanasia.

8. Occupational Health and Safety

It is the UCHC's responsibility for providing an adequate occupational health and safety program (OHSP) in which **all animal users must be enrolled**. The OHSP is responsible for assessing risks associated with animal contact (e.g., zoonoses, chemical, microbiological, and physical hazards), communicate those risks to personnel, provide training to help protect personnel (e.g., with respect to personal hygiene, protective equipment, and competent care and use methods), and implement procedures to monitor personnel. At the Health Center, this program is administered primarily by Employee Health Services (EHS) with some input from the Research Safety Office. It is the responsibility of the ACC to review and assess the effectiveness of the OHSP as part of the semi-annual program review.

Enrollment in the occupational health surveillance program is simple. An individual needs to go to the OHS page of the ACC website (http://clacc.uchc.edu/ACC/OccHealthandSafetywithAnimals.htm). The first thing they should do is to perform a risk analysis in the context of their work with animals. The risk assessment is at (http://clacc.uchc.edu/ACC/Occupational%20Health%20and%20Safety/HazardAssessment.htm) and is categorized by species. Once a person is aware of this preliminary assessment of hazards working with particular species, they should then fill out a Mandatory Annual Certificate of Enrollment (MACE) for which is located on the web. This needs to be completely filled out and the person needs to determine if they are going to participate or not participate in the OHS program. Either action meets the requirement of enrollment in the program. The completed MACE must be mailed as a hard copy to Employee Health Service at MC-6210.

The foundation of a good occupational health and safety program is one that addresses employee risks of illness and injury associated with the care and use of research animals. Program design requires an understanding of the tasks of at-risk employees; those employees' diversity in experience, education, and language proficiency; characteristics of the work environment; and the institutional mission. The work environment and mission are of paramount importance because they determine the nature of the hazards presented by the animal research activities. Areas of importance are:

- Knowing the hazard(s)
- Avoiding and controlling exposures
- Training and education
- Rules and guidelines
- Consistency
- Recordkeeping and monitoring
- Commitment and coordination

An important overall concept which is important in terms of running and effectively operating program depends on interaction among distinct functional parts of an institution. These functional parts include:

- Animal care and use
- Research
- Environmental health and safety
- Occupational health
- Administration and management

There are various areas within an effective occupational health and safety program which should be addressed by the institution. These areas include knowing the physical, chemical, and protocol-related hazards, allergens, zoonoses, and occupational health care services. Principal elements of an occupational health and safety program include:

- Administrative procedures
- Facility design and operation
- Exposure control
- Education and training
- Occupational health
- Equipment performance
- Information management
- Emergency procedures
- Program evaluation

The goal of an occupational health and safety program is to prevent occupational injury and illness. The program must be consistent with federal, state, and local regulations, but the principal focus of the program should be on the control of hazards and the reduction of risks, as opposed to merely satisfying regulations. The strategies that promote health and safety in the care and use of research animals are similar to those applied generally in a research laboratory. The use of animals in research is an extension of other experimentation that occurs in the laboratory. Research animals and the procedures and techniques that attend their use can present unique problems and challenges, many of which increase the hazards of experimentation. Those problems and challenges must be considered in the management of occupational health and safety programs.

Knowing the hazards

Determining the level of protection that is needed in any given situation depends on understanding the hazard in question. Defining and quantifying a hazard is sometimes referred to as risk assessment. The assessment, insofar as possible, should be based on scientific information. In the case of infectious agents, dose-response relationships, virulence, communicability, prevalence, routes of exposure, shedding patterns, stability, and availability of prophylaxis and therapy are important considerations. For

chemical agents, one has to know about toxic doses, stability, form (liquid, gas, or solid), type of toxicity (irritation, corrosion, carcinogenicity, narcosis, lethality, etc.), severity of reaction, mode of action, and metabolic products. The main sources of information for risk assessment are the scientific literature and professionals and consultants with unpublished field experience.

Avoiding and Controlling Exposures

It is common sense that it is better to avoid a hazard than to deal with the consequences of exposure to it. Measures related to the principle include training, work practices, containment equipment, personal protective equipment, control of access to hazardous areas, and use of purpose-bred animals. Safety measures should be implemented in advance rather than after a problem emerges. Although reducing risk to employees is the primary goal of an occupational health and safety program, it should be recognized that it is impossible to totally eliminate risk.

Training and Education

Once a hazard is known, this knowledge must be communicated to animal care and use employees most directly involved and other employees (such as janitorial and maintenance workers) who might be at risk of exposure. Employee training begins with orientation immediately after hiring. Standard operating procedures should include methods for performing duties safely. New employees should be carefully instructed in those procedures by an experienced co-worker before assuming duties independently. Laboratory procedures can be reinforced with signs and posters. Periodic meetings to encourage safe work practices are advisable, and safety newsletters and electronic bulletin boards sometimes can be beneficial in keeping employees updated on changes. An institution has a crucial role in ensuring that its employees remain both well-informed of relevant health and safety information and proficient in the use of safe practices.

Rules and Guidelines

Rules are necessary to ensure safety in the workplace. Rules governing the training of personnel, adherence to work procedures, use of disinfectants and decontaminants, access, waste disposal, use and maintenance of equipment and safety devices, emergency procedures, reporting of accidents and exposures, and personnel behavior (smoking, eating, and hand-washing) should be rigidly enforced. Rules are “musts” whereas guidelines are recommendations and suggestions that allow for some judgment.

Consistency

Consistency is essential to the success of an occupational health and safety program, including consistency in rules, enforcement, and application to all workers. Lack of consistency can undermine a program. However, too-rigid safety rules, at times considered unreasonable by employees, can undermine the credibility of a program.

Recordkeeping and Monitoring

Developing and maintaining records is essential in an occupational health and safety program. It might start with a medical history of each employee to discover any facts that would bear on the general susceptibility of the employee to injury or illness. Reports of accidents, exposures, and work-related illnesses are absolutely necessary and sometimes required by law. Other forms of recordkeeping can provide useful information for monitoring safety programs and identifying deficiencies.

Commitment and Coordination

Commitment to safety must be a feature of an organization from top to bottom. Even the best safety program will fail if employees ignore the rules. The hierarchy of management must be committed if a safe attitude is to be instilled in workers. Animal facilities are rarely autonomous organizations; coordination is

required among administrators, research scientists, veterinarians, technicians, and maintenance workers. Every person's role should be clearly defined because safety programs can fail if responsibilities are diffuse and not well understood.

II. REGULATIONS

1. Overview

As stated previously, there are two federal agencies governing the use of laboratory animals, the United States Department of Agriculture (USDA) and the Public Health Service (PHS):

- **Animal Welfare Act**- specifically governs the use of animals under the jurisdiction of the USDA and includes all warm-blooded vertebrate animals other than mice of the genus *Mus* and rats of the genus *Rattus* bred for research purposes and birds.
- **Health Research Extension Act of 1985**- specifically governs the use of all vertebrate animals in agencies utilizing PHS funds.
- **PHS Policy on the Humane Care and Use of Laboratory Animals**- is the policy stated to require institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities (hereinafter referred to as activities) conducted or supported by the PHS.
- **US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training**- principles used to implement the Health Research Extension Act of 1985.

These two federal agencies vary in their requirements to animal care and use programs. UCHC has made a concerted effort to ensure that the policies and procedures used comply with both agencies, as we use both USDA covered species and PHS funding.

In addition, PHS policy states that animal care facilities should use the standards and recommendations set forth in the *Guide*. The American Association for the Accreditation of Laboratory Animal Care (AAALAC) so require the use of the *Guide* in laboratory animal care programs and facilities.

The following pages contain some of the regulations which must be adhered to.

2. Animal Welfare Act

The Animal Welfare Act was first introduced in 1966 partly as a response to animal welfare groups. It has been amended at various points: the 1986 amendment introduced the requirements for exercise for dogs, requirements for the psychological well-being of non-human primates; requirements for pain alleviation, and justification requirements for multiple survival surgery.

Regulatory authority under the AWA is vested in the secretary of the U.S. Department of Agriculture (USDA) and implemented by the USDA's Animal and Plant Health Inspection Service (APHIS). Rules and regulations pertaining to implementation are published in the Code of Federal Regulations, Title 9 (Animals and Animal Products), Chapter 1, Subchapter A (Animal Welfare).

The following is a summary only. For full text go to: www.nal.usda.gov/awic/legislat/usdaleg1.htm

For more than a quarter of this century, the U.S. Department of Agriculture (USDA) has enforced the Animal Welfare Act (AWA) to protect certain animals from inhumane treatment and neglect. Congress passed the AWA in 1966 and strengthened the law through amendments in 1970, 1976, 1985, 1990, and 2005. The USDA's Animal and Plant Health Inspection Service (APHIS) administers the AWA, its standards, and its regulations.

The Law

The AWA requires that minimum standards of care and treatment be provided for certain animals bred for commercial sale, used in research, transported commercially, or exhibited to the public. Individuals who operate facilities in these categories must provide their animals with adequate care and treatment in the areas of housing, handling, sanitation, nutrition, water, veterinary care, and protection from extreme weather and temperatures. Although Federal requirements establish acceptable standards, they are not ideal. Regulated businesses are encouraged to exceed the specified minimum standards.

Exemptions

The AWA regulates the care and treatment of warm-blooded animals, except those, such as farm animals, used for food, fiber, or other agricultural purposes.

Currently, cold-blooded animals, such as snakes and alligators, are exempt from coverage under the Act. Retail pet shops are not covered under the Act unless the shop sells exotic or zoo animals or sells animals to regulated businesses. Animal shelters and pounds are regulated if they sell dogs or cats to dealers. Pets owned by private citizens are not regulated.

Pet Protection

To help prevent trade in lost or stolen animals, regulated businesses are required to keep accurate records of acquisition and disposition and a description of the animals that come into their possession. Animal dealers also must hold the animals that they acquire for a period of 5 to 10 days to verify their origin and allow pet owners an opportunity to locate a missing pet.

Animal Fighting

The AWA prohibits staged dogfights, bear or raccoon baiting, and similar animal fighting ventures.

Licensing and Registration

The AWA also requires that all individuals or businesses dealing with animals covered under the law must be licensed or registered with APHIS.

Research Facilities

In addition to providing the required standards of veterinary care and animal husbandry, regulated research facilities must provide dogs with the opportunity for exercise and promote the psychological well-being of primates used in laboratories. Researchers must also give regulated animals anesthesia or pain-relieving medication to minimize the pain or distress caused by research if the experiment allows. The AWA also forbids the unnecessary duplication of a specific experiment using regulated animals.

Research facilities must establish an institutional animal care and use committee to oversee the use of animals in experiments. This committee is responsible for ensuring that the facility remains in compliance with the AWA and for providing documentation of all areas of compliance to APHIS. The committee must be composed of at least three members, including one veterinarian and one person who is not affiliated with the facility in any way.

The AWA also does not permit APHIS to interfere with research procedures or experimentation. Regulated research facilities include hospitals, colleges and universities, diagnostic laboratories, and many private firms in the pharmaceutical and biotechnology industries.

AWA Enforcement

APHIS ensures that all regulated commercial animal breeders, dealers, brokers, transportation companies, exhibitors, and research facilities are licensed or registered. APHIS also searches for unlicensed or unregistered facilities.

Before APHIS will issue a license, the applicant must be in compliance with all standards and regulations under the AWA. To ensure that all licensed and registered facilities continue to comply with the Act, APHIS inspectors make unannounced inspections at least once annually.

If an inspection reveals deficiencies in meeting the AWA standards and regulations, the inspector instructs the facility to correct the problems within a given timeframe. If deficiencies remain uncorrected at the unannounced follow-up inspection, APHIS documents the facility's deficiencies and considers possible legal action.

APHIS also conducts reviews and investigates alleged violations. Some cases are resolved with Official Notices of Warning or agency stipulation letters, which set civil penalties for the infractions. Civil penalties include cease-and-desist orders, fines, and license suspensions or revocations. If APHIS officials determine that an alleged AWA violation warrants additional action, APHIS submits all evidence to the USDA for further legal review.

Cooperation

In addition to conducting regular inspections, APHIS will perform inspections in response to public input about the conditions of regulated facilities. Concerned individuals also are encouraged to inform APHIS about facilities that should be licensed or registered.

Many State and local governments have passed additional animal welfare legislation. The public is encouraged to work with Federal, State, and local officials as well as local humane organizations to help eliminate inhumane treatment of animals.

3. Health Research Extension Act of 1985

The Health Research Extension Act of 1985, Public Law 99-158, "Animals In Research" (November 20, 1985) provides the statutory mandate for the PHS Policy. In 1986, the HREA incorporated the **U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training** (see section 5). The Principles were incorporated into the PHS Policy in 1986 and continue to provide a framework for conducting research in accordance with the Policy.

Sec.495.

(a) The Secretary, acting through the Director of NIH, shall establish guidelines for the following:

"(1) The proper care of animals to be used in biomedical and behavioral research.
"(2) The proper treatment of animals while being used in such research. Guidelines under this paragraph shall require-

"(A) the appropriate use of tranquilizers, analgesics, anesthetics, paralytics, and euthanasia for animals in such research; and
"(B) appropriate pre-surgical and post-surgical veterinary medical and nursing care for animals in such research.

Such guidelines shall not be construed to prescribe methods of research.

"(3) The organization and operation of animal care committees in accordance with subsection (b).

"(b)

(1) Guidelines of the Secretary under subsection (a)(3) shall require animal care committees at each entity which conducts biomedical and behavioral research with funds provided under this Act (including the National Institutes of Health and the national research institutes) to assure compliance with the guidelines established under subsection (a).

"(2) Each animal care committee shall be appointed by the chief executive officer of the entity for which the committee is established, shall be composed of not fewer than three members, and shall include at least one individual who has no association with such entity and at least one doctor of veterinary medicine.

"(3) Each animal care committee of a research entity shall-

"(A) review the care and treatment of animals in all animal study areas and facilities of the research entity at least semiannually to evaluate compliance with applicable guidelines established under subsection (a) for appropriate animal care and treatment;

"(B) keep appropriate records of reviews conducted under sub-paragraph (A); and

"(C) for each review conducted under subparagraph (A), file with the Director of NIH at least annually (i) a certification that the review has been conducted, and (ii) reports of any violations of guidelines established under subsection (a) or assurances required under paragraph (1) which were observed in such review and which have continued after notice by the committee to the research entity involved of the violations.

Reports filed under subparagraph (C) shall include any minority views filed by members of the committee.

"(c) The Director of NIH shall require each applicant for a grant, contract, or cooperative agreement involving research on animals which is administered by the National Institutes of Health or any national research institute to include in its application or contract proposal, submitted after the expiration of the twelve-month period beginning on the date of enactment of this section-

"(1) assurances satisfactory to the Director of NIH that-

"(A) the applicant meets the requirements of the guidelines established under paragraphs (1) and (2) of subsection (a) and has an animal care committee which meets the requirements of subsection (b); and

"(B) scientists, animal technicians, and other personnel involved with animal care, treatment, and use by the applicant have available to them instruction or training in the humane practice of animal maintenance and experimentation, and the concept, availability, and use of research or testing methods that limit the use of animals or limit animal distress; and

"(2) a statement of the reasons for the use of animals in the research to be conducted with funds provided under such grant or contract. Notwithstanding subsection (a)(2) of section 553 of title 5, United States Code, regulations under this subsection shall be promulgated in accordance with the notice and comment requirements of such section.

"(d) If the Director of NIH determines that-

"(1) the conditions of animal care, treatment, or use in an entity which is receiving a grant, contract, or cooperative agreement involving research on animals under this title do not meet applicable guidelines established under subsection (a);

"(2) the entity has been notified by the Director of NIH of such determination and has been given a reasonable opportunity to take corrective action; and

"(3) no action has been taken by the entity to correct such conditions; the Director of NIH shall suspend or revoke such grant or contract under such conditions as the Director determines appropriate.

"(e) No guideline or regulation promulgated under subsection (a) or (c) may require a research entity to disclose publicly trade secrets or commercial or financial information which is privileged or confidential."

4. Public Health Service Policy on Humane Care and Use of Laboratory Animals

The first PHS Policy on Humane Care and Use of Laboratory Animals was passed in 1979. This was the first PHS Policy to require an IACUC by the institution. It also required that assurances were held in institutions before funding is received from PHS, covered all live vertebrates, and recommended protocol review. Like the Animal Welfare Act, it has been amended on various occasions, most recently in 2002. The 1985 Policy included the Health Research Extension Act (see section 3), required a more detailed PHS assurance, mandated that the IO is ultimately responsible for all animal research, required a CEO to appoint IACUC members, set forth minimum requirements of an IACUC, and finally required protocol review.

The following 2002 reprint of the **Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals** reflects the August 7, 2002 PHS Policy amendment permitting institutions with PHS Animal Welfare Assurances to submit verification of Institutional Animal Care and Use Committee (IACUC) approval for competing applications or proposals subsequent to peer review but prior to award (67 FR 51289). New footnotes (6 and 12) are incorporated to provide institutions with the option of coding the names of IACUC members in materials routinely submitted to the Office of Laboratory Animal Welfare (OLAW). Citations and addresses are also updated in this reprint, and language specifying that information be submitted on institutional letterhead or in letter form is eliminated to allow for electronic submission of information to OLAW in the future. OLAW, which has responsibility for the general administration and coordination of the Policy, provides specific guidance, instruction, and materials to institutions that must comply with the Policy.

I. Introduction

It is the Policy of the Public Health Service (PHS) to require institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities (hereinafter referred to as activities) conducted or supported by the PHS. The PHS endorses the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals

Used in Testing, Research, and Training" developed by the Interagency Research Animal Committee. This Policy is intended to implement and supplement those Principles.

II. Applicability

This Policy is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution and conducted in the United States, the Commonwealth of Puerto Rico, or any territory or possession of the United States. Institutions in foreign countries receiving PHS support for activities involving animals shall comply with this Policy, or provide evidence to the PHS that acceptable standards for the humane care and use of the animals in PHS-conducted or supported activities will be met. No PHS support for an activity involving animals will be provided to an individual unless that individual is affiliated with or sponsored by an institution which can and does assume responsibility for compliance with this Policy, unless the individual makes other arrangements with the PHS. This Policy does not affect applicable state or local laws or regulations which impose more stringent standards for the care and use of laboratory animals. All institutions are required to comply, as applicable, with the Animal Welfare Act, and other Federal statutes and regulations relating to animals.

III. Definitions

A. *Animal* - Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes.

B. *Animal Facility* - Any and all buildings, rooms, areas, enclosures, or vehicles, including satellite facilities, used for animal confinement, transport, maintenance, breeding, or experiments inclusive of surgical manipulation. A satellite facility is any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours.

C. *Animal Welfare Act* - Public Law 89-544, 1966, as amended, (P.L. 91-579, P.L. 94-279 and P.L. 99-198) 7 U.S.C. 2131 et. seq. Implementing regulations are published in the Code of Federal Regulations (CFR), Title 9, Chapter 1, Subchapter A, Parts 1, 2, and 3, and are administered by the U.S. Department of Agriculture.

D. *Animal Welfare Assurance or Assurance* - The documentation from an institution assuring institutional compliance with this Policy.

E. *Guide* - *Guide for the Care and Use of Laboratory Animals*, National Academy Press, 1996, Washington, D.C., or succeeding revised editions.

F. *Institution* - Any public or private organization, business, or agency (including components of Federal, state, and local governments).

G. *Institutional Official* - An individual who signs, and has the authority to sign the institution's Assurance, making a commitment on behalf of the institution that the requirements of this Policy will be met.

H. *Public Health Service* - The Public Health Service or PHS currently includes the Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, the Food and Drug Administration, the Health Resources and Services Administration, the Indian Health Service, the National Institutes of Health, and the Substance Abuse and Mental Health Services Administration.

I. *Quorum* - A majority of the members of the Institutional Animal Care and Use Committee (IACUC).

IV. Implementation by Institutions

A. Animal Welfare Assurance

No activity involving animals may be conducted or supported by the PHS until the institution conducting the activity has provided a written Assurance acceptable to the PHS, setting forth compliance with this Policy. Assurances shall be submitted to the Office of Laboratory Animal Welfare (OLAW), Office of the Director, National Institutes of Health.[1] The Assurance shall be signed by the Institutional Official. OLAW will provide the institution with necessary instructions and an example of an acceptable Assurance. All Assurances submitted to the PHS in accordance with this Policy will be evaluated by OLAW to determine the adequacy of the institution's proposed program for the care and use of animals in PHS-conducted or supported activities. On the basis of this evaluation OLAW may approve or disapprove the Assurance, or negotiate an approvable Assurance with the institution. Approval of an Assurance will be for a specified period of time (no longer than five years) after which time the institution must submit a new Assurance to OLAW. OLAW may limit the period during which any particular approved Assurance shall remain effective or otherwise condition, restrict, or withdraw approval. Without an applicable PHS-approved Assurance no PHS-conducted or supported activity involving animals at the institution will be permitted to continue.

1. Institutional Program for Animal Care and Use

The Assurance shall fully describe the institution's program for the care and use of animals in PHS-conducted or supported activities. The PHS requires institutions to use the *Guide for the Care and Use of Laboratory Animals (Guide)* as a basis for developing and implementing an institutional program for activities involving animals.[2] The program description must include the following:

a. a list of every branch and major component of the institution, as well as a list of every branch and major component of any other institution, which is to be included under the Assurance;

b. the lines of authority and responsibility for administering the program and ensuring compliance with this Policy;

c. the qualifications, authority, and responsibility of the veterinarian(s) who will participate in the program and the percent of time each will contribute to the program;

d. the membership list of the Institutional Animal Care and Use Committee(s) (IACUC) established in accordance with the requirements set forth in IV.A.3. of this Policy;[3]

e. the procedures which the IACUC will follow to fulfill the requirements set forth in this Policy;

f. the health program for personnel who work in laboratory animal facilities or have frequent contact with animals;

g. a synopsis of training or instruction in the humane practice of animal care and use, as well as training or instruction in research or testing methods that minimize the number of animals required to obtain valid results and minimize animal distress, offered to

scientists, animal technicians, and other personnel involved in animal care, treatment, or use;

h. the gross square footage of each animal facility (including satellite facilities), the species housed therein and the average daily inventory, by species, of animals in each facility; and

i. any other pertinent information requested by OLAW.

2. Institutional Status

Each institution must assure that its program and facilities are in one of the following categories:

Category 1 - Accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). All of the institution's programs and facilities (including satellite facilities) for activities involving animals have been evaluated and accredited by AAALAC, or another accrediting body recognized by PHS.[4] All of the institution's programs and facilities (including satellite facilities) for activities involving animals have also been evaluated by the IACUC and will be reevaluated by the IACUC at least once every six months, in accordance with IV.B.1. and 2. of this Policy, and reports prepared in accordance with IV.B.3.of this Policy.

Category 2 - Evaluated by the Institution. All of the institution's programs and facilities (including satellite facilities) for activities involving animals have been evaluated by the IACUC and will be reevaluated by the IACUC at least once every six months, in accordance with IV.B.1. and 2. of this Policy, and reports prepared in accordance with IV.B.3. of this Policy. The most recent semi-annual report of the IACUC evaluation shall be submitted to OLAW with the Assurance.

3. Institutional Animal Care and Use Committee (IACUC)

a. The Chief Executive Officer shall appoint an Institutional Animal Care and Use Committee (IACUC), qualified through the experience and expertise of its members to oversee the institution's animal program, facilities, and procedures.[5]

b. The Assurance must include the names,[6] position titles, and credentials of the IACUC chairperson and the members. The committee shall consist of not less than five members, and shall include at least:

(1) 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 (see IV.A.1.c.);

(2) one practicing scientist experienced in research involving animals;

(3) one member whose primary concerns are in a nonscientific area (for example, ethicist, lawyer, member of the clergy); and

(4) 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.

c. An individual who meets the requirements of more than one of the categories detailed in IV.A.3.b.(1)-(4) of this policy may fulfill more than one requirement. However, no committee may consist of less than five members.

B. Functions of the Institutional Animal Care and Use Committee

As an agent of the institution, the IACUC shall with respect to PHS - conducted or supported activities:

1. review at least once every six months the institution's program for humane care and use of animals, using the *Guide* as a basis for evaluation;[7]

2. inspect at least once every six months all of the institution's animal facilities (including satellite facilities) using the *Guide* as a basis for evaluation;

3. prepare reports of the IACUC evaluations conducted as required by IV.B.1. and 2. of this Policy, and submit the reports to the Institutional Official;[8] (NOTE: The reports shall be updated at least once every six months upon completion of the required semiannual evaluations and shall be maintained by the institution and made available to OLAW upon request. The reports must contain a description of the nature and extent of the institution's adherence to the *Guide* and this Policy and must identify specifically any departures from the provisions of the *Guide* and this Policy, and must state the reasons for each departure. The reports must distinguish significant deficiencies from minor deficiencies. A significant deficiency is one which, consistent with this Policy, and, in the judgment of the IACUC and the Institutional Official, is or may be a threat to the health or safety of the animals. If program or facility deficiencies are noted, the reports must contain a reasonable and specific plan and schedule for correcting each deficiency. If some or all of the institution's facilities are accredited by AAALAC International or another accrediting body recognized by PHS, the report should identify those facilities as such.)

4. review concerns involving the care and use of animals at the institution;

5. make recommendations to the Institutional Official regarding any aspect of the institution's animal program, facilities, or personnel training;

6. review and approve, require modifications in (to secure approval) or withhold approval of those components of PHS-conducted or supported activities related to the care and use of animals as specified in IV.C. of this Policy;

7. review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities; and

8. be authorized to suspend an activity involving animals in accordance with the specifications set forth in IV.C.6 of this Policy.

C. Review of PHS-Conducted or Supported Research Projects

1. In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy. In making this determination, the IACUC shall confirm that the research project will be conducted in accordance with the Animal Welfare Act insofar as it applies to the research project, and that the research project is consistent

with the *Guide* unless acceptable justification for a departure is presented.[9] Further, the IACUC shall determine that the research project conforms with the institution's Assurance and meets the following requirements:

a. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design.

b. Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.

c. Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

d. The living conditions of animals will be 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.

e. Medical care for animals will be available and provided as necessary by a qualified veterinarian.

f. Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.

g. Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia (PDF), unless a deviation is justified for scientific reasons in writing by the investigator.[10]

2. Prior to the review, each IACUC member shall be provided with a list of proposed research projects to be reviewed. Written descriptions of research projects that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full committee review of those research projects. If full committee review is not requested, at least one member of the IACUC, designated by the chairperson and qualified to conduct the review, shall review those research projects and have the authority to approve, require modifications in (to secure approval) or request full committee review of those research projects. If full committee review is requested, approval of those research projects may be granted only after review at a convened meeting of a quorum of the IACUC and with the approval vote of a majority of the quorum present. No member may participate in the IACUC review or approval of a research project in which the member has a conflicting interest (e.g., is personally involved in the project) except to provide information requested by the IACUC; nor may a member who has a conflicting interest contribute to the constitution of a quorum.

3. The IACUC may invite consultants to assist in the review of complex issues. Consultants may not approve or withhold approval of an activity or vote with the IACUC unless they are also members of the IACUC.

4. The IACUC shall notify investigators and the institution in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or

of modifications required to secure IACUC approval. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

5. The IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this Policy at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1.-4. at least once every three years.

6. The IACUC may suspend an activity that it previously approved if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the *Guide*, the institution's Assurance, or IV.C.1.a.-g. of this Policy.[11] The IACUC may suspend an activity only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present.

7. 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 a full explanation to OLAW.

8. Applications and proposals that have been approved by the IACUC may be subject to further appropriate review and approval by officials of the institution. However, those officials may not approve an activity involving the care and use of animals if it has not been approved by the IACUC.

D. Information Required in Applications-Proposals for Awards Submitted to PHS

1. All Institutions

Applications and proposals (competing and non-competing) for awards submitted to PHS that involve the care and use of animals shall contain the following information:

a. identification of the species and approximate number of animals to be used;

b. rationale for involving animals, and for the appropriateness of the species and numbers used;

c. a complete description of the proposed use of the animals;

d. a description of procedures designed to assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research, and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals; and

e. a description of any euthanasia method to be used.

Non-competing applications and contract proposals for other than full and open competitions need not repeat the information required by IV.D.1.a.-e. if the information was complete in the last competing application or proposal and there are no significant changes to that information. However, the application or proposal must contain a statement to that effect. If there are significant changes in the information, then the application or proposal must specifically identify them and state the reasons for the changes.

2. Institutions That Have an Approved Assurance

Applications or proposals (competing and non-competing) covered by this Policy from institutions which have an approved Assurance on file with OLAW shall include verification of approval (including the date of the most recent approval) by the IACUC of those components related to the care and use of animals. For competing applications or proposals only, such verification may be filed at any time prior to award unless specifically required earlier by the funding component. If verification of IACUC approval is submitted subsequent to the submission of the application or proposal, the verification shall state the modifications, if any, required by the IACUC. The verification shall be signed by an individual authorized by the institution, but need not be signed by the Institutional Official.

3. Institutions That Do Not Have an Approved Assurance

For applications and proposals covered by this Policy from institutions that do not have an approved Assurance on file with OLAW, the signature of the official signing for the applicant organization shall constitute a declaration that the institution will submit an Assurance when requested by OLAW. Upon such request, the institution shall prepare the Assurance as instructed by OLAW and in accordance with IV.A. of this Policy. The authorized IACUC shall review those components of the application or proposal as required by IV.C. of this Policy. Upon IACUC approval of those components of the application or proposal the institution shall submit the Assurance to OLAW.

E. Recordkeeping Requirements

1. The awardee institution shall maintain:

a. a copy of the Assurance which has been approved by the PHS;

b. minutes of IACUC meetings, including records of attendance, activities of the committee, and committee deliberations;

c. records of applications, proposals, and proposed significant changes in the care and use of animals and whether IACUC approval was given or withheld;

d. records of semiannual IACUC reports and recommendations (including minority views) as forwarded to the Institutional Official; and

e. records of accrediting body determinations.

2. All records shall be maintained for at least three years; records that relate directly to applications, proposals, and proposed significant changes in ongoing activities reviewed and approved by the IACUC shall be maintained for the duration of the activity and for an additional three years after completion of the activity. All records shall be accessible for inspection and copying by authorized OLAW or other PHS representatives at reasonable times and in a reasonable manner.

F. Reporting Requirements

1. At least once every 12 months, the IACUC, through the Institutional Official, shall report in writing to OLAW:

a. any change in the institution's program or facilities which would place the institution in a different category than specified in its Assurance (see IV.A.2.of this Policy);

b. any change in the description of the institution's program for animal care and use as required by IV.A.1.a.-i. of this Policy;

c. any changes in the IACUC membership;[12] and

d. notice of the dates that the IACUC conducted its semiannual evaluations of the institution's program and facilities and submitted the evaluations to the Institutional Official.

2. At least once every 12 months, the IACUC, at an institution which has no changes to report as specified in IV.F.1.a.-c. of this Policy, shall report to OLAW in writing, through the Institutional Official, that there are no changes and inform OLAW of the dates of the required IACUC evaluations and submissions to the Institutional Official.

3. The IACUC, through the Institutional Official, shall promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to:

a. any serious or continuing noncompliance with this Policy;

b. any serious deviation from the provisions of the *Guide*;[13] or

c. any suspension of an activity by the IACUC.

4. Reports filed under IV.F. of this Policy shall include any minority views filed by members of the IACUC.

V. Implementation by PHS

A. Responsibilities of the Office of Laboratory Animal Welfare (OLAW)

OLAW is responsible for the general administration and coordination of this Policy and will:

1. request and negotiate, approve or disapprove, and, as necessary, restrict or withdraw approval of Assurances;

2. distribute to Scientific Review Administrators of initial review and technical evaluation groups, and to PHS awarding units, lists of institutions [domestic and foreign] that have an approved Assurance;

3. advise awarding units and awardee institutions concerning the implementation of this Policy;

4. evaluate allegations of noncompliance with this Policy;

5. have the authority to review and approve or disapprove waivers to this Policy (see V.D. of this Policy); and

6. conduct site visits to selected institutions.

B. Responsibilities of PHS Awarding Units

PHS awarding units may not make an award for an activity involving animals unless the prospective awardee institution and all other participating institutions have approved Assurances on file with OLAW, and the awardee institution has provided verification of approval by the IACUC of those components of the application or proposal related to the care and use of animals. If any one of these institutions does not have an approved Assurance on file with OLAW, the awarding unit will ask OLAW to negotiate an Assurance with the institution(s) before an award is made. No award shall be made until all required Assurances have been submitted by the institution(s), been approved by OLAW, and the institution(s) have provided verification of approval by the IACUC of those components of the application or proposal related to the care and use of animals.

C. Conduct of Special Reviews/Site Visits

Each awardee institution is subject to review at any time by PHS staff and advisors, which may include a site visit, in order to assess the adequacy or accuracy of the institution's compliance or expressed compliance with this Policy.

D. Waiver

Institutions may request a waiver of a provision or provisions of this Policy by submitting a request to OLAW. No waiver will be granted unless sufficient justification is provided and the waiver is approved in writing by OLAW.

FOOTNOTES

Footnote 1:

Assurances should be sent to the Office of Laboratory Animal Welfare (OLAW), National Institutes of Health, Rockledge I, Suite 360, MSC 7982, 6705 Rockledge Drive, Bethesda, Maryland 20892-7982 (for express or hand delivered mail use zip code 20817).

Footnote 2:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the applicable regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

Footnote 3:

The name Institutional Animal Care and Use Committee (IACUC) as used in this Policy is intended as a generic term for a committee whose function is to ensure that the care and use of animals in PHS-conducted or supported activities is appropriate and humane in accordance with this Policy. However, each institution may identify the committee by whatever name it chooses.

Footnote 4:

As of the 2002 revision of this Policy, the only accrediting body recognized by PHS is the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

Footnote 5:

The Health Research Extension Act of 1985 requires the IACUC to be appointed by the chief executive officer (CEO) of the entity for which the committee is established. OLAW considers the CEO to be the highest operating official of the organization (such as the President of a University). If the CEO delegates authority to appoint the IACUC then the delegation must be specific and in writing. The CEO may or may not be the Institutional Official as defined by this Policy (see definition at III.G.).

Footnote 6:

Institutions may, at their discretion, represent the names of members other than the chairperson and veterinarian with program authority (see IV.A.3.), by using numbers or other symbols in submissions to OLAW. Sufficient information for OLAW to determine that all appointees are appropriately qualified must be provided. The identity of each member must be readily ascertainable by the institution and available to authorized OLAW or other PHS representatives upon request.

Footnote 7:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

Footnote 8:

The Institutional Animal Care and Use Committee (IACUC) may, at its discretion, determine the best means of conducting an evaluation of the institution's programs and facilities. The IACUC may invite ad hoc consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report.

Footnote 9:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the applicable regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

Footnote 10:

Journal of the American Veterinary Medical Association (JAVMA), 2001, Vol. 218, No. 5, pp. 669-696 (PDF), or succeeding revised editions.

Footnote 11:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the applicable regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

Footnote 12:

Institutions may, at their discretion, represent the names of members other than the chairperson and veterinarian with program authority (see IV.A.3.), by using numbers or other symbols in submissions to OLAW. Sufficient information for OLAW to determine that all appointees are appropriately qualified must be provided. The identity of each member must be readily ascertainable by the institution and available to authorized OLAW or other PHS representatives upon request.

Footnote 13:

This Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals* and that they comply with the applicable regulations (9 CFR, Subchapter A) issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The *Guide* may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

5. 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 following is a copy of these Principles:

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:

I. 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.*

II. 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.

III. 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.

IV. 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.

V. 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.

VI. 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.

VII. 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.

VIII. 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.

IX. 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.

*For guidance throughout these Principles, the reader is referred to the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources, National

III. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

1. Role and Charge of the Animal Care Committee (ACC)

An Institutional Animal Care and Use Committee (IACUC) is a federally mandated committee with the job to oversee the animal care program at any given institution. It has been approximately 17 and 12 years, respectively, since the implementation of the current PHS Policy and Part 2 of the USDA regulations which first defined the federal requirements for IACUCs. Since then, the IACUC has evolved as the premier instrument of animal welfare oversight within the majority of biomedical research institutions in the US.

The Health Center's IACUC is called the Animal Care Committee (ACC). The ACC is lead by the chair person of the committee and the committee reports directly to the Institutional Official (IO) of the Health Center- the Associate Vice President of Research. Members of the ACC are appointed by the Executive Vice President of the Health Center. The committee membership is federally mandated and must include:

- A doctor of veterinary medicine who is certified or has training or experience in laboratory animal science and medicine or the use of the species in question
- At least one practicing scientist experienced in research involving animals
- At least one public member to represent general community interests in the proper care and use of animals. Public members should not be laboratory animal users, be affiliated with the institution, or be members of the immediate family of a person who is affiliated with the institution
- At least one non-scientist member

The committee is responsible for oversight and evaluation of the animal care and use program and its components. Its functions include: inspection of facilities, evaluation of programs and animal-activity areas; submission of reports to the IO; review of proposed uses of animals (i.e., protocols); training program for animal users; and establishment of a mechanism for receipt and review of concerns involving the care and use of laboratory animals; suspension of animal activities (if necessary); and make recommendations to the IO regarding any aspect of the animal care program.

There is no federal or state mandate dealing with how often an IACUC should meet, except the statement that "the IACUC must meet as often as necessary to fulfill its responsibilities, but it should meet at least once every 6 months". Our ACC meets once per month, generally on the last Thursday of the month. ACC meeting dates are posted on the CLAC website (http://clacc.uchc.edu/ACC/Calander.htm). Generally, the deadline to submit new applications and modifications is at noon on the 10th of the month.

Federally mandated functions of an IACUC are as follows:

1. Review, at least once every six months, the research facility's program for the humane care and use of animals, using the 1996 *Guide for the Care and Use of Laboratory Animals* (PHS) and 9 CFR, chapter 1, subchapter A (USDA) as a basis for evaluation.
2. Inspect, at least once every six months, all of the institution's animal facilities using the 1996 *Guide for the Care and Use of Laboratory Animals* (PHS) and 9 CFR, chapter 1, subchapter A (USDA) as a basis for evaluation. Satellite holding facilities and areas in which surgical manipulations are performed must always be included.
3. Prepare reports of the IACUC evaluations and submit the reports to the Institutional Official (IO).
4. Review, and if warranted, investigate concerns involving the care and use of animals resulting from public complaints and from reports of non-compliance received from laboratory or research facility personnel or employees.
5. Make recommendations to the IO regarding any aspects of the animal program, facilities, or personnel training.

6. Review and approve, require modifications, or withhold approval of animal care and use protocols. Continuing review of activities required not less than annually and a complete review (e.g., resubmission) are required at least once every 3 years.
7. Review and approve, require modifications in, or withhold approval of proposed changes regarding the use of animals in ongoing activities.
8. Be authorized to suspend an activity involving animals in accordance with specifications in IV.C.6 of PHS *Policy* and/or 9 CFR. This action may only be taken after review of the matter at a convened meeting of a quorum of the IACUC and a vote for suspension by the majority of the quorum present.

In addition to the above federally-mandated Functions of an IACUC, the Health Center's ACC has been charged with the following institution-mandated functions:

1. The ACC shall serve as an advisory committee to the Assistant Vice President of Research.
2. The ACC shall concern itself with the budget of the Center for Laboratory Animal Care (CLAC) and the status of the animal care per diem charges.
3. The ACC shall concern itself with recommendations to the Space Committee for allocation and space utilization.
4. The ACC shall concern itself with procedures and technology to maintain disease-free health animals.
5. The ACC shall concern itself with the long-term development of the facility and broad policy issues, such as scientific and ethical use of animals in research.
6. The ACC shall be responsible for recommending procedures and policies which will ensure compliance with federal and state regulations concerning the use of animals in research.
7. The ACC shall be responsible for recommending procedures and policies which will ensure full accreditation status by the American Association for Accreditation of Laboratory Animal Care (AAALAC).
8. The ACC shall be responsible for reviewing and approving training curricula required by appropriate federal and state regulations.

2. Composition of the UCHC ACC

Current ACC Members

Dr. Joseph Lorenzo, Chair
Dr. Stephen Clark, Vice-Chair
Dr. Srdjan Antic
Dr. Lisa Conti
Dr. Theresa Digiulio, attending vet
Dr. Gustavo Fernandez, ad hoc member
Ms. Tiffany Gough, alternate member
Dr. John Harrison
Dr. Sandra Hewett
Dr. Mina Mina
Mr. John Pasnau, non-affiliated member
Ms. Alison Pohl, compliance monitor / coordinator
Dr. Lynn Puddington
Dr. Ernst Reichenberger
Mr. Dennis Scranton
Dr. David Waitzman
Dr. Ronald Wallace
Dr. Stephen Wikel
Dr. Catherine Wu

3. Application for Animal Care and Use Protocols

One of the primary functions of the UCHC ACC is to review animal care and use protocols. An adequate review of a protocol depends upon the ACC receiving a thorough, well-written document that conforms to USDA and PHS policies as well as recommendations set forth by AAALAC and the *Guide*.

New applications

All new animal care and use protocol must be submitted electronically to the ACC office (ooacc@uchc.edu). Current versions of the protocol form may be downloaded from the CLAC website (http://clacc.uchc.edu/ACC/SubmittingProtocols.htm). Once the completed form is received by the ACC office, it will be reviewed for completeness. If it is determined that the application form is incomplete, it will be returned to the submitter to be completed. Once the ACC office receives a complete form, it will be reviewed in order to evaluate whether it meets criteria for a DMR review or if the submission must go to the full committee of the ACC. Either way, the protocol application is sent to reviewers and placed on the ACC agenda.

Yearly reviews

All animal care and use protocols must have a yearly review. The review form can be downloaded from the CLAC website (http://clacc.uchc.edu/ACC/SubmittingProtocols.htm) and submitted electronically to the ACC office (ooacc@uchc.edu). Typically, the yearly review form is sent to principal investigators when it is time for a yearly review of a protocol. This form must be filled out and mailed back to the ACC office (MC-2806). Failure to provide information for the yearly review may result in a suspension of the protocol until the form is received.

Modifications

All modifications to animal care and use protocols must be submitted to the ACC coordinator and approved by the ACC prior to implementation. The modification form may be downloaded from the CLAC website http://clacc.uchc.edu/ACC/SubmittingProtocols.htm) and must be submitted electronically to the ACC office (ooacc@uchc.edu).

Renewals

3-year renewals follow the same procedures as new applications. This is done to satisfy both the USDA and PHS regulations. Under no circumstances may protocols be granted an "administrative extension"; once a protocol is expired, all work on that protocol must cease until a replacement animal care and use protocol has been approved for the work.

4. Reporting of Animal Welfare Concerns

The following is the ACC's official policy on reporting animal welfare concerns, as required by the AWA and PHS policy:

> The Health Center's Animal Care Committee (ACC) is committed to the humane care and use of laboratory animals. To ensure that laboratory animals receive humane care and use or treatment in accordance with the highest ethical standards, laws, regulations, and policies governing animal research, the ACC must review and, if warranted, address any animal-related concerns by the public or University of Connecticut Health Center employees. The following will outline the established procedure to ensure that concerns are communicated to the ACC. The ACC must review each concern in a timely and systematic manner and, when necessary, take prompt and appropriate corrective action.
>
> Reports of animal welfare concerns may be made anonymously, if desired. However, if the complainant would like to know the resolution of the investigation, s/he must provide a name. All reports will be handled confidentially, although anonymity cannot be guaranteed.
>
> This policy is subject to the UCHC Whistle Blower's Protection Policy.

Action:

1. Letter-sized posters outlining how to report animal care and use concerns are available and posted throughout the health center: in the main department offices, and on each floor where animal rooms are located.

2. When alleged incidences of non-compliance are reported to the ACC, these incidences will be investigated with the utmost concern for confidentiality and due process, without compromising the welfare of the animals.

3. If the incidence directly involves animal health and safety, a Center for Laboratory Animal Care (CLAC) veterinarian will assess the health and well-being of the animal(s) and will verify the concern. If there is animal suffering, the veterinarian will take immediate action, including supportive care or euthanasia. While a good faith effort will be made to contact the principal investigator (PI), the immediate animal welfare situation may necessitate that immediate action be taken without the PI's knowledge.

4. Once the animal(s)'s welfare is assessed and addressed (or in those situations where animals are not directly involved), the alleged concern or issue will be investigated by an ACC subcommittee:
   a. This subcommittee will usually consist of the ACC chair, the ACC coordinator, the Associate VP of Research, an attending veterinarian, and another member of the ACC.
   b. This subcommittee will initiate an investigation within 5 working days of receiving the report. All reports will be brought to a meeting of the ACC.
   c. It is the responsibility of the ACC subcommittee to review the concern, determine appropriate action, communicate with the PI involved, and follow-up on the corrective action plan.
   d. Once the subcommittee informs the ACC of the results of the investigation, the ACC- via the chair- will inform the PI and the Associate VP of Research of the results of the investigation
   e. The Associate VP of Research will then, if necessary, inform the NIH Office of Laboratory Animal Welfare, the USDA Animal and Plant Health Inspection Service, and the grant institution.

5. If the complainant disclosed his/her name, s/he will then be contacted by the ACC coordinator with the results of the investigation.

6. If allegations of misuse of laboratory animals or non-compliance with federal, state, or institutional policies or regulations have been established by the investigation, the potential consequences to the involved individual(s) may include: mandatory retraining, suspension of animal protocol(s), termination of animal protocol(s), or permanent withdrawal of ACC approval to use laboratory animals.

5. Investigator Responsibilities Regarding ACC Approved Protocols

It is the responsibility of the principal investigator (PI) to maintain the "approval" status of his protocol(s). The ACC coordinator will generally give advanced notice when protocols need yearly reviews (forms are sent out 6-8 weeks prior to review date) and 3-year renewals (approximately 4 months and 2 months prior to expiration date) and will provide help when requested. There is no such thing as an "extension" of animal protocol approvals— such actions are strictly prohibited in USDA and PHS regulations. Please do not request extensions of the approvals of your protocols.

It is the responsibility of the PI to ensure that professionally acceptable, ethical, and humane standards governing the care, treatment, and use of laboratory animals will be followed. The PI must also ensure that discomfort, and injury to animals will be limited to that which is unavoidable in the conduct of

scientifically valuable research and that appropriate anesthetic, analgesic, and tranquilizing drugs will be used to relieve all unnecessary pain and distress for the subject animals during teaching, research, testing, and post-operative care.

It is the responsibility of the PI to ensure that protocols do not unnecessarily duplicate previous experiments.

It is the responsibility of the PI to ensure that personnel conducting procedures on the animals will comply with all the pertinent institutional, state, and federal laws, rules, and policies; that personnel are adequately trained in the procedures they are required to perform during the course of their work; and that personnel are enrolled in an occupational health and safety program.

It is the responsibility of the PI to ensure that any changes in the protocol procedures or personnel will be submitted to, and approved by, the ACC prior to implementation. The PI is also responsible for having a current copy of the approved protocol posted in a place where all individuals working on the protocol have access to it.

It is the responsibility of the PI to notify the ACC coordinator regarding any unexpected study result(s) that impact the animals— including any unanticipated pain and/or distress, morbidity, and mortality.

It is the responsibility of the PI to cooperate with the ACC and attending veterinarian(s) in their supervision of all laws, rules, and policies and to cooperate fully with semi-annual reviews and any compliance audits performed by the ACC.

It is the responsibility of the PI to ensure that a copy of the approved protocol will be posted in a place where all individuals working on the protocol will have access to it. In addition, the **Signature of Compliance** sheet must be signed by all individuals working on the protocol and kept with the copy of the protocol.

IV. CONCEPTS OF VETERINARY CARE

1. Use of Anesthetics, Analgesics, and Tranquilizers

An integral component of veterinary medical care is prevention or alleviation of pain associated with procedural and surgical protocols. Pain is a complex experience that typically results from stimuli that damage tissue or have the potential to damage tissue. Pain is a stressor and, if not relieved, can lead to unacceptable levels of stress and distress in animals. The proper use of anesthetics and analgesics in research animals is an ethical and scientific imperative. *Recognition and Alleviation of Pain and Distress in Laboratory Animals* (NRC, 1992) is a source of information about the basis and control of pain.

Earlier, the clinical signs of pain in animals was listed and knowing these signs is fundamental to the relief of pain in the animals. The selection of the most appropriate analgesic or anesthetic should reflect professional judgment as to which best meets clinical and humane requirements without compromising the scientific aspects of the research protocol. Preoperative or intra-operative administration of analgesics might enhance post-surgical analgesia. As the selection of the most appropriate analgesic depends on many factors, the attending veterinarians of the health center should be consulted on analgesia options.

Some classes of drugs— such as sedatives, anxiolytics, and neuromuscular blocking agents— are not analgesic or anesthetic and do not relieve pain; however, they might be used in combination with appropriate analgesics and anesthetics. Neuromuscular blocking agents are sometimes used to paralyze skeletal muscles during surgery in which general anesthetics have been administered.

Anesthetic Drugs Guidelines for Rodents (mg/kg of body weight):

Drug	Category	Mice	Rats	Gerbils	Guinea Pigs	Hamsters
Atropine	Anti-cholinergic	0.04 IM or SQ	0.05 IM, IP	0.02-0.05 SQ, IM, IP	0.02-0.05 SQ, IM, IP	0.02-0.05 SQ, IM, IP
Ketamine + Xylazine	Dissociative Anesthetic	100 + 15 IM	40-90 + 15 IM	50 + 2 IP	50 + 5 IP	200 + 10 IP
Ketamine + Xylazine + Acepromazine	Dissociative Anesthetic	30 + 6 + 1 IM	22-44 + 2.5 + 0.75 IM	May precipitate seizures		
Ketamine + Acepromazine	Dissociative Anesthetic	100 + 2.5 IM	30-75 + 2.5-3 IM		125 + 5 IM	150 + 5 IM
Thiopental	Barbiturate	25-50 IV	30 IV			
Pentobartital	Barbiturate	Neonate: 5 IP 35-70 IV 40-90 IP	30-40 IP	25-30 IP	25-30 IP	9-11.2 IP
Isoflurane (vapors must be controlled- see page 99)	Inhalant Anesthetic	1.5-4% to effect	1.5	4% to effect	1.5	4% to effect

Postoperative Analgesics for Rodents (mg/kg body weight):

Analgesic	Mice	Rats	Gerbils	Guinea Pigs	Hamsters
Buprenorphine	0.05-2.5 IP/SQ 6-12 hours	0.2-0.5 IP/SQ 8-12 hours	0.1-0.2 SQ 8-12 hours	0.05 SQ 6-12 hours	0.05-0.5 SQ 8-12 hours
Butorphanol	0.05-5.0 SQ q 4 hours	0.05-2.0 SQ q 4 hours			
Meperidine	10-20 SQ/IP 2-4 hours	25-50 SQ 2-3 hours		10-20 SQ/IM 2-3 hours	20 SQ/IM 2-3 hours
Pentazocine	10 SQ 2-4 hours	10 SQ 2-4 hours			

It should be noted that non-pharmacologic control of pain is often effective; the attending veterinarians should be able to provide you with information regarding these options.

2. Euthanasia

Euthanasia is the act of killing animals by methods that induce rapid unconsciousness and death without pain or distress. Unless a deviation is justified for scientific or medical reasons, methods should be consistent with the 2007 AVMA Euthanasia Guidelines (http://clacc.uchc.edu/ACC/euthanasia.pdf). In evaluating the appropriateness of methods, some of the criteria that should be considered are: the ability to induce loss of consciousness and death with no or only momentary pain, distress, or anxiety; reliability; non-reversibility; the time required to induce unconsciousness; species and age limitations; compatibility with research objectives; and the safety and emotional effects on personnel.

Euthanasia might be necessary at the end of a protocol or as a means to relieve pain or distress that cannot be alleviated by analgesics, sedatives, or other treatments. Protocols should include criteria for initiating euthanasia, such as degree of a physical or behavioral deficit or tumor size that will enable a prompt decision to be made by the veterinarian and the investigator to ensure that the end point is humane and the objective of the protocol is achieved.

It is essential that euthanasia be performed by personnel who are skilled in methods for the species in question and that it be performed in a professional and compassionate manner. Death should be confirmed by personnel who can recognize cessation of vital signs in the species being euthanized. General, acceptable methods of euthanasia for commonly laboratory species are as follows:

Species	Acceptable Method of Euthanasia (2000 AVMA Panel Guidelines)
Amphibians	Barbiturates, Tricaine methane sulfate, Benzocaine hydrochloride, Double pithing
Cats	Barbiturates, Inhalant anesthetics, Potassium chloride with general anesthesia, Carbon dioxide, Carbon monoxide
Dogs	Barbiturates, Inhalant anesthetics, Potassium chloride with general anesthesia, Carbon dioxide, Carbon monoxide
Fish	Barbiturates, Inhalant anesthetics, Tricaine methane sulfate, Benzocaine hydrochloride, 2-phenoxyethanol
Nonhuman Primates	Barbiturates
Rabbits	Barbiturates, Inhalant anesthetics, Potassium chloride with general anesthesia, Carbon dioxide, Carbon monoxide
Rodents	Barbiturates, Inhalant anesthetics, Potassium chloride with general anesthesia, Carbon dioxide, Carbon monoxide

Unacceptable methods of euthanasia include: air embolism, blow to the head, burning, chloral hydrate (unacceptable in dogs, cats, and small mammals), chloroform, cyanide, decompression, drowning, exsanguinations (unless performed under general anesthesia), direct immersion into formalin, household products and solvents, hypothermia, neuromuscular blocking agents, rapid freezing (unless anesthetized), strychnine, and stunning.

3. Physical Restraint

Physical restraint is the use of manual or mechanical means to limit some or all of an animal's normal movement for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation. Animals are restrained for brief periods in many research applications.

Animals can be physically restrained briefly either manually or with restraint devices. These devices should be suitable in size, design, and operation to minimize discomfort or injury to the animal. Prolonged restraint should be avoided unless it is essential for achieving research objectives and is approved by the ACC. Less-restrictive systems that do not limit an animal's ability to make normal postural adjustments should be used when compatible with the protocol objectives. The following are important guidelines for restraint:

- Restraint devices are not to be considered normal methods of housing
- Restraint devices should not be used simply as a convenience in handling or managing the animals.
- The period of restraint should be the minimum required to accomplish the research objectives
- Animals to be placed in restraint devices should be given training to adapt to the equipment and personnel
- Provision should be made for observation of the animal at appropriate intervals, as determined by the ACC; and
- Veterinary care should be provided if lesions or illnesses associated with restraint are observed.

4. Multiple Major Survival Surgery Procedures

Major surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic function. Multiple major survival surgery procedures on a single animal are discouraged by the ACC but may be permitted if scientifically justified by the user and approved by the ACC. If multiple major survival surgery is approved, the ACC will pay particular attention to animal well-being through continuing evaluation of outcomes. Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures according to federal regulations (Animal Welfare Regulations).

The 1996 *Guide* contains recommendations for the use of aseptic techniques for rodent survival surgery. These recommendations apply to all live vertebrate animals used in research and, thus, include laboratory rats and mice as well as other rodents and vertebrates.

Surgical procedures on rodents can be done in a dedicated surgical facility of in a laboratory. If done in a laboratory, the surgery must be conducted on a clean, uncluttered lab bench or table surface in a low traffic area. The surface should be wiped with a disinfectant before and after use and covered with a clean drape. Intra-operative care should aim to maintain a near-normal state of the animal's physiology.

All people involved with a study need appropriate training to adequately perform the duties required of them. Adequate surgical training must be provided to ensure that good surgical technique is practiced including asepsis, gentle tissue handling, minimal dissection of tissue, appropriate use of instruments, effective hemostasis and suturing techniques.

5. Food or Fluid Restriction

When experimental situations require food or fluid restriction, at least minimal quantities of food and fluid should be available to provide for development of young animals and to maintain long-term well-being of all animals. Restriction for research purposes should be scientifically justified, and a program should be established to monitor physiologic or behavioral indexes, including criteria for temporary or permanent removal of an animal from the experimental protocol.

Animals on food or fluid restriction should be weighted at least once a week— or more often as might be needed for small animals such as rodents. The least restriction that will achieve the scientific objective should be used. In the case of conditioned-response research protocols, use of a highly preferred food or fluid as positive reinforcement, instead of restriction, is recommended.

6. Routine Animal Husbandry

Proper housing and management of animal facilities are essential to animal well-being, to the quality of the research data and teaching or testing programs in which animals are used, and to the health and safety of personnel. Many factors are considered when planning for adequate appropriate physical and social environment and housing of research animals. These include:

- The species, strain, and breed of the animal and individual characteristics, such as sex, age, behavior, experiences, and health
- The ability of the animals to form social groups with conspecifics through sight, smell, and possibly contact, whether the animals are maintained singly or in groups
- The design and construction of housing
- The availability or suitability of enrichments
- The project goals and experimental design
- The intensity of animal manipulation and invasiveness of the procedures to be conducted
- The presence of hazards or disease-causing materials, and
- The duration of the holding period.

Animals are housed with a goal of maximizing species-specific behaviors and minimizing stress-induced behaviors. For social species, this normally requires housing in compatible pairs or groups. The environment in which animals are maintained should be appropriate to the species, its life history, and its intended use.

An animal's space needs are complex and consideration of only the animal's body weight or surface area is insufficient. The *Guide* has recommendations regarding space for a variety of laboratory animals. CLAC has guidelines available as to what constitutes routine husbandry procedures for all species used at the health center. Any deviation from these guidelines, and the standards set forth in the *Guide*, requires scientific justification and approval from the ACC.

7. Controlled Substances

Controlled substances require special handling at the University of Connecticut Health Center. The following are requirements for controlled substance use:

Scheduled drugs must be securely locked behind 2 locked storage areas. Federal regulations promulgated by 21 CFR1301.72 states: "… housing schedule I or II drugs …. secure building or room … and (for) small quantities, a safe or steel cabinet …. If (the safe or cabinet) weighs less than 750 pounds, is bolted or cemented to the floor or wall in such a way that it cannot be readily removed…."

Controlled substances must be returned to CLAC when expired. Federal regulations promulgated by 21 CFR 1207.21 state: "….. schedule drugs ….. (must be) disposed of by an authorized disposal agency …"

Logsheets are needed for dispensing controlled drugs. Federal regulations promulgated by 21 CFR 291.505 state: "… accurate records traceable to specific (individuals) are maintained showing dates, quantity, and batch or code marks of the drugs dispensed. These records must be retained for a period of 3 years from the date of dispensing…"

8. Outdated Materials

Drugs used on laboratory animals cannot be expired. Regulations promulgated by APHIS/AC Policy #3 state: the use of expired medical materials such as pharmaceuticals "is not considered to be acceptable veterinary practice and does not constitute adequate veterinary care".

9. Use of Non-Pharmaceutical Grade Compounds

OLAW and USDA consider that the use of non-pharmaceutical grade compounds should be based on:

- scientific necessity;
- no availability of an acceptable veterinary or human pharmaceutical-grade compound; and
- specific review and approval by the IACUC.

Investigators and IACUCs should consider relevant animal welfare and scientific issues including safety, efficacy, and the inadvertent introduction of new variables. Cost savings alone do not adequately justify the use of non-pharmaceutical-grade compounds in animals. Although the potential animal welfare consequences of complications are less evident in non-survival studies, the scientific issues remain the same and the principles and need for professional judgment outlined above still apply. This includes the use of 2,2-tribromoethanol (Avertin).

V. Center for Laboratory Animal Care (CLAC)

1. Contact Information

Main CLAC number		x2731
Director and Attending Veterinarian	VACANT	x2248
Interim Attending Veterinarian	Dr. Theresa Digiulio	x2731
CLAC Administrative Assistant	Ms. Debbie Heard	x2731
Administrative Coordinator	Ms. Normal Mallet	x2303
Animal Care Supervisor	Ms. Sara Fraize	x4075
Animal Facility Supervisor	Ms. Gina Gates	x2485
Veterinary Services	Ms. Sandy Kuester	x8751
	Ms. Lisa Chuba	x4726

If you need any additional information not found in this training manual regarding the use of animals at the UCHC, please contact CLAC at x2731.

2. Animal Facility Access

Access to the CLAC facilities requires that individuals have completed initial animal users training or have completed continuing training, whichever is appropriate. In addition, individuals must be enrolled in the UCHC Occupational Health Surveillance (OHS) Program and be listed as an animal user on an approved animal care and use protocol.

Once an individual has fulfilled all of these requirements, s/he must inform the CLAC administrative assistant to request access to the facility by email. The Public Safety office will be notified by CLAC and the individual requesting access will make arrangements to go to public safety to have a new ID badge or have a new ID badge activated with CLAC access. This ID badge is your responsibility; if it is lost, CLAC and Public Safety must be notified immediately. Card sharing is NOT ALLOWED.

This activated ID card will allow access to the CLAC facility. Access to individual animal rooms is given by CLAC personnel; you must contact CLAC when individual room access is required. Doors to the animal rooms or main CLAC facility must NOT be propped open.

If an individual fails to maintain their training and/or OHS requirements, access to the facility will be terminated until training and/or OHS enrollment is completed.

3. General CLAC Facility Rules

- No food or drinks are allowed in animal rooms.
- No smoking is allowed in the animal facility.
- No children, pets, or unauthorized visitors are allowed into the animal facility.
- All animal users must follow the established traffic flow patterns:
  - 1.0 is the cleanest traffic flow number in the facility
  - 7.5 is the dirtiest traffic flow number in the facility
  - If you enter any room, you may not enter a room with a lower traffic flow number within 24 hours without showering.
  - These traffic flow numbers are posted on each animal room door
- Non-USDA regulated species may not be housed outside the facility for >24 hours unless permission to do so has been given by the ACC.
- USDA regulated species may not be housed outside the facility for >12 hours unless permission to do so has been given by the ACC.

4. Personal Protective Equipment (PPE)

All individuals must adhere to the person protective equipment (PPE) posted on the door of the animal room to be entered. PPE may include masks, gowns, gloves, face shields, safety glasses, bonnets, booties, and/or respirators. Open-toe shoes and shorts should not be worn in the facility.

Masks versus Respirators

Masks are meant to protect against splashes only in either direction. Respirators are designed to protect the respiratory system as well as protecting against splashes. Respirator use is highly recommended; however, in order to use respirators at the Health Center, an individual must fill out a respiratory questionnaire and send it to Employee Health (EHS). EHS will evaluate the responses given on the questionnaire and determine if the individual is able to use a respirator. If EHS feels the individual meets the criteria for using a respiratory, notification will be sent to the office of Research Safety (ORS) which will contact the individual requesting the use of a respiratory to arrange for a fit test. This fit test must be performed annually.

5. Animal Imports, Exports, and Quarantine

Import from approved vendors

All animal orders are submitted through the Granite on-line ordering system. If any individual requires training on how to use the Granite computer system, please contact CLAC to arrange for this training. Animal orders must be placed by noon on Wednesday to be received the following week. Currently, approved vendors include Harlan, Taconic, Jackson Labs, Charles River Labs, Milbrook, Covance, Liberty, and NASCO. For any further help, please contact CLAC.

Import from unapproved vendors

Mice are able to be imported from non-approved vendors for either re-derivation or short-term experimental use. Researchers requiring mice from unapproved vendors must contact Veterinary Services.

Exports

Animal exports are performed when requested by the PI. Please contact Veterinary Services if you need to export animals to another institution.

Per Diem Rates

Current per diem rates (as of 2/1/08) are as follows:

Mice	0.588 per cage/day
Rats	0.945 per cage/day
Hamsters	0.588 per animal/day
Gerbils	0.588 per animal/day
Guinea pigs	1.176 per animal/day
Rabbits	2.174 per animal/day
Cats	3.738 per animal/day
Fish	0.126 per tub (< 20 L)
Frogs	0.336 per tub (> 20 L)
NHP	Contact CLAC

Cage Identification

Granite cage cards are generated by CLAC for all active cages; these cage cards have a unique bar-coded number. Every cage must have a Granite generated cage card. PIs must contact the CLAC office for additional cage cards which may be needed (e.g., future weaning).

Quarantine

Mice imported from non-approved vendors will be placed into a quarantine room. Mice imported to be re-derived will be placed in a room with restricted access to CLAC personnel only. Mice for import for short-term experimental use require the approval of Veterinary Services. These mice will be placed into a room with limited access and a strict quarantine policy. Please contact Veterinary Services for information specific to your mice.

6. Animal Care and Notifications

Reporting Sick Animals

If CLAC personnel find a sick animal, they will place a yellow “sick report” sticker with a unique sick report number which is on a plastic transparent card placed over the Granite cage card. The research contact person associated with that cage card will be contacted by CLAC via email. Veterinary Services will work with the contact person regarding the treatment or disposition of the sick animals.

Research personnel should be aware that certain sick animals should be reported to the veterinarian if found by research staff. This includes, but is not limited to, animals that are moribund, bleeding, suffering from debilitating diarrhea, exhibiting self-induced trauma, showing ambulatory difficulties, and inability to gain access to food or water. Researchers are responsible for notifying the ACC with any unusual or unexpected morbidity and/or mortality associated with their research protocol in order to comply with the ACC Policy on Unexpected Morbidity and Mortality.

Pregnancy and Weaning

If CLAC personnel find a pregnant animal, they will place a pink “pregnancy/weaning” sticker on a plastic transparent card which is then placed over the Granite cage card. If no dates are recorded on this sticker, the animals are pregnant. If dates are on the sticker, it will reflect the date of birth (DOB) and date of weaning (DOW). Research staff are responsible for weaning animals according to the approved ACC Policy on Cage Density and Weaning Activities for Mice. If animals are not weaned by the research staff, CLAC will wean the animals and the researchers will be charged for this service.

Medicated Water Treatment

If the ACC approved protocol dictates the use of medicated water, CLAC will place a blue “medicated water” sticker on a plastic transparent card which is placed over the Granite cage card. Please contact the CLAC animal care supervisor if medicated water is necessary for your animals. CLAC will administer the medicated water treatments and the researchers will be charged for this service.

Malocclusion

If an animal has malocclusion, CLAC will place a yellow “malocclusion” sticker on a plastic transparent card which is placed over the Granite cage card. CLAC will trim the malocclusion as necessary for the health of the animal. Researchers will be charged for this service.

Breeding Diet / Special Food

If an animal requires a special diet, CLAC will place a green “special diet” sticker on a plastic transparent card which is placed over the Granite cage cared. Please contact the CLAC animal care supervisor if a breeding or special diet is necessary for your animals.

Death Report

If CLAC personnel find a dead animal, they will place an orange “death report” sticker with a unique death report number on a plastic transparent card which is placed over the Granite cage card. Research staff will be contacted with the death report number by email. Carcasses will be placed in the necropsy refrigerator along with the death report. Researchers are responsible for notifying the ACC with any unusual or unexpected morbidity and/or mortality associated with their research protocol in order to comply with the ACC Policy on Unexpected Morbidity and Mortality.

7. Animals and Hazards

If a researcher needs to expose the animals to any biological or chemical hazards (including carcinogens, suspected carcinogens, and unknown chemicals), s/he needs to coordinate with the Biological Safety Officer (BSO) to develop a safety protocol specific to the experiment to be performed. Animals requiring ABSL-2 for biohazard containment will be housed in the biocontainment suite. Animals exposed to chemical hazards will be housed in the chemical isolation room. Veterinary Services must be given at least 3 days notice prior to the start of the experiment. Use of hazardous agents requires that the research staff work closely with Veterinary Services and the BSO and comply with all directives throughout the course of the experiment.

Biohazards

If animals are exposed to an infectious agent (including human cells) during the course of the experiment, an additional orange cage card will be labeled with the international biohazard symbol sticker and the safety protocol HAZ number. All cages with biohazards require a safety protocol approved by the Biological Safety Officer. Please note that this card is placed in front of the Granite cage card.

Carcinogens / Chemical Hazards

If animals are exposed to a potential carcinogen or chemical hazard during the course of the experiment, an additional orange cage card will be labeled with the carcinogen, suspected carcinogen, or chemical hazard sticker and the safety protocol HAZ number.

8. Animal Transfers

If an approved protocol has expired, and the researcher must continue to breed the animals, the cages may be transferred to the appropriate institutional animal holding protocol. Researchers must contact the attending veterinarian (AV) in order to do this and must provide the AV with the following information: the number of animals needing to be transferred, the species, the transgenic strain (if applicable), and the names of the research staff who will be responsible for any breeding (including genetic analysis) of the transferred animals. The AV will give this information to the ACC office and a modification to the institutional holding protocol will be generated and approved according to established procedures. Once this modification to transfer the animals is approved, it will be approved for 3 months to allow the original PI time to write a new animal care and use protocol and have it approved by the ACC. Animals transferred to this holding protocol will be euthanized, or otherwise disposed of, once the 3 month expiration date is reached. A PI may request a one-time 3 month extension submitted in writing to the AV.

Animals may also be transferred between protocols. The PI who is supplying the animals to be transferred must inform the ACC office (ooacc@uchc.edu) that the animal will be transferred to ensure that the animal is being transferred to an approved animal care and use protocol. Animals which have had experimental procedures performed may not be transferred between protocols; exceptions to this must have approval by the ACC. In addition, any protocol which has USDA-regulated species being transferred must explicitly state that the transfer of animals is an approved animal disposition method and this may require a modification to the protocol. Researchers should contact the ACC office if they have any questions regarding animal transfers between experimental protocols.

9. Cage Density Requirements for Mice

Overcrowded cages are unacceptable and are a violation of PHS Policy and do not adhere to the guidelines promulgated by the *Guide for the Care and Use of Laboratory Animals*. Researchers should maintain familiarity with the ACC Policy on Cage Density and Weaning Activity for Mice. There is a maximum allowance of 125 grams total mouse mass per cage with few exceptions. If weaning is necessary in a cage, CLAC personnel will place a "PLEASE WEAN" label on the cage and wait for approximately 24 hours for the research staff to wean the animals; after this time, CLAC personnel will wean the animals and the researchers will be charged for this service. Exceptions to the cage density policy require prior approval by the ACC.

10. General Animal Husbandry

- Mice may be housed on conventional or ventilated racks depending upon the housing location and requirements of the experimental procedure.
- Most cages are changed once per week; in some cases this may be more or less frequent.
- When using ventilated racks, never force a cage into its slot- please ask for help if you experience any difficulties returning a cage to its position on the rack.
- CLAC uses sentinel animals in order to perform regular and quarantine health monitoring for animals. These sentinel cages are clearly labeled with a red transparent card; DO NOT REMOVE THEM OR CHANGE THEIR POSITION ON THE RACK. This monitoring is done on a quarterly basis.
- Health reports may be obtained from the CLAC office.

11. Surgery Rooms and Equipment

The use of the CLAC facility surgical suites and equipment are reserved on a first-come, first-served basis. Researchers will need to contact Veterinary Services to inquire about services and the availability of the surgery rooms and equipment. Researchers are charged for the use of surgical suites, equipment, and supplies.

VI. Self-Assessment Questions

1. Which is not a function of the IACUC?
   A. Purchase healthy animals on behalf of the investigators
   B. Conduct reviews of the animal care and use program on a 6-month basis
   C. Inspect the animal facilities on a 6-month basis
   D. Review and approve animal use protocols submitted by investigators

2. The USDA AWA regulations do not currently apply to:
   A. Non-human primates
   B. Dogs, pigs, and sheep
   C. Non-vertebrates, laboratory-bred mice and rats, and birds
   D. Hamsters and gerbils

3. Which of the following institutions must follow PHS guidelines for animal research?
   A. Those that use vertebrate animals for research, teaching, or testing
   B. Those that use any animals for research, teaching, or testing
   C. Those that accept USDA research funds
   D. Those that accept PHS funding

4. Unlike the USDA AWA regulations, when applicable, PHS Policy applies to:
   A. All animal species used in research
   B. All animal species except mice and rats
   C. All vertebrate species used in research
   D. Invertebrate species used in research

5. Before making a change in your animal procedures, you must:
   A. Be confident that the ACC would have approved it upon review
   B. Get approval for the change from the IACUC
   C. Consult with the Institutional Official
   D. Consult with the appropriate chief or dean of research

6. If procedures involving more than momentary or slight pain or distress to animals are proposed, the AWA Regulations and Standards require:
   A. A consultation with a veterinarian in the planning stages of the animal experiments
   B. That a veterinarian be appointed as a consultant on the project
   C. A consultation with the ACC chairperson in the planning stages of the experiments
   D. That the ACC chairperson be appointed as a consultant on the project

7. Which of the following is **not** true regarding the assurance provided by an investigator to the ACC that alternatives to painful/distressful procedures are not available?
   A. If a database search is used, the name of the database, date of the search, time period covered, and keywords or search strategy must be given in the narrative
   B. The assurance must be written, usually as part of the animal protocol form
   C. All three “Rs” by Russell and Burch must be addressed, not just replacement
   D. A report of the lab’s experience with the current technique may be used in place of an alternatives search

8. Which of the following is **true** regarding the USDA AWA Regulations and Standards and duplication of experiments?
   A. The investigator may decide of duplication is necessary
   B. The ACC is not allowed to decide if duplication is necessary
   C. The institution can overrule an ACC decision and allow a duplicative experiment
   D. Unnecessary duplication of experiments is not allowed

9. Humane endpoint criteria describe when it is time to:
    A. Submit an updated animal protocol form
    B. Notify the ACC of the need for more animals to achieve statistical significance
    C. Intervene in a study, sometimes by euthanizing the animal
    D. Seek medical care from a veterinarian

10. Euthanasia is:
    A. The act of killing animals by methods that preserve physiologic function after death
    B. The act of killing animals by methods that induce rapid unconsciousness and death without pain or distress
    C. The act of killing animals for experimental purposes
    D. The emotional state of a human or animal under distress

11. Annually, an institution must report the number of animals used by pain/distress category to:
    A. The United States Department of Agriculture (USDA)
    B. Public Health Service (PHS)
    C. Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC)
    D. American Association for Laboratory Animal Science (AALAS)

12. Who is given institutional responsibility for deciding if an individual researcher is properly trained to perform animal procedures, as required by law?
    A. The investigator
    B. The research technicians who perform the animal experiments
    C. The ACC
    D. The institutional official in charge of the research program

13. All personnel performing animal procedures must be properly trained to do so:
    A. Before any procedures are performed
    B. By the end of the experiments
    C. Unless they have doctoral level or medical degrees
    D. Unless they receive a waiver from their supervisor

14. Which statement is **false** regarding the occupational health and safety program?
    A. Risk assessment for hazards is a necessary component of the program
    B. The program should include health care procedures
    C. Personnel should receive training about the program
    D. The program may be limited to employees

15. In the animal protocol form, the investigator should:
    A. Identify hazardous agents to be used in the proposed animal study
    B. Verify that personnel are informed or enrolled in the OHSP
    C. Assure that personnel exposure to hazardous agents will be avoided or minimized
    D. All of the above

16. Which of the following is **false** concerning prolonged restraint of animals?
    A. It should not be considered a normal method of housing
    B. The period of restraint should be the minimum required to achieve objectives
    C. It can be justified as a convenience for research staff
    D. The restraint method used should be the least restrictive possible

17. When proposing to restrict food or water for animals, which of the following is **true**?
    A. Short-term restriction is allowed without scientific justification
    B. Restriction for periods longer than pre-surgical preparation is considered to cause pain and distress
    C. ACC approval is necessary only for long-term restriction
    D. Animal monitoring procedures are necessary only for restriction periods greater than 24 hours

18. Which of the following is **true** regarding allegations of misuse or mistreatment of animals or non-compliance with federal mandates on animal welfare?
    A. Individuals should first report an allegation to the institutional official
    B. Allegations must be investigated by the ACC
    C. Allegations are investigated only when made by the institution's employees
    D. When allegations are proven true, only the institutional official can impose disciplinary procedures

19. Surgery that penetrates and exposes a body cavity of produces substantial physical impairment is described as:
    A. Minor
    B. Major
    C. Survival
    D. Non-survival

20. Which of the following would not be accepted by the ACC as the sole justification for performing multiple major survival surgeries?
    A. Cost savings
    B. Scientific need
    C. Conservation of rare or endangered species
    D. Clinical need due to medical complications

21. A dedicated surgery suite must be used for which type of surgery?
    A. Non-survival surgery
    B. Major survival surgery on rodents
    C. Major survival surgery on non-rodent mammals
    D. Major non-survival surgery on non-rodent vertebrates

22. Which of the following statements is **false** regarding post-operative analgesia?
    A. If a procedure is expected to cause pain in a human, it must be assumed to cause pain in an animal
    B. If an animal does not overtly display pain following a procedure, it does not need an analgesic
    C. A veterinarian must be consulted on the analgesic agent, dose, route, frequency, and duration of treatment
    D. Post-operative analgesia may be initiated by the use of analgesics prior to surgery

23. Which of the following statements is **true** regarding care of an anesthetized animal during surgery?
    A. Intra-operative care does not need to be documented for USDA-covered species
    B. Intra-operative care refers to the quality of surgical and aseptic technique
    C. Intra-operative care should aim to maintain a near-normal state of the animal's physiology
    D. If adequate intra-operative care is provided, vital signs monitoring can be omitted

24. Which of the following statements is **true** regarding the description of surgical complications in the protocol form?

A. May omit describing possible surgical complications if the same surgical procedure has been performed previously without problem
B. May state only that all surgical complications will be referred to the veterinary staff
C. Can use professional qualifications to assure that surgical complications will not occur
D. Should describe expected surgical complications and methods of addressing each complication

25. Which of the following statements are **false** regarding controlled substances / pharma-ceuticals?

A. Controlled substances commonly used in the health center must be kept secure
B. Expired pharmaceuticals may be used on laboratory animals
C. Controlled substances must be disposed of through a federally-authorized disposal agency
D. Logsheets for dispensing controlled drugs must be kept for 3 years

ANSWERS TO THESE QUESTIONS FOLLOW ON THE NEXT PAGE

ANSWERS

1. **A**. Purchase healthy animals on behalf of the investigators (see pp. 32-33)
2. **C**. Non-vertebrates, laboratory mice, and laboratory rats (see pp. 15)
3. **D**. Those that accept PHS funding (see p. 19)
4. **C**. All vertebrate animals used in research (see p. 19)
5. **B**. Get approval for the change from the ACC (see p. 34)
6. **A**. A consultation with a veterinarian in the planning stages of animal experiments (see p. 7)
7. **D**. A report of the lab's experience with the current technique may be used in place of an alternatives search (see p. 5)
8. **D**. Unnecessary duplication of experiments is not allowed (see p. 5)
9. **C**. Intervene in a study, sometimes by euthanizing an animal (see pp. 5-9)
10. **B**. The act of killing animals by methods that induce rapid unconsciousness and death without pain or distress (see p. 43)
11. **A**. The United States Department of Agriculture (see p. 15)
12. **C**. The ACC (see p. 33)
13. **A**. Before any procedures are performed (see p. 11)
14. **D**. The program may be limited to employees (see pp. 11-13)
15. **D**. All of the above (see pp. 11-13)
16. **C**. It can be justified as a convenience for the research staff (see p. 44)
17. **B**. Restriction for periods longer than pre-surgical preparation is considered to cause pain and distress (see p. 44)
18. **B**. Allegations must be investigated by the ACC (see pp. 34-35)
19. **B**. Major (see p. 44)
20. **A**. Cost savings (see p. 44)
21. **C**. Major survival surgery on non-rodent mammals (see p. 44)
22. **B**. If an animal does not overtly display pain following a procedure, it does not need an analgesic (see p. 42)
23. **C**. Intra-operative care should aim to maintain a near-normal state of the animal's physiology (see p. 44)
24. **D**. Should describe expected surgical complications and methods of addressing each complication (see pp. 5-6)
25. **B**. Expired pharmaceuticals may be used on laboratory animals (see p. 46)

University of Connecticut Health Center

VII. Approved ACC Policies

1. Animal Training Requirements

Purpose: The Animal Welfare Act, Animal Welfare Regulations, and PHS Policy require institutions to provide training for all personnel engaged in animal research to include, but not limited to: Principal Investigators (including those that do not work directly with animals), research associates, post-doctorate fellows, students, animal facility personnel, and IACUC members.

The Institutional Animal Care and Use Committee, at the Health Center known as the Animal Care Committee (ACC), is charged with ensuring that all personnel who use animals are adequately trained.

Action:

1. All new personnel who require animal use training must contact the ACC office (ooacc@uchc.edu) to schedule attendance at a 3-hour core lecture series on vertebrate animal use.

2. Continuing training will be accomplished by web-based training. The UCHC will be using the CITI training site for continuing education in laboratory animal use. Details on how to access training is maintained on the CLAC/ACC training website (http://clacc.uchc.edu/Training/Onlinetraining.htm).

3. Additional training in specific procedures may be required and will be scheduled through the Center for Laboratory Animal Care. For individuals using USDA-regulated species, procedural training must be documented on the Animal Training Record form located on the ACC website (http://clacc.uchc.edu/ACC/SubmittingProtocols.htm). Please refer to the ACC policy on Training Requirements when using USDA Regulated Species (http://clacc.uchc.edu/ACC/Policies/TrainUSDA.htm).

4. The ACC office will be responsible for notifying all personnel who require continuing training and informing on what on-line course(s) must be completed and the date the training must be completed by.

5. The ACC office will be responsible for documenting all training activities of animal users at the Health Center.

6. No person shall attempt to work with animals until they have completed the required training. Failure to obtain approved training constitutes non-compliance with this policy.

7. Individuals who do not complete the required training by the due date will have their access privileges to CLAC facilities withdrawn and protocols may be suspended at the discretion of the ACC.

8. Principal Investigators who do not complete the required training by the due date may have their protocols suspended at the discretion of the ACC.

Effective Dates: April 26, 2007 thru April 25, 2010

University of Connecticut Health Center

2. Animal Transportation

Purpose: In order to ensure a safe environment for both employees of the Health Center, and the laboratory animals, the ACC has implemented a policy regarding the transport of animals in the Health Center.

Action:

1. Animals must be transported in closed caging (either microisolator lids or soft bonnet type covers)

2. If more than 1 cage of animals is being transported, it is suggested that transport be on a cart because of the possibility of dropping the cages.

3. Animals may not be transported on a common-use elevator. CLAC elevators only are to be used to transport animals between floors.

4. Animal caging (with or without animals) may NOT be placed, unsupervised, in the hallways. All caging must be kept in the laboratory areas.

Effective Dates: October 25, 2007 thru October 24, 2010

3. Cage Density Control and Weaning Activity for Mice

Purpose: In order to comply with government regulations (PHS and USDA) and the American Association for the Accreditation of Laboratory Animal Care (AAALAC) and *The Guide for the Care and Use of Laboratory Animals, 7th edition* (NRC, 1996) the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy concerning cage densities and weaning activities.

Action: 1. The ACC allows a housing maximum of 125 grams to be the total post- weaned mouse mass that is housed per standard 67 sq. in. (floor space) mouse cage. Post-weaned mice are defined as no longer suckling or greater than 21 days old. An exception to this 125 gram rule is granted for large or obese mice (e.g., NOD) where two mice are permitted per cage even if the combined weight exceeds 125 grams. The benefits of social housing takes preference over body mass, but such cages must be flagged with the 125 gram exception sticker.

2. Monogam Breeding (one male to one female)- the ACC recommends one male to one female in a permanent breeding arrangement as the optimal use of the 67 sq. in. cage size available in CLAC. In this arrangement, cage densities may temporarily exceed the 125 gram combined mouse mass for large parents / litters such as out-bred strains of mice (e.g., CD-1 mice). However, birthdates must be noted on such cages, the 21 day weaning time limit must be observed and such cages must be flagged with the 125 gram exception sticker if the weight limit is exceeded.

3. Bigam Breeding (one male to two females)- the ACC recognizes the necessity for difficult breeders (need for cross fostering and utilizing post partum estrus) to be set up in a bigam breeding arrangement with a permanent presence of the male with two females. Such cages must be within the 125 gram maximum mouse mass limit at the time of breeding unit set-up. Pups less than 9 grams may stay past the 21 day weaning deadline, but no more than 10 pups from a maximum of two litters are allowed per cage at any given time. Cages exceeding the maximum 125 gram total mouse mass must be flagged with the 125 gram exception sticker.

4. Multigam Breeding (one male to more than two females)- Harem breeding is permitted provided the total mouse mass at the time of breeding cage set up is less than 125 grams including the male and the non-pregnant females. Due to pregnancies, the total mouse mass may temporarily exceed the 125 gram rule; however, females must be separated prior to parturition even if this means that the post partum estrus will be missed. Cages exceeding the maximum 125 gram total mouse mass must be flagged with the 125 gram exception sticker.

5. Investigators and research staff should maintain familiarity with this density policy and CLAC's flagging system. CLAC staff will flag, with a pink sticker, cages with pregnant females. On the same sticker, CLAC staff will record the Date of Birth (DOB) and the Date of Weaning (Wean). Once the date of weaning is reached, CLAC staff will post a "PLEASE WEAN" sticker as a last reminder. After that, CLAC staff will wean without further notice if a cage is in violation of this cage density policy.

Effective Dates: February 22, 2007 thru February 21, 2010

University of Connecticut Health Center

4. Cage Identification

Purpose: The ACC has implemented a policy stating that all animal care and use at the Health Center will comply with the recommendations set forth in the *Guide for the Care and Use of Laboratory Animals*, 7th edition, 1996. This policy will detail the requirements for cage identification.

Action: 1. All animal cages must be appropriately labeled. It is the responsibility of the Primary Investigator to ensure that each cage is clearly identified with the following:

- **a.** PI Name
- **b.** Active Protocol Number
- **c.** Species
- **d.** Strain / Stock/ Genetic Designation
- **e.** Sex
- **f.** Date of Birth or Arrival Date / Age at Arrival

2. All cages housing animals exposed to or presenting a hazard must also be labeled with the Hazard Protocol Identification Number, the type of hazard associated with that cage (e.g., carcinogen, infectious agent), the specific hazard involved (e.g., infection with *Leishmania spp*.), the application date (when inoculated, exposed), and if appropriate, the clearance date.

Effective Dates: September 27, 2007 thru September 26, 2010

5. Code of Ethics for the Care and Use of Animals

Purpose: In order to comply with government regulations (PHS and USDA) and the American Association for the Accreditation of Laboratory Animal Care (AAALAC) the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy regarding a code of ethics for the care and use of animals

Action:

1. It is recognized that in many research protocols there is simply no alternative to the use of live animals. All investigators have an ethical obligation to explore ways in which animals can be partially or totally replaced by biological or mathematical/computer systems. When a research question can be pursued using reasonably available non-animal or *in vitro* models and still result in scientifically relevant conclusions, the investigator should choose those alternatives.

2. When live animals are used in research or biological testing, there must be a reasonable expectation that such utilization will contribute to the enhancement of human or animal health, the advancement of knowledge, and /or the good of society. The relative value of the study is a particularly important consideration in potentially painful experiments where there is an ethical imperative that the benefits of the research clearly outweigh any pain, discomfort, and distress experienced by the animals.

3. Selection of an appropriate animal model is an important consideration, particularly at a time when alternative models for animal research are being emphasized. It is the investigator's responsibility to select the optimal species for a particular project. In addition, the number of animals utilized in a protocol should be minimized consistent with sound scientific and statistical standards. It is also the investigator's responsibility to consider the source of the animal and ensure that all animals used for experimental research are acquired in a manner consistent with IACUC policies.

4. When animals are used in a research project, the investigator has an ethical obligation to seek the least painful techniques feasible that will allow the protocol objective(s) to be pursued adequately. If a procedure has associated pain, discomfort, or distress, it is imperative that the investigator estimate the probably occurrence, magnitude, and duration of the pain, discomfort, or distress in order to adequately plan for the treatment of pain.

5. In potentially painful procedures, the investigator must take all necessary steps to assess and monitor pain as well as discomfort and distress. In assessing pain, the investigator should use behavioral signs based on the normal behavior pattern of the species under study.

6. If a procedure will cause more than momentary slight pain or distress to the animal, the pain must be minimized both in intensity and duration through the administration of appropriate anesthetics, analgesics, and tranquilizers consistent with acceptable standards of veterinary medicine. It should be emphasized that the requirement for the alleviation/reduction of pain applies not only at the time the procedure is being conducted, but also following the procedure until such time when the pain is either alleviated or reduced to an acceptable tolerance level.

7. Potentially painful experiments should not be conducted on an awake animal under the influence of a paralytic or curarizing drug without the concomitant use of an appropriate anesthetic.

8. Research in which painful stimuli are used should be so designed as to provide a means of escape from that pain by the animals.

9. It is recognized that in certain research protocols, the administration of appropriate anesthetics and/or analgesics will compromise the scientific validity of the experiment. Such experiments must be justifiable in terms of scientific design and value, and the deletion of these drugs should be based on referenceable scientific fact or experimental data and not intuition. In addition, pain, discomfort, and distress levels should be carefully monitored. There is a limitation on the pain to which an experimental animal may be exposed. Investigators should choose the earliest possible end-point in order to minimize pain and discomfort. An animal that is observed to be in a state of severe pain that cannot be alleviated or reduced to an acceptable tolerance level should be immediately euthanized.

10. No animal should be subjected to multiple survival surgeries, except where they are inter-related and essential to the primary research objective.

11. Physical restraint procedures should be used on an awake animal only after alternative procedures have been considered and found to be inadequate. If a restraint will be utilized, the animal should be trained or conditioned to the restraining device, using positive reinforcement, prior to the beginning of the experiment. The restraining device should provide the minimum restraint consistent with the maximum security and comfort of the animal. In addition, the restraining device should provide the animal with the greatest possible opportunity to assume its normal postural adjustments. Awake animals should not be subjected to prolonged physical restraint.

12. It is the responsibility of the investigator to ensure that adequate post-surgical/procedural care is provided to all animals. This care must meet acceptable standards of veterinary medicine and be provided as long as necessary, including during non-duty hours.

13. Euthanasia is the act of inducing painless death. The proposed method of euthanasia must be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia (2000). See http://www.avma.org/resources/euthanasia.pdf. If an animal will not be subjected to euthanasia at the completion of a research protocol, it is the responsibility of the investigator to ensure that the final disposition of the animal is both humane and acceptable.

14. Procedures involving the use of animals should be performed by or under the immediate supervision of an individual with the appropriate training and experience relative to the procedures to be carried out on live animals.

Effective Dates: September 27, 2007 thru September 26, 2010

6. Collecting Samples for Genomic Analysis From Genetically Engineered Mice

Action: In order to comply with government regulations governing the use of vertebrate animals and to ensure the well-being of animals at the University of Connecticut Health Center, the Animal Care Committee (ACC) has implemented a policy regarding the collection of samples for genomic analysis from genetically engineered mice.

Background: To determine if genetically-engineered mice carry a gene of interest, tail biopsies are commonly performed to obtain samples for DNA analysis. DNA for polymerase chain reaction (PCR) analysis can also be obtained from ear punches and digits clipped during identification procedures, blood samples, or saliva swabs. To obtain larger amounts of DNA for Southern Blot testing, tail biopsy is usually performed. Tail biopsy is safe and humane when it is performed correctly.

Action:

Procedure for Mice Between 10-21 Days of Age

1. The tail biopsy procedure should be described in the approved animal care and use protocol.
2. Mice should be between 10 and 21 days old. At this age, the tail is still soft and the tail vertebrae have not yet calcified. Prompt analysis allows mice to be genotyped prior to weaning.
3. Local anesthetics are recommended, but not required. The tip of the tail may be immersed in ice-cold isopropyl alcohol for 10 seconds.
4. The size of the biopsy should not exceed 5 mm of tissue.
5. The tail biopsy procedure must be performed using clean gloves and a sterile sharp scalpel, sharp scissors, or razor blade. Tail skin should be disinfected with alcohol prior to incising the tip. Make one clean cut through the tail. Do not use iodine solutions because they may interfere with DNA analysis.
6. Following the biopsy procedure, bleeding should be controlled using local pressure. After releasing the mouse back into the cage, it should be observed to make certain that the bleeding has stopped. The presence of blood in the cage may cause aggression between cagemates. If bleeding occurs, it may be necessary to cauterize the tip of the tail with silver nitrate. Please consult the Attending Veterinarians for advice when using cauterizing agents,as they may be toxic if they are ingested by the mouse.

Procedure for Mice Older than 21 Days of Age

1. The procedure should be described in the approved animal care and use protocol. The rationale for testing older mice should be explained.
2. The use of a general or local anesthetic is suggested, but not required as long as the length of the biopsy does not exceed 5mm. Please consult the surgery guidelines for general anesthetic details. The tip of the tail may be numbed with ice or immersed in ice-cold isopropyl alcohol for 10 seconds.
3. Steps 4-6 should be followed as described above. Plastic restrainers are useful to hold the mouse.

Removal of more than 5 mm of tail in mature rodents is only allowed in exceptional cases, and it must be approved by the Animal Care Committee. If repeat sampling is necessary, anesthesia must be used and only small amounts of tissue may be taken.

References: 1. Blickman, A. and C. Vogelweid. ISUM IACUC Guidelines, February, 2003.
2. *The Guide for the Care and Use of Laboratory Animals*. National Research Council, 1996.

Effective Dates: March 20, 2008 thru February 28, 2011

University of Connecticut Health Center

7. Compliance with *The Guide for the Care and Use of Laboratory Animals*

Purpose: In order to comply with government regulations (PHS and USDA) and the American Association for the Accreditation of Laboratory Animal Care (AAALAC) the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy stating that the ACC will use the recommendations and standards set forth by *The Guide for the Care and Use of Laboratory Animals* (NRC, 1996) in determining appropriate standards of laboratory animal care.

Action: Any protocols or situations which require a deviation from the *Guide* must be submitted to the ACC in writing with a justification of why the deviation is required. This justification must be scientifically sound and not for the convenience of the investigator or for monetary reasons.

Effective Dates: August 25, 2005 thru August 24, 2008

8. Counting Pre-Weaned Animals

Purpose: The ACC has an obligation to ensure compliance with federal regulations regarding the use of laboratory animals. PHS policy states that if animals are used, they must be counted in the protocol without regard to the age of the animals. NIH guidelines state that if animals are genotyped and found to be a genotype inappropriate for the experiment and subsequently will be euthanized at weaning, those animals do not have to be counted as used in the protocol. These two policies appear to be contradictory. The ACC has adopted the following policy on counting pre-weaned animals.

Action: 1. If a pre-weaned animal is genotyped and found to be a genotype inappropriate for the experiment and subsequently will be euthanized *at weaning*- no other experimental procedures will be performed- the animal will not have to be counted as being used toward the protocol.

2. If a pre-weaned animal has any other experimental procedures performed other than genotyping- including behavioral studies- that animal must be counted toward the total number of animals used on the protocol.

3. If an animal is not used experimentally, but is euthanized post-weaning (e.g., the genotyping was performed post-weaning), it must be counted toward the number of animals used in the protocol.

Effective Date: August 25, 2005 through August 24, 2008

University of Connecticut Health Center

9. Death as an Endpoint

Purpose: In order to comply with Federal Regulations (USDA and PHS) and the *Guide for the Care and Use of Laboratory Animals, 7th edition*, 1996, the University of Connecticut Health Center's Animal Care Committee has established a policy on death as an endpoint in research projects.

Action: 1. Death as an endpoint will not be approved by the ACC except in these specific circumstances, where there is a:

- Specific scientific rationale
- Inability to scientifically justify other endpoints
- Justification of the number of animals used for this endpoint
- Plan describing the monitoring of these animals
- Description of data to be obtained between morbidity and mortality.

2. Cages housing animals in studies in which death is the endpoint should be tagged to make animal care technicians and other responsible people aware, viz. should be clearly indicated.

Effective Dates: September 27, 2007 thru September 26, 2010

University of Connecticut Health Center

10. Utilizing Designated Member Review

Purpose: In order to comply with government regulations and to simplify the approval process, the ACC has established a policy on the ability to utilize the designated member review (DMR) for approval of new protocols.

Action:

IF THE ORIGINAL FULL COMMITTEE REVIEW RESULT IS "MINOR MODIFICATIONS REQUIRED", THEN:

1. The changes requested to the protocol are forwarded by the program coordinator to the Primary Investigator (PI) of the protocol.
2. When the PI has responded to the request for changes, the critique, the PI's changes and the revised protocol are placed into the shared folder in the month of the original review and are also sent to the reviewers (Primary, veterinarian, research safety) of the protocol via email.
3. When all three (3) reviewers have indicated *in writing* their approval of the change(s) to the program coordinator, the coordinator will complete the paperwork required to approve the protocol.

IF THE ORIGINAL REVIEW RESULT IS "DEFERRED", THEN:

1. In exceptional circumstances, a vote may be taken at the ACC meeting that the subsequent, secondary review will be by the DMR process.
2. The changes requested to the protocol are forwarded by the program coordinator to the PI of the protocol.
3. When the PI has responded to the request for changes, the changes and the revised protocol are placed into the shared folder in the month of the original review and are also sent to the reviewers (primary, veterinary, and research safety) of the protocol via email.
4. When all three (3) reviewers have indicated *in writing* their approval of the change(s) required to the program coordinator, the coordinator will complete the paperwork required to approve the protocol.
5. The designated reviewers may not subsequently disapprove the protocol. If the changes are not satisfactory to the designated reviewers, the protocol must be brought to a full committee for discussion.
6. At any time in this process, any designated reviewer may request full committee review.

Effective Dates: September 27, 2007 thru September 26, 2010

University of Connecticut Health Center

11. Use of Expired Drugs and Biomaterials in Research Involving Animals

Purpose: The use of expired medical materials such as drugs, fluids, or sutures on animals is not considered to be acceptable veterinary practice and does not constitute adequate veterinary care as required by current animal care and use regulations.

Action: 1. No expired drugs, fluid replacements, or surgical/medical materials are allowed for use in animals utilized for research, testing, or teaching purposes.

2. All expired materials must be discarded on, or before, their expiration date, in accordance with the label or product sheet.

Effective Dates: September 27, 2007 thru September 26, 2010

12. Training New ACC Members

Purpose: The Animal Welfare Act, Animal Welfare Regulations, and PHS Policy require institutions to provide training for all personnel appointed to the Institutional Animal Care and Use (IACUC) committee at an institution. The UCHC IACUC, known as the Animal Care Committee (ACC), is charged with ensuring that all personnel who are appointed are adequately trained.

Action: 1. All new individuals who are being considered for an appointment to the ACC will meet with the ACC Chair, coordinator, and the Institutional Official. This meeting will cover topics including, but not limited to, the following: the function of the ACC, logistical aspects of appointment (meeting dates, times, location, etc.), and the responsibilities of the member related to the committee position they will hold (e.g., scientific member, community member, etc.).

2. If the individual agrees to an oral invitation to the committee by the Institutional Official, an appointment letter will be sent to them by the Executive Vice President of Health Affairs.

3. Once the individual is appointed, they will meet with the ACC coordinator. In this discussion, the new committee member will be introduced to the federal and state laws and regulations which govern the use of laboratory animals as well as institutional policies and procedures.

4. The new committee member will be given a copy of the following:

- The ACC Committee Member Handbook
- *The Guide for the Care and Use of Laboratory Animals*
- Public Health Service Policy on Humane Care and Use of Laboratory Animals. This document includes the Health Research Extension act of 1985 and the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
- Animal Welfare Act and Regulations
- Animal Care (USDA) Policies
- AVMA Panel on Euthanasia Guidelines
- *Institutional Animal Care and Use Committee Guidebook*

5. The new committee member will be required to complete two training modules through ResearchTraining.org. These include “Working with the IACUC” and “Essentials for IACUC Members”. The new committee member will be required to pass the examinations associated with these training modules.

6. The new committee member will be required to review the Office of Laboratory Animal Welfare, NIH tutorial located at http://grants.nih.gov/grants/olaw/tutorial/index.htm.

7. In order to satisfy requirements of the Department of Defense, new community members of the IACUC will complete a minimum of 8 hours of training to include a minimum of 4 hours of instruction on regulations and protocol review and a minimum of 4 hours on the concepts of humane animal care and the ethics of animal use. This may be accomplished by any combination of the following:

- Meetings with the ACC coordinator and/or chair
- On-line training modules and tutorials
- Attendance at sponsored training courses (e.g., IACUC 101)
- Attendance at national meetings (e.g., PRIM&R IACUC conference)

8. The new committee member will be trained on how to access InfoEd and access the ACC Committee shared folder, if required, by the ACC coordinator.

9. The ACC office will be responsible for documenting all training activities of ACC members here at the Health Center.

Effective Dates: July 27, 2006 thru July 26, 2009

University of Connecticut Health Center

13. Inter-Agency IACUC Reviews

Purpose: There are many circumstances that involve partnerships between collaborating institutions or relationships between institutional animal care programs. OLAW and USDA-APHIS agree that review of a research project or evaluation of a program or facility by more than one recognized IACUC is not a federal requirement.

It is imperative that institutions define their respective responsibilities. PHS Policy requires that all awardees and performance sites hold an approved Animal Welfare Assurance. OLAW negotiates Inter-institutional Agreement Assurances of Compliance when an awardee institution without an animal care and use program or IACUC will rely on the program of an Assured Institution. Assured institutions also have the option to amend their Assurance to cover non-assured performance sites, which effectively subjugates the performance site to the Assured institution and makes the Assured institution responsible for the performance site.

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. Similarly, an IACUC would want to know about any significant questions or issues raised during a semi-annual program inspection by another IACUC of a facility housing a research activity for which that IACUC bears some responsibility or exposure. This policy defines when the University of Connecticut Health Center will accept another institution's IACUC approval and/or require submission to the Health Center's ACC.

Action: 1. Work performed at the University of Connecticut Health Center with the funding administered through another institution:

- The University of Connecticut Health Center's ACC will review and approve all animal care and use activities performed at this institution. The work must have a Health Center faculty member sponsor and the principal investigator must complete the Health Center's animal care and use protocol form. All personnel involved in the study performed at this institution must comply with all ACC policies and procedures.

2. Work performed at another institution with the funding administered through the University of Connecticut Health Center:

- The Health Center's ACC will accept the review and approval of the institution performing the work if the following are met:
  - the Health Center's ACC receives a copy of the protocol approval letter from the institution.
  - the Health Center's ACC receives a copy of the IACUC approved protocol from the institution.
  - additional documentation may be requested at the discretion of the ACC chair.

- If any of the above requirements are not met, then the PI will be required to submit a protocol to the Health Center for review.

3. Work performed at the University of Connecticut Health Center and another institution with the funding administered through the University of Connecticut Health Center:

- This will be handled for each institution as described in 1 and 2 above.

4. Work performed at the University of Connecticut Health Center under an agreement which may be for pay or collaboration for an institution or company:

● If the institution or company has an IACUC, the Health Center's ACC will accept the review and approval of the institution performing the work if the following are met:

- the Health Center's ACC receives a copy of the protocol approval letter from the institution.
- the Health Center's ACC receives a copy of the IACUC approved protocol from the institution.

● If the institution or company does not have an IACUC, the work will be performed as described in 1 above.

Effective Dates: July 27, 2006 thru July 26, 2009

University of Connecticut Health Center

14. Modification Approvals

Purpose: In order to comply with government regulations and to make the modification approval process as simple as possible for the primary investigators, the ACC has established a policy on modification approvals.

Action:

1. Request for modifications goes to the program administrator of the Animal Care Committee
2. The request is posted in the shared folder and an email gets sent to the original primary reviewer of the protocol.

IF THE MODIFICATION IS MINOR: (e.g., addition of qualified personnel, addition of faculty collaborator, addition of another strain of the same animal species, small increase (<10%) in animal numbers, need to repeat an experiment, addition of sample collection times)

3. Notification of the submission of the modification will be sent to the entire committee on Thursdays to allow everyone the chance- for the following Friday- to call for a full committee review of the protocol. If no one calls for a full committee review AND the primary reviewers have approved the modification, the modification may be formally approved.
4. The modification will remain on the agenda covering the request period for documentation purposes
5. It is the responsibility of the ACC members to review the modification folder for all modifications that will be on the monthly agenda
6. Any member of the ACC has the right to request a full-committee discussion regarding any modifications
7. For qualified personnel, the designated reviewer will be the ACC coordinator

IF THE MODIFICATION IS MAJOR: (e.g., change in purpose or specific aim of study, change in primary investigator, change of species, addition of USDA-regulated species, large increase (>10%) in animal numbers, addition of surgical procedures, addition of painful procedures)

8. This will require full-committee review with a chance it must be resubmitted as a new protocol

Effective Date: September 27, 2007 thru September 26, 2010

University of Connecticut Health Center

15. New Protocol Submissions

Purpose: In order to comply with NIH-PHS government regulations which state that all vertebrate animal procedures described in a PHS grant must be approved by the institutional animal care and use committee, the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy regarding new animal care and use protocol submissions.

Action: 1. All animal care and use protocol submissions must be submitted electronically as a Word document to the coordinator of the ACC (pohl@uchc.edu)

2. If the protocol is new (not a 3-year renewal) and will be performed under the auspices of a grant, the grant application must accompany the protocol.

Effective Dates: April 13, 2006 thru April 12, 2009

University of Connecticut Health Center

16. Notification of Suspension of Protocols

Purpose: The Animal Welfare Regulations (9 CFR, Ch 1, 2.31 (c)(8)) and PHS Policy (IV.B.8) charge the IACUC (Institutional Animal Care and Use Committee), also known as the Animal Care Committee (ACC) with the authority to suspend an activity involving animals in accordance with the specifications set forth in the Animal Welfare Act and/or PHS Policy or because it has determined that the activity is not being conducted in accordance with the description of that activity as provided by the principal investigator in the animal care application. The following will outline the established procedure which will be used to notify Principal Investigators (PI) of the decision of the ACC to suspend protocols.

Action: There are three ways a protocol can be suspended:

1. The decision to suspend a protocol may be reached by a majority vote of a convened meeting of a quorum of the ACC.
    a. The PI will be notified by phone or email by the chair of the ACC within 24 hours of this action being taken by the ACC.
    b. The PI will also receive a letter from the ACC stipulating the actions taken by the ACC.

2. In exceptional circumstances where there is a clear threat to animal health, the Attending Veterinarian (AV) has the authority to suspend animal activities on a protocol. This action needs to be followed by a convened meeting of the ACC as soon as possible to review the cause of the suspension of animal activity.
    a. The PI will be notified by phone or email by the AV within 24 hours of this action being taken by the AV.
    b. The PI will also receive a letter from the ACC stipulating the actions taken by the AV and/or a description of actions prospectively to be taken as a result of the ACC meeting following the suspension of activities by the AV.

3. The Institutional Official (IO) may suspend an activity that the ACC has previously approved in the case of serious or continuing non-compliance with ACC approved protocol or governmental law or regulation, misuse, or mistreatment of research laboratory animals, or previously unanticipated risk to the laboratory research personnel. This action needs to be followed by a convened meeting of the ACC as soon as possible to review the cause of the suspension of animal activity.
    a. The PI will be notified by phone or email by the IO within 24 hours of this action being taken by the IO.
    b. The PI will also receive a letter from the ACC stipulating the actions taken by the IO and/or a description of actions prospectively to be taken as a result of the ACC meeting following the suspension of activities by the IO.

4. All further actions of investigating animal welfare issues, complaints, and cases of non-compliance with animal care and use protocols are outlined in the ACC Policy on Reporting Animal Welfare Concerns.

Effective Dates: September 29, 2005 thru September 28, 2008

University of Connecticut Health Center

17. Protocol Reviews

Purpose: In order to ensure adequate review of animal care and use protocols, the University of Connecticut Health Center's Animal Care Committee has established a policy on protocol reviews.

Action:

1. All protocols to be reviewed at an ACC meeting must be submitted to the ACC coordinator by the 10th of the month in which the protocol will be reviewed.

2. The principal investigator (PI) will be notified of the results of the ACC review of their protocol within 5 working days of the date of the ACC meeting in which the review occurred. This is typically done by email.

3. If the ACC review was **DEFERRED**:
   - The PI will need to respond to all comments outlined by the ACC
   - The PI will need to submit a revised protocol
   - The protocol will have to be reviewed by the full ACC
   - The PI will have 3 months to respond to an ACC review
   - If no response is received in 3 months, the protocol will be considered withdrawn unless the PI writes a letter to the committee requesting an extension

4. If the ACC review was **MINOR MODIFICATIONS REQUIRED**:
   - The PI will need to respond to all comments outlined by the ACC
   - The PI will need to submit a revised protocol
   - The PI will have 3 months to respond to an ACC review
   - If no response is received in 3 months, the protocol will be considered withdrawn unless the PI writes a letter to the committee requesting an extension

5. If the ACC review was **APPROVED**:
   - No further action is required by the PI

6. If the ACC review was **DISAPPROVED**:
   - The ACC will include a statement of the reasons for its decision
   - The PI will have the opportunity to respond in writing to the disapproval

Effective Dates: July 28, 2005 thru July 27, 2008

University of Connecticut Health Center

18. Approved Animal Care and Use Protocol Signatures

Purpose: In order to comply with government regulations (PHS and USDA) and the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC), the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy requiring signatures on all approved animal care and use protocols.

Action: 1. The final approved copy of an animal care and use protocol must be signed by the Principal Investigator (PI) in section 19: Investigator Assurances. It will be the responsibility of the ACC office to ensure that the signature of the PI is on the official final ACC document.

2. All individuals who are listed as animal users on the protocol must sign on a "Sign-Off Sheet" verifying that they have read the protocol and will comply with the procedures detailed in the protocol.

3. These "Sign-Off Sheets" must be maintained with the copy of the final animal care and use protocol which is posted either in the laboratory or in a place where all animal users have access to it. Copies must be provided to the ACC upon request.

Effective Dates: September 28, 2006 thru September 27, 2009

19. Reporting Animal Welfare Concerns

Purpose: The Health Center's Animal Care Committee (ACC) is committed to the humane care and use of laboratory animals. To ensure that laboratory animals receive humane care and use or treatment in accordance with the highest ethical standards, laws, regulations, and policies governing animal research, the ACC must review and, if warranted, address any animal-related concerns by the public or University of Connecticut Health Center employees. The following will outline the established procedure to ensure that concerns are communicated to the ACC. The ACC must review each concern in a timely and systematic manner and, when necessary, take prompt and appropriate corrective action.

Reports of animal welfare concerns may be made anonymously, if desired. However, if the complainant would like to know the resolution of the investigation, s/he must provide a name. All reports will be handled confidentially, although anonymity cannot be guaranteed.

This policy is subject to the UCHC Whistle Blower's Protection Policy.

Action: 1. Letter-sized posters outlining how to report animal care and use concerns are available and posted throughout the health center: in the main department offices, and on each floor where animal rooms are located.

2. When alleged incidences of non-compliance are reported to the ACC, these incidences will be investigated with the utmost concern for confidentiality and due process, without compromising the welfare of the animals.

3. If the incidence directly involves animal health and safety, a Center for Laboratory Animal Care (CLAC) veterinarian will assess the health and well-being of the animal(s) and will verify the concern. If there is animal suffering, the veterinarian will take immediate action, including supportive care or euthanasia. While a good faith effort will be made to contact the principal investigator (PI), the immediate animal welfare situation may necessitate that immediate action be taken without the PI's knowledge.

4. Once the animal(s)'s welfare is assessed and addressed (or in those situations where animals are not directly involved), the alleged concern or issue will be investigated by an ACC subcommittee:

a. This subcommittee will usually consist of the ACC chair, the ACC coordinator, the Associate VP of Research, an attending veterinarian, and another member of the ACC.
b. This subcommittee will initiate an investigation within 5 working days of receiving the report. All reports will be brought to a meeting of the ACC.
c. It is the responsibility of the ACC subcommittee to review the concern, determine appropriate action, communicate with the PI involved, and follow-up on the corrective action plan.
d. Once the subcommittee informs the ACC of the results of the investigation, the ACC- via the chair- will inform the PI and the Associate VP of Research of the results of the investigation
e. The Associate VP of Research will then, if necessary, inform the NIH Office of Laboratory Animal Welfare, the USDA Animal and Plant Health Inspection Service, and the grant institution.

5. If the complainant disclosed his/her name, s/he will then be contacted by the ACC coordinator with the results of the investigation.

6. If allegations of misuse of laboratory animals or non-compliance with federal, state, or institutional policies or regulations have been established by the investigation, the potential consequences to the involved individual(s) may include: mandatory retraining, suspension of animal protocol(s), termination of animal protocol(s), or permanent withdrawal of ACC approval to use laboratory animals.

Effective Dates: November 29, 2007 thru November 28, 2010

20. Retro-Orbital Bleeding

Purpose: In order to comply with government regulations (PHS and USDA) and the American Association for the Accreditation of Laboratory Animal Care (AAALAC) and *The Guide for the Care and Use of Laboratory Animals, 7th edition* (NRC, 1996) and standard veterinary care techniques, the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy concerning retro-orbital eye bleeding.

Action: 1. Investigators should consult with the Center for Laboratory Animal Care standard operating procedures regarding retro-orbital plexus bleeding. Investigators should be proficient in the procedure or receive assistance from the CLAC veterinarian.

2. All animals must be appropriately anesthetized prior to performing procedure unless exempted by the CLAC veterinarian.

3. Mouse: Maximum blood collection volumes
   - Weekly sampling (0.6% body weight): 150 µL (25 g mouse)
   - Biweekly sampling (0.8% body weight): 200 µL (25 g mouse)
   - Monthly sampling (no fluid replacement 0.8%): 200 µL (25 g mouse)
   - Monthly sampling (with fluid replacement 1.5%): 350 µL (25 g mouse)

4. Rat: Maximum blood collection volumes
   - Biweekly sampling
     (without fluid replacement 1.25% body weight): 3.1 mL (250 g rat)
   - Biweekly sampling
     (with fluid replacement 1. 5% body weight): 3.7 mL (250 g rat)

5. Multiple retro-orbital plexus bleeding requires the use of alternate eyes each time the procedure is performed.

6. No bleeding may be performed from a damaged eye. In the event that both eyes are damaged, eye bleeding must cease.

7. Volumes greater than the maximum volumes listed above require scientific justification and prior approval by the ACC.

Effective Dates: September 27, 2007 thru September 26, 2010

21. Semi-Annual Program Review and Facility Inspections

Purpose: In order to comply with government regulations (PHS and USDA), the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC), and the *Guide for the Care and Use of Laboratory Animals*, the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy regarding semi-annual program review and facility inspections.

Action:

1. Animal study area is defined as "any building, room, area, enclosure, or other containment outside of a core facility of centrally designated or managed area in which animals are housed for more than 12 hours if it houses a USDA species and more than 24 hours for other species."

2. The Office of Laboratory Animal Welfare (OLAW), NIH, has issued a document which states "when considering IACUC responsibilities for semi-annual review, it is important to keep in mind that the institution, acting through the IACUC, is responsible for all animal-related activities of the institution, regardless of where animals are maintained or the duration of their stay."

3. In June and December of any calendar year, the ACC will conduct a facility inspection to include all CLAC areas including, but not limited to: animal holding rooms (including any satellite facilities), animal study areas, cagewash areas, food and bedding storage area, and any other area deemed appropriate. In addition, all laboratories where survival and non-survival surgeries are performed will be inspected along with laboratories where animals are held for more than 12 or 24 hours.

4. Laboratories where only non-surgical animal procedures are performed will be inspected on a rotating basis during a 5-year cycle. Lists of all surgical and procedure rooms will be maintained by the coordinator of the ACC and updated prior to the semi-annual inspections.

5. Once the inspections are completed, the ACC will hold a special meeting to review the animal care and use program and the results of the facility and laboratory inspections. A report will be generated by the ACC coordinator which will be signed by a majority of a quorum of the ACC and will include any minority views. This report will then be submitted to the institutional official.

Effective Dates: July 27, 2006 thru July 26, 2009

University of Connecticut Health Center

22. Training Requirements when Using USDA Regulated Species

Purpose: In order to comply with government regulations (USDA Animal Welfare Act and Animal Welfare Regulations) the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy implementing a training form for individuals who are performing research, testing, or training on USDA-regulated species.

Action:

1. All individuals who perform research, testing, or training on a USDA regulated species are required to fill out and maintain an "Animal Training Record". This form can be found on the ACC website (http://clacc.uchc.edu/ACC/SubmittingProtocols.htm).

2. This form is to be maintained by each individual using the regulated species.

3. Training forms must be copied and submitted to the ACC office with the annual review form for the protocol on which the regulated species are used.

Effective Dates: May 25, 2006 thru May 24, 2009

University of Connecticut Health Center

23. Reporting Unusual or Unexpected Morbidity and Mortality

Purpose: In order to comply with Federal Regulations (USDA and PHS) and the *Guide for the Care and Use of Laboratory Animals,* the University of Connecticut Health Center's Animal Care Committee (ACC) has established a policy on requirements for reporting unusual or unexpected morbidity and/or mortality in a research project.

Action:

1. If, during the course of a research project, any unusual animal deaths or significant health related problems occur, the Principal Investigator must report the incident within 72 hours from time of discovery to the ACC (via the program coordinator) and the Director of the Center for Laboratory Animal Care (CLAC). The attending veterinarian should also report any incidences of unusual animal illnesses and deaths to the ACC via the program coordinator when they are discovered during review of animal morbidity and mortality reports.

2. It is at the discretion of the attending veterinarians what action, immediate or otherwise, is needed to prevent, reduce, or minimize any further animal suffering. This may include removal of the animal(s) from the study and/or euthanasia of the remaining animal(s).

3. There should be a combined effort of the ACC, the attending veterinarians, and the principal investigator to arrive at a workable plan to prevent further morbidity and mortality for the duration of the research project.

Effective Dates: May 25, 2006 thru May 24, 2009

24. Use of Complete Freund's Adjuvant (CFA)

Purpose: In order to ensure appropriate use of Complete Freund's Adjuvant (CFA), the University of Connecticut's Animal Care Committee (ACC) has implemented a policy on the use of CFA.

Background: CFA is an oil-in-water emulsion containing mycobacterial cell wall components. It is used as an agent to potentiate antibody response to injected immunogens by eliciting a local inflammatory response. CFA should be used only when absolutely necessary (e.g., weak antigens, induction of auto-immune response) and may only be used for the initial immunization. Incomplete Freund's Adjuvant (IFA) or other adjuvants that produce less intensive inflammatory responses (e.g., RIBI® or TiterMax®) should be used whenever possible. Improper use of Freund's adjuvant can cause undesirable and painful side effects such as excessive inflammation and swelling, abscess formation, ulceration, and tissue necrosis.

Any proposed deviation from these guidelines must be fully explained and justified to the Animal Care Committee in the research proposal.

Occupational Health and Safety

Due to the fact that CFA contains killed mycobacteria, accidental inoculation into personnel handling this agent can result in subsequent positive tuberculin titers and/or local inflammatory lesions, which have poor response to antibiotic therapy. These lesions can be severe and result in granulomas, abscesses, and/or tissue necrosis. Extreme caution should be taken when using CFA.

Personnel Protective Equipment (PPE), especially gloves and eye protection, must be worn when handling CFA. Needles should not be recapped, Luer lock syringes should be used, and anesthesia or sedation of animals being injected is recommended to minimize the risk of accidental exposures to personnel.

Action: Procedure

CFA may be used only for the first (priming) immunization. IFA should be used for any subsequent, booster immunizations. Inoculum should be free of extraneous microbial or chemical contamination. Filtration of the antigen before mixing with adjuvant is recommended.

Sites of administration of the CFA should be chosen so as to avoid anatomic sites used for handling or restraint of the animals being inoculated. Intravenous administration of CFA is prohibited. Intramuscular, intradermal, and footpad administrations (rodents only, one footpad only) are permitted only with scientific justification and approval of the ACC.

Injection sites should be clean and free of debris as contamination is likely to result in local infections. Clipping of hair and surgical preparation of the injection sites will reduce the potential for the development of infection and/or abscess formation. Sterile Luer lock syringes and needles should be utilized. Needles should be 25 to 31 gauge in size. The number of injection sites should be limited to the minimum necessary to accommodate the volume of material being administered. Injection sites should be sufficiently separated to prevent coalescing of any inflammatory responses from different injection sites.

Animals may receive booster immunizations of IFA or another adjuvant, as required, to develop the desired immune response as long as no adverse effects

from prior immunizations are present. There should be a minimum interval of two weeks between initial and subsequent immunizations.

The following is a list of acceptable routes of administration and volumes of CFA for the indicated species:

Species	Subcutaneous	IM	SubQ via Footpad	ID	IP
Mouse	0.1 ml/site 4 sites maximum	NR (Not Recommended)	Requires Scientific Justification	0.05 ml/site 4 sites maximum	0.25 ml maximum
Rat	0.2 ml/site 4 sites maximum	NR	Requires Scientific Justification	0.05 ml/site 4 sites maximum	0.5 ml maximum
Rabbits	0.25 ml/site 4 sites maximum	0.25 ml/site 4 sites maximum Requires Scientific Justification	NR	0.05 ml/site 1.0 ml total	Not permitted

Animals must be closely monitored for complications following CFA administration. Daily observation of injection sites must be documented in written records for the initial 7 days post immunization and a minimum of once weekly thereafter. Injection sites should be closely monitored for the development of severe lesions. When the adjuvant has been administered intraperitoneally in rodents, the animals must be monitored closely for excessive abdominal distension.

References:

1. ARAC Guidelines: *Recommendations for Consideration in the Research Use of Inflammatory Agents*. NIH Office of animal Care and Use. May, 1996.
2. Jackson, LR and Fox, JG. *Institutional Policies and Guidelines on Adjuvants and Antibody Production*. ILAR Journal, Vol. 37(3): 141-152, 1995.

Effective Dates: April 13, 2006 thru April 12, 2009

University of Connecticut Health Center

25. Use of Tribromoethanol (Avertin)

Purpose: In order to ensure appropriate use of Tribromoethanol, the University of Connecticut's Animal Care Committee (ACC) has implemented a policy on the use of this drug. The ACC encourages the use of ketamine/xylazine and isoflurane rather than Tribromoethanol.

Background: Tribromoethanol (Avertin) is an anesthetic that provides rapid induction and recovery for single use, short duration (approximately 15-20 minutes) surgical procedures in rodents. Tribromoethanol has been commonly used in the production of transgenic animals to facilitate procedures such as embryo transfer, vasectomy, or distal tail amputation for Southern Blot analysis. Improper preparation, storage, or use of tribromoethanol can result in high mortality losses. In particular, tribromoethanol degrades in the presence of heat and light, producing toxic byproducts that are potent gastrointestinal irritants. Adverse effects are common in mice following any second exposure to Tribromoethanol regardless of the dosing interval; therefore, this anesthetic is approved for one administration only as a survival anesthetic in mice.

Any proposed deviation from these guidelines must be fully explained and justified to the Animal Care Committee in the research proposal.

Action:

Preparation

Tribromoethanol must be prepared as follows:

- Dissolve 2.5 grams of 2,2,2-tribromoethanol in 5 ml of tert-amyl alcohol. This requires heating to approximately 40°C and stirring vigorously
- Add distilled water, stirring continuously, up to a final volume of 200 ml
- Filter sterilize through a 0.5 micron filter
- Aliquot the final solution into light protected containers. Containers must be labeled:
    - Tribromoethanol
    - 12.5 mg solution
    - Date of preparation
    - Date of expiration (two weeks from reconstitution)
    - Initials of person who prepared the solution

Storage

Tribromoethanol must be stored at 2-8°C in light protected containers.

Use

Tribromoethanol may be approved after scientific and/or medical justification has been provided in the animal care and use protocol and after ACC review for a single, survival administration to adult mice. If a second administration of tribromoethanol is given, the animals must be euthanized prior to awakening from the anesthetic. The anesthetic should be administered at a dose of 250 mg/kg given **IP**.

Dispose of any solution that is past the two-week expiration date, has crystals, or has changed from a clear solution to a yellow solution.

References: 1. Papaioannou, VE and Gox, JG. Efficacy of Tribromoethanol Anesthesia in Mice. *Laboratory Animal Science*, 1993. April, 43(2): 189-192.
2. Zeller, WM; Burki, G; and Panoussis, B. Adverse Effects of Tribromoethanol as Used in the Production of Transgenic Mice. *Laboratory Animal Science*, 1998. October, 32(4): 407-413.
3. Kohn, DF; Wixson, SK, White, WJ, and Benson, GJ. *Anesthesia and Analgesia in Laboratory Animals.* 1997.

Effective Dates: October 26, 2006 thru October 25 2009

University of Connecticut Health Center

26. Utilizing Designated Member Review for New Protocol Submissions

Purpose: In order to comply with governmental regulations and to simplify the review process, the ACC has established a policy on the ability to use the Designated Member Review (DMR) on new protocol submissions.

Action: 1. New protocols will be reviewed by the ACC coordinator to see if they meet the review criteria for a DMR protocol.[1]

2. If a protocol meets these criteria, it will be assigned a primary (scientific), a veterinary, and a safety reviewer. These individuals will act as agents of the ACC and can require and perform any function of the ACC with the sole exception of withholding approval of a protocol. Only a full committee vote may do that.

3. Notification of the submission of the protocol will be sent to the entire committee on Thursdays to allow everyone the chance- for the following Friday- to call for a full committee review of the protocol.

4. Written reviews are expected from DMR reviews and are posted in the shared folder in the same manner as full committee reviews (FCR). These reviews are forwarded to the Principal Investigator and the subsequent DMR review process is the same as the FCR review process.

	Designated Member Review	**Full Committee Review**
Pain/Distress Level	B and / or C	D and / or E
Species	Non-USDA Regulated	USDA Regulated
Invasiveness	Euthanasia only (tissue harvest) Breeding / holding protocols Injections Routine blood collections Minor surgery Non-survival surgery	Survival surgery Death as an Endpoint Prolonged restraint Food / fluid restriction Any exceptions to the regulations

1. Table of Criteria for Designated Member Review versus Full Committee Review

Effective Dates: November 17, 2005 thru November 16, 2008

University of Connecticut Health Center

27. Food Placement for Impaired Rodents

Purpose: The *Guide for the Care and Use of Laboratory Animals* states that animals should be fed palatable, non-contaminated, and nutritionally adequate food daily, or according to their particular requirements, unless the protocol in which they are being used requires otherwise. In addition, the *Guide* states that feeders should be designed and placed to allow easy access to food and to minimize contamination with urine and feces. Placement of rodent chow in an appropriate feeder may not be in the animal's best interest if that animal is unable to reach the food hopper. In this situation, the ACC recognizes that placement of rodent chow on the floor of the cages of sick, injured, or otherwise impaired rodents will ensure that animals will be able to access the food.

Actions:

1. An appropriate amount of rodent chow or powdered food in a Petri dish should be placed in the cage of animals that cannot reach the food hopper or have an impairment which affects their ability to chew rodent food.

2. The cage should be identified as being a cage where food is being placed on the floor of the cage because of an impaired animal.

3. Food should be changed minimum weekly, or as needed, so as to minimize potential contamination with the animals' urine and feces.

4. Food should be placed on the floor of the cage for the least amount of time necessary to ensure adequate nutrition of the impaired animal.

Effective Dates: March 29, 2007 thru March 28, 2010

28. Annual Reviews and Expired Protocols

Purpose: In order to comply with both NIH-PHS government regulations that cover all vertebrate animals and USDA government regulations that cover most warm-blooded vertebrate animals, the University of Connecticut Health Center's Animal Care Committee (ACC) has implemented a policy regarding the expiration of protocols and the requirements for annual review.

Actions: **FOR USDA COVERED SPECIES** (All warm-blooded vertebrate animals except mice of the genus *Mus* and rats of the genus *Rattus* bred for research purposes and birds)

1. Protocols expire approximately three years from the approval date with the requirement that they are reviewed every year. USDA regulations are clear that a review of the protocol must occur "no less than annually".

2. Annual review forms are mailed to the Principal Investigator (PI). These forms must be completed and mailed to the ACC office by the 10th of the month that the annual review is scheduled to occur. Due dates for the annual review forms are clearly marked on the forms.

3. If the review form is not received by the date of the ACC meeting for the month of the protocol being reviewed, the protocol will be suspended. The PI and CLAC will be notified by letter. All work on that protocol must cease and no more animals may be ordered. If breeding must be maintained, the animals must be transferred to the approved renewal protocol, another approved protocol, or the CLAC holding protocol.

4. Suspension of a protocol requires that the USDA, OLAW (NIH), and the funding agency be informed.

FOR PHS COVERED SPECIES (all vertebrate animals)

1. Protocols expire approximately three years from the approval date with reviews at appropriate intervals as determined by the ACC. PHS requires a triennial *de novo* review.

2. Annual review of the protocol is required by institutional policy to comply with our PHS assurance document. Annual review forms are mailed to the PI. These forms must be completed and mailed to the ACC office by the 10th of the month that the annual review is scheduled to occur. Due dates for the annual review forms are clearly marked on the forms.

3. If the review form is not received by the date of the ACC meeting for the month of the protocol being reviewed, a one month grace period will be given to the PI to submit the completed annual review form. If the review form is not received by the second month, the protocol will be suspended. The PI and CLAC will be notified by letter. All work on that protocol must cease and no more animals may be ordered. If breeding must be maintained, the animals must be transferred to the approved renewal protocol, another approved protocol, or the CLAC holding protocol.

4. Suspension of a protocol requires that OLAW (NIH) and the funding agency be informed.

FOR ALL ANIMALS

1. All protocols require a new submission once every 3 years (approximately).

2. Letters are sent to the PI approximately four (4) months prior to the protocol expiration date stating that the protocol is expiring and a new application will be due approximately two (2) months prior to the expiration date.

3. All protocols will be terminated on the expiration date and **EXTENSIONS ARE NOT ALLOWED UNDER FEDERAL REGULATIONS OR OUR PHS ASSURANCE DOCUMENT**. If a new replacement protocol has not been approved, all experimental animal use must cease. If breeding must be maintained, all animals must be transferred to the approved renewal protocol, another approved protocol, or the CLAC holding protocol.

4. A “stop census” in granite must be performed on the day the protocol expires and animals must be transferred to another active protocol (e.g., the PI’s renewal protocol or the CLAC holding protocol). The transferred animals will be counted against the renewal or holding protocol.

Effective Dates: March 29, 2007 thru March 28, 2010

University of Connecticut Health Center

29. Animal Transfers to Institutional Breeding and Holding Protocols

Purpose: The Animal Welfare Act, Animal Welfare Regulations, and PHS Policy state that no animal work may be performed on protocols without IACUC approval which includes protocols that have expired. The Center for Laboratory Animal Care (CLAC) has breeding and holding protocols on which animals may be temporarily transferred from a previously approved protocol (which has expired) so that the breeding and maintenance of these animals can be assured.

Action:

1. All Principal Investigators (PI) who wish to transfer animals from an expired protocol must contact the attending veterinarian (AV) for permission to transfer the animals from the original expired protocol to a holding protocol. The following information must be given to the AV: the number of animals needing to be transferred, the species, the transgenic strain (if applicable), and the names of the research staff who will be responsible for breeding (including genetic analysis) of the transferred animals.

2. The AV will, in turn, give the above information to the Animal Care Committee (ACC) office. A modification to the holding protocol will be generated to include the above information.

3. The modification will require the approval of the ACC according to established procedures.

4. Once the modification request is approved, it will be approved for 3 months to allow the original PI time to write a new animal care and use protocol and have it approved by the ACC.

5. Animals transferred to a holding protocol will be euthanized, or otherwise appropriately disposed of, once the 3 month expiration date is reached unless the PI of the original expired protocol requests a one-time extension of an additional 3 months.

Effective Dates: April 26, 2007 thru April 25, 2010

University of Connecticut Health Center

30. Animal Holding in Investigator Laboratories

Purpose: In order to ensure a safe environment for both employees of the Health Center and the laboratory animals, the ACC has implemented a policy regarding the holding of animals outside of the main CLAC animal facility in the Health Center.

Action:

1. Animals must be transported from the animal holding room to the PI laboratory in closed caging (either microisolator lids or soft bonnet type covers) where appropriate (e.g., rodent caging).

2. Animals may only be held in the PI laboratory for ≤12 hours if it is a USDA-regulated species or ≤24 hours if it is any other species without prior ACC approval. Housing for longer periods of time requires scientific and/or medical justification and prior ACC approval.

3. Animals must be held in a laboratory room that has been listed on the PI's approved animal care and use protocol. In addition, if animals are to be kept unsupervised in the PI laboratory, the doors to the laboratory must be kept closed and locked.

4. Animals involved with experiments that use hazardous materials or organisms which are required to be housed in the PI laboratory are to be removed from CLAC facilities, transported to, and held in the PI laboratory in accordance with additional specific instructions in the safety protocol governing the hazardous work approved by the Biological Safety Officer and the ACC.

5. Animal caging (with or without animals) may NOT be placed, unsupervised, in the hallways.

Effective Dates: May 31, 2007 thru May 30, 2010

31. Post Approval Monitoring

Purpose: The Animal Care Committee (ACC) recognizes that ensuring compliance with approved animal care and use protocols is an important aspect of a laboratory animal program. The purpose of a post approval monitoring (PAM) program is to work with investigators to facilitate their animal research and to be proactive in identifying potential problems in their compliance with active ACC protocols. The PAM program at the University of Connecticut Health Center will operate under the acronym PAWS: Post-Approval Animal Welfare Support.

Action:

1. All PAM will be under the supervision of the ACC and will be performed by a designated Compliance Liaison Officer (CLO) accompanied by one member of the Animal Care Committee.

2. Review of approved protocols will be conducted at a rate of up to four per month.

3. All active animal care and use protocols are eligible for PAM review. Criteria which may increase the frequency of PAM protocol review include:

- Animal use in pain categories D or E
- Significant personnel changes
- Significant increases in protocol activity
- The use of biohazards and/or carcinogens
- The use of physical restraint
- The use of food and/or water restrictions

4. The procedure for the performance of a PAM review will be as follows:

- The CLO will notify a PI that his or her protocol has been selected for review at least one month before the review will occur. At this time, the PI will receive the "PAWS checklist" for the review of items that will be addressed during the PAM review (different checklists will be devised with core elements to be addressed during all reviews and broad categories with special activities such as survival surgery).
- All visits will be scheduled at the convenience of the PI and the senior research staff of the laboratory.
- During the PAM review, the CLO will ask the PI and the laboratory staff that are present to describe their animal procedures verbally. These verbal reports will then be checked against the approved procedures in the protocol that is being reviewed. Specific attention will be paid to drugs administered, procedures performed, and all surgeries (survival and non-survival).
- During the PAM review, the CLO will identify any inconsistencies between the verbal record of what the laboratory is actually doing with animals and the procedures that are described in the ACC approved protocol. If the CLO determines that the laboratory is performing an unapproved procedure, or discovers that an inconsistency exists between the details of an approved procedure and the way it is currently being performed, the CLO will instruct the PI to discontinue that procedure immediately. If warranted, the PI must submit an application to modify the protocol to the ACC office. It is only after the modification is approved by the ACC that the procedure may be re-instated by the laboratory. The PI should ask questions of the CLO/ACC committee member and seek clarification of any issues that have been raised during the PAM review.

5. The PI and the senior research staff for the reviewed protocol are required to be present during a PAM review to facilitate the review.

6. After the PAM review, a written report of the monitoring results will be presented to the ACC. These written reports will be kept on file. Issues that pose a significant threat to animal welfare will be referred immediately to the attending veterinarian for resolution and to the ACC for further action.

7. A summary of the findings of PAM reviews during a given month will be reported to the ACC at its monthly meeting.

8. The PI will have 28 calendar days from the date of the initial PAM review to respond to the identified deficiencies and/or recommended corrective actions. Investigators who disagree with PAM review results, recommendations, or corrective actions can appeal their concerns to the ACC. Procedures not approved by the ACC cannot be performed until ACC approval has been obtained.

9. The ACC chair (or designee) will review and approve the PI's responses. If the response is deemed acceptable, no further action will be taken. Should the response be deemed unacceptable, the ACC chair (or designee) will seek further revisions and the PI will have 14 additional days to respond.

10. If the PI does not respond to the inspection findings of the CLO within the appropriate time frame as outlined above, the ACC will then decide on how to proceed.

Effective Dates: October 25, 2007 thru October 24, 2010

University of Connecticut Health Center

32. Animal Stabilization

Purpose: The *Guide for the Care and Use of Laboratory Animals* states that newly received animals should be given a period for physiological, psychological, and nutritional stabilization before their use. This allows animals to recover from shipping stress and permits them to adapt to their new surroundings. The length of time for stabilization will depend on the type and duration of animal transportation, the species involved, and the intended use of the animals. This policy will guide the amount of time an animal should be allowed to acclimate to the facility after their arrival from another institution.

Action: Rodents to be used for non-survival surgery or non-surgical procedures should be housed for a minimum of 48 hours prior to such use. This policy does not apply to animals euthanized prior to 48 hours.

Rodents to be used for survival surgical procedures should be housed for a minimum of 1 week prior to such use.

All non-rodent animals used for any procedure should be housed for a minimum of 2 weeks prior to such use.

Effective Dates: October 25, 2007 thru October 24, 2010

University of Connecticut Health Center

33. Assigning Reviewers to New Protocols

Purpose: In order to ensure adequate review of animal care and use protocols, and to be compliant with both PHS Policy and recent clarification from the USDA, the ACC has established a policy on assigning reviewers to new protocols.

Action:

1. All protocols are submitted to the ACC mailbox (ooacc@uchc.edu) by the Principal Investigator.

2. The ACC office will initially assign a primary (scientific) reviewer to the protocol. The primary reviewer assignment will be on a rotating basis with consideration of a reviewer's particular area of expertise. In addition, the Attending Veterinarian (AV) and Biological Safety Officer (BSO) will also review all submitted protocols. If there are more than one AV and/or BSO on the ACC, this assignment will be performed on a rotating basis.

3. The ACC office will then inform the Chair of the reviewer assignment. The chair may approve the assignment of the reviewers, in which case no further action is warranted. The chair may choose to re-assign the reviewers, in which case the Chair will inform the ACC office of the new reviewer(s) designated by the Chair. The ACC office will then relate this change to the reviewers.

4. The primary reviewers will remain for the life of the protocol; the initial primary reviewers will serve as the reviewers for all subsequent modifications to the protocol. If the initial primary reviewer not be a voting member of the ACC when a future modification is received, the primary reviewer will be the Chair of the ACC. If the initial AV or BSO reviewer not be a voting member of the ACC when a future modification is received, these reviews will be performed by the current AV or BSO on the ACC committee.

Effective Dates: February 28, 2008 thru January 31, 2011

University of Connecticut Health Center

34. Animal Transfers to Approved Protocols- USDA Species

Purpose: The Animal Welfare Act, Animal Welfare Regulations, and PHS Policy state that no animal work may be performed on protocols without IACUC approval which includes protocols that have expired. In addition, all approved protocols must completely describe the disposition of animals. This policy only applies to protocols which utilize USDA regulated species.

Action: 1. All Principal Investigators (PI) who wish to transfer animals from an approved protocol to an approved protocol of another PI must have, in the original protocol, a statement that the disposition of animals includes the transfer of animals to another approved protocol.

2. The PI will need to inform CLAC and the ACC office of the request to transfer animals. The PI will need to give the following information: species and number of animals to be transferred, the name of the PI to whom the animals will be transferred, and the new ACC protocol number. The ACC office will confirm that the new protocol is approved.

3. This process may require that the original protocol be modified to include transfer of animals as disposition method; this modification will require the approval of the Animal Care Committee (ACC) according to established procedures.

Effective Dates: February 28, 2008 to January 31, 2011

VIII. Resources:

1. Internet resources

Animal Welfare Act	www.nal.usda.gov/awic/legislat/usdaleg1.htm
Animal Care Regulations	www.aphis.usda.gov/ac/publications.html
Animal Care Policy Manual	www.aphis.usda.gov/ac/polmanpdf.html
PHS Policy	www.grants.nih.gov/grants/olaw/olaw.htm
2000 Report of the AVMA Panel on Euthanasia	www.avma.org/resources/euthanasia.pdf
US Government Principles	www.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples
The *Guide*	www.nap.edu/readingroom/books/labrats/
To order your own copy of the *Guide*:	send request to: OLAW@od.nih.gov
ACC Home page	http://clacc.uchc.edu/ACC/Animal_Care_Committee.htm
CLAC Home page	http://clacc.uchc.edu

2. Top ten actions for new animal users

As new animal users, you have a responsibility to ensure that you use laboratory animals in an appropriate and ethical manner. The Animal Care Committee (ACC) office is available to all animal users who have questions regarding the proper use of laboratory animals and regulations that affect the use of laboratory animals. The ACC wants to ensure that all animal users get the information they need.

In order to use laboratory animals here at the Health Center, *all vertebrate animal users* must do the following:

1. Enroll in animal training. If an individual will be using live, vertebrate animals they ***MUST*** have animal training. This is both federal law (Animal Welfare Act, HREA of 1985, PHS Policy) and institutional policy.

2. Enroll in the occupational health surveillance program. Please take the time to read the occupational health website- it provides a wealth of information from how to enroll in the program to potential risks associated with common laboratory animal species. This is both federal law (PHS Policy) and institutional policy.

3. Familiarize yourself with the approved policies of the UCHC ACC. Everyone who works with animals is expected to comply with all ACC policies. Failure to do so may lead to the revocation of your ability to use laboratory animals.

4. Familiarize yourself with the federal regulations that govern the use of vertebrate animals. All animal users, especially Principal Investigators, should be cognizant of these regulations. Ignorance of the laws governing animal use is not an excuse to not follow these laws and policies. Violation of federal laws governing the use of live vertebrate animals is reportable to the Office of Laboratory Animal Welfare, National Institutes of Health, and the United States Department of Agriculture, and your funding agency. It is in a Principal Investigator's best interest ***not*** to allow this to happen.

5. Write and submit animal care and use applications prior to using animals. Federal laws are clear: all research involving the use of live vertebrate animals ***must be approved*** by an Institutional Animal Care and Use Committee (an IACUC)- here at the Health Center, this committee is called the ACC- ***prior to using the animals***. It is the responsibility of the Principal Investigator to submit an application to the ACC. Failure to do so is a serious violation of federal law and is reportable to the Office of Laboratory Animal Welfare, National Institutes of Health, and the United States Department of Agriculture, and your funding agency. It is in a Principal Investigator's best interest ***not*** to allow this to happen.

6. Read the section on the ethics of animal use. Using animals in an ethical and responsible manner is expected at the Health Center. The issues of animals and ethics and the use of animals in biomedical research are ones that are important for all researchers and personnel who use animals to take some time to think about. It is not the intent of the Animal Care Committee to tell you how you should feel about these topics; however, it is important that information be available to the research and animal care community so that each individual can explore these topics.

7. Notify the ACC of any ***unexpected study result(s) that impact the animals***; including any unanticipated pain and/or distress, morbidity, and mortality. It is the Principal Investigator's responsibility to do this.

8. Inform the ACC of any animal users that will be using live, vertebrate animals. The ACC needs to confirm that the individuals have adequate training and are enrolled in the occupational health surveillance program. Individuals must also be added to the protocol(s) they will be working on by submitting a modification to the ACC for that protocol(s). It is the responsibility of the Principal Investigator to ensure that this is accomplished.

9. Read The ACC Connection newsletters. New documents are mailed to all Principal Investigators who use live, vertebrate animals at the Health Center. Read the old issues that are on the website- they contain information that is helpful to you as a PI and/or animal user.

10. Read the Animal Users Training Handbook. This document, located on the web, will give you supplemental information to what was presented in the initial animal users training. We are required by federal law to provide this information.

3. Occupational Health Surveillance Program

In order to be compliant with both PHS Policy on the Humane Care and Use of Laboratory Animals and the UCHC Policy on Occupational Health Surveillance Program for Principal Investigators, Researchers, Technicians, Center for Laboratory Animal Care Staff, and Students Utilizing Animals in Research or Educational Programs, you and everyone listed on your protocol as animal users ***must enroll*** in the UCHC Occupational Health Surveillance Program for Animal Users.

It would be helpful to all animal users to perform a preliminary risk assessment prior to filling out the Mandatory Annual Certification of Enrollment (MACE). All you need to do is click on the species that you are using.

In order to enroll, please:

1. Obtain a copy of the MACE form. Forms are located in your department administrator's office, the ACC office, the ORS office, and EHS.

2. You must fill out the MACE.

NOTE 1: The MACE may contain medical information and, as such, is subject to HIPAA rules and will be kept in your confidential medical file at Employee Health Service (EHS). Only the information that you are enrolled in the program and whether you have accepted or declined participation in surveillance will go back to the Animal Care Committee (ACC) office and the Office of Research Safety (ORS) for tracking purposes (e.g., page 2).

NOTE 2: Prior to consulting with each person listed on the protocol, the PI is advised to come to a consensus with the Biological Safety Officer (BSO) about what will be considered hazards in the ACC protocol.

NOTE 3: Mail the top copy (white) to EHS, attn: Dr. Marcia Trape, MC-6210. Mail the bottom copy (yellow) to the ACC office, MC-2806.

3. You may **participate** in medical surveillance or not: It is ***HIGHLY RECOMMENDED*** that you participate in surveillance. If you know you want to participate in surveillance, or if you wish to consult about participation, you must go to EHS for an appointment. To do so, call EHS at x8005. If no one answers, leave a message stating that you are enrolling in the occupational health surveillance program and would like an appointment, your name, your department, and an extension. EHS will call you back and set up an appointment. At this appointment, you will be able to discuss surveillance with a health care professional who will be able to advise each individual in the context of their particular health status, about the risks associated with working with laboratory animals, and other risks identified in the ACC protocol that you bring to the discussion. Bring the completed MACE with you to the EHS appointment.

4. Protecting yourself with Personal Protective Equipment, including respirators is ***HIGHLY RECOMMENDED*** whether you participate in surveillance or not. If you chose to protect yourself with a respirator or other protective equipment, you should consult in EHS, or with the Biological Safety Officer (BSO), about how to do this. For respirators, the UCHC follows OSHA requirements for medical clearance and fit testing although your choice to wear a respirator is strictly voluntary. Medical clearance for respirators is separate from the surveillance and involves filling out a different questionnaire which should be taken to your medical surveillance consultation along with the MACE. Respirator fit testing and training is performed by the Office of Research Safety and must be done after written medical clearance is received by ORS. You may also send the Respiratory Questionnaire directly to EHS (MC-6210) without visiting there, but if you wish to participate in surveillance, you must visit EHS.

5. Should you decide **not to participate** in medical surveillance: you may do so without speaking with EHS. You will still need to fill out the MACE, sign that you have read the materials about the program, that you understand the risks in your research and wish to decline participation, and then send the form to EHS (MC-6210) in an envelope **marked confidential**.

6. For those participating in surveillance, the MACE form will have to be filled out annually. Whether you participate in surveillance or not, this process will ***enroll*** you in the Occupational Health Surveillance Program for Animal Users, which is required by laws governing the use of animals at the UCHC.

Please note that ***no new protocols or annual renewal protocols will be approved until all personnel associated with these protocols are enrolled in the Occupational Health Surveillance Program for Animal Users***; therefore, please make this a priority in your laboratory.

4. Using recombinant DNA (rDNA) or Hazardous Materials.

The UCHC is required, as a condition of both Institutional and individual PIs' funding, to comply with the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (a.k.a. *NIH Guidelines, NIH rDNA Guidelines, nihG).* Use of rDNA must be either registered with the Institutional Biosafety Committee (IBC) or exempted to the *NIH rDNA Guidelines.* The contact person for doing this is the IBC Coordinator, Ron Wallace (rwallace@adp.uchc.edu, x3781), who can also tell you if your experiment is exempt or not. Sometimes people look at experiments and because they see they are safe, they reason that they are exempt to the NIH rDNA Guidelines. This is not always the case. Sometimes safe experiments are not exempt.

Your ACC Protocol (ACCprot) will be reviewed for human occupational health, safety and compliance issues by the IBC Coordinator, who is also the Biological Safety Officer (BSO). Those ACCprot that have human occupational health, safety and/or compliance issues must be approved by the BSO before the ACC will grant approval. These issues will mainly be for *in vivo* experiments, which are the purview of the ACC. Occasionally, *in vivo* issues transfer into the lab for *in vitro* analysis. Those *in vitro* issues that originate *in vivo* will also be addressed by the BSO. You will be notified by the ACC after the Committee meeting if such issues exist in your ACCprot and asked to contact the BSO with information, clarifications, to fill out an application for the IBC, or to fill out an ACC Safety Protocol (ACC SP). Please note that the IBC is a separate committee from the ACC. It is possible that you will be asked to fill out both forms for the ACC SP and for IBC registration. There has been confusion, because the BSO collaborates with PIs or designees on both documents, that after the BSO was encountered once, all of the requirements had been met. Please see that all of the requirements listed by the ACC in their review are addressed by their respective committees. In order to be in compliance, fiscal packages will not be set up without all approvals indicated on the routing sheet and research with rDNA must not start without IBC approval and research with animals must not start without ACC approval.

The following is a partial list of experiments typical to ACCprot and modifications and their exempt or non-exempt status in the *NIH rDNA Guidelines.* Even if you know that your experiment is exempt, please document how this is true in your ACCprot to avoid being contacted by the BSO for verification and documentation.

Description of Experiment or Procedure	***Needs IBC Regis-tration***	***nihG Exempt***	***Notes for ACC Protocol***
Transgenic (Tg) or Gene Targeted (GT) rodents will be constructed for you in the GTTF at UCHC.	X		Please make a table of all of your Tg/GT strains and indicate where they were constructed or from where acquired.
Tg or GT rodents will be acquired from a *domestic* institution or vendor.		X	Please make a table of all of your Tg/GT strains and indicate where they were constructed or from where acquired.
Tg or GT rodents will be imported from outside the US.	X		Please make a table of all of your Tg/GT strains and indicate where they were constructed or from where acquired.
You will construct your own Tg or GT rodent strains.	X		Please make a table of all of your Tg/GT strains and indicate where they were constructed or from where acquired.
You will cross Tg or GT rodent strains with other strains. *Not exempt, but in most cases your description in the ACC protocol/modification will become the IBC registration.	X*		Please make *another* table of all of your Tg/GT strain crosses. Please indicate if each parent was constructed using plasmids or viral vectors or if unknown. Please indicate if potentially hazardous sequences were incorporated into either parent.
You will transfer non-infected, non-transfected, non-Tg/GT eukaryotic cells into animals. If cells are human, see table below.		X	Please state in your ACCprot that the transferred cells are not recombinant or infectious unless they are human.
Description of Experiment or Procedure Involving Animals	***Needs IBC Regis-tration***	***nihG Exempt***	***Notes for ACC Protocol***
You will introduce rDNA into animals either directly or using viral vectors.	X		Please indicate this in your ACCprot.
You will transfer recombinant cells (transfected by any means) or that come from a Tg/GT animal into other animals.	X		Please indicate this in your ACCprot.
You will infect animals with recombinant, infectious organisms or viruses.	X		Please indicate this in your ACCprot.
You will transfer untransfected hESC into animals. (see table below)		X	Please indicate this in your ACCprot. ESCRO approval is required.
You will transfer recombinant hESC (transfected by any means) into animals. (see table below)	X		Please indicate this in your ACCprot. ESCRO approval is required.

Exemptions for Tg/GT animals are in Section III-E-3 and Appendix C-VI in the nihG. Most of the transfer of recombinant materials into animals experiments fall under Section III-D-4 of the nihG. The requirement for registering crosses of Tg/GT animals comes from a letter of clarification from NIH/OBA.

The following is a partial list of experiments typical to ACCprot that need safety documentation: either a sentence in the ACCprot, or an ACC SP (independent of an IBC registration).

Description of Experiment or Procedure	***Needs ACC Safety Protocol?***	***Notes for ACC Protocol***
Use of paraformaldehyde or formalin in perfusion or fixation (carcinogen, sensitizer). Check 'yes' for hazardous chemicals in Section 7 of the ACCprot.	No	State in ACCprot that you will use this in a chemical fume hood. If you cannot, please consult the BSO.
Use of anesthetic gases (isoflurane) with a chamber or other than with a vaporizer and scavenger. Check 'yes' for hazardous chemicals in Section 7 of the ACCprot.	No	State in ACCprot that you will use this in a chemical fume hood. If you cannot, please consult the BSO.
Use of toxicologically hazardous or uncharacterized chemical compounds and toxins. Check 'yes' for hazardous chemicals in Section 7 of the ACCprot.	Yes	Please define chemical acronyms using the full chemical name, the CAS# and/or supply the MSDS.
Use of ionizing and non-ionizing radiation producing instruments and/or radioactive materials	Possible	Please indicate whether or not you are in contact with the Office of Radiation Safety regarding this use.
Use of human or non-human primate tissues, blood or body fluids, including cultured human cell lines (e.g. hESC, HeLa, HEK 293, etc.) for transfer into animals or any other purpose.	Yes	Under the OSHA Bloodborne Pathogen Standard, Universal Precautions and/or BSL-2 containment must be used with animals that contact these materials.
Use with animals of organisms or viruses pathogenic for humans, animals or plants. This includes recombinant organisms and viruses, select agents and most viral vectors even if replication incompetent.	Yes	Please indicate the name(s) and strain(s) of the organism(s) or virus(es) and the time course of infection and clearing. You may also be required to register your lab.
Use of disease carrying vectors (arthropods, etc.)	Yes	Please specify species/strain of vectors and containment conditions.

A positive answer in both tables generally means that both requirements will need to be fulfilled. Because the IBC meets every two months (http://ors.uchc.edu/bio/ibc/ibc.html) it may be more efficient to prepare the IBC registration in advance or in parallel with the ACC protocol and ACC Safety Protocol. Please consult the biosafety web site or contact the BSO for details and answers to questions about this. In addition, if hESC are involved, please allow time for consideration by the ESCRO committee.

5. Contact Information

Trying to find information on:	Contact this individual:	Contact information:
ACC ADMINISTRATIVE		
Animal regulations, laws, policies	Alison D. Pohl, ACC Coordinator	pohl@uchc.edu; ooacc@uchc.edu
Adverse events involving animal research	Alison D. Pohl, ACC Coordinator	pohl@uchc.edu; ooacc@uchc.edu
Information regarding your protocol	Alison D. Pohl, ACC Coordinator	pohl@uchc.edu ooacc@uchc.edu
Animal training class registration	Alison D. Pohl, ACC Coordinator	pohl@uchc.edu ooacc@uchc.edu
Occupational Health Surveillance	Alison D. Pohl, ACC Coordinator Marcia Trape-Cardoso, Director EHS	pohl@uchc.edu trape@nso.uchc.edu
Training dates, OHS dates for people	ACC website	http://clacc.uchc.edu
SAFETY/COMPLIANCE ADMINISTRATIVE		
ACC Safety Protocols for Chemical, Infectious, Bloodborne Pathogens Issues	Ron Wallace, Biosafety Officer See section 4, Using rDNA and Hazardous Materials, above.	rwallace@adp.uchc.edu
Recombinant DNA use	Ron Wallace, Biosafety Officer	rwallace@adp.uchc.edu
Biosafety issues	Ron Wallace, Biosafety Officer	rwallace@adp.uchc.edu
Institutional Biosafety Committee	Ron Wallace, IBC Coordinator	rwallace@adp.uchc.edu
CT Dept. Public Hlth. registration	Ron Wallace, Biosafety Officer	rwallace@adp.uchc.edu
Select Agents program	Ron Wallace, Biosafety Officer	rwallace@adp.uchc.edu
Radiation / Radioactive materials	James Fomenko, Asst. RSO	fomenko@adp.uchc.edu
Laser Safety	James Fomenko, Asst. RSO	fomenko@adp.uchc.edu
Blood Borne Pathogens	Steve Jacobs, Asst. Director ORS Ron Wallace, Biosafety Officer	Jacobs@adp.uchc.edu rwallace@adp.uchc.edu
Chemical hazards	Steve Jacobs, Asst. Director ORS	Jacobs@adp.uchc.edu; x2723
Hazardous waste	Steve Jacobs, Asst. Director ORS	Jacobs@adp.uchc.edu; x2723
Shipping hazardous materials	James Fomenko, Asst. RSO Ron Wallace, Biosafety Officer	fomenko@adp.uchc.edu rwallace@adp.uchc.edu
Respiratory fit testing	All members of ORS	ORS office: 860-679-2723
URGENT ISSUES		
Chemical/Biological **Spills/ Exposures** in CLAC **controllable** by personnel present	Director CLAC & PI of Protocol; for exposures, EHS or JDH ED (off hours),	x2731 EHS, Dowling North x2893 JDH ED hospital x2588
Chemical/Biological **Spills/ Exposures** in CLAC ***NOT*** **controllable** by personnel present	Contact the Office of Research Safety x2723 - Steve Jacobs and/or Ron Wallace; then contact those above.	ORS office: 860-679-2723
EMERGENCIES where **Fire, EMT/ Rescue, Police** personnel are required. Fire, Man/Woman Down	Call x7777, then contact those above.	860-679-7777 x7777
If animals appear to be sick	Veterinary services	veterinaryservices@uchc.edu
Problems with ACC Safety Protocols where human **safety is in question**	Ron Wallace, Biosafety Officer	rwallace@adp.uchc.edu
Animal Welfare Issues (animal mistreatment, neglect, etc.)	Alison D. Pohl, ACC Coordinator Director CLAC	pohl@uchc.edu x2731
Animal Allergies	Marcia Trape-Cardoso, Director EHS Ron Wallace, Biosafety Officer	trape@nso.uchc.edu rwallace@adp.uchc.edu
Ergonomic Issues	Patti Wawzyniecki, CIH	wawzyniecki@uchc.edu

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CLAC ADMINISTRATIVE		
Ordering animals	Normal Mallett, CLAC Coordinator	mallet@nso.uchc.edu
Imports / Exports of animals	Sandy Kuester	kuester@uchc.edu
Give 3 days notice for setting up animals in Biocontainment or Chemical Isolation	Veterinary Services	veterinaryservices@uchc.edu
Problems with Granite	CLAC	X2731
Procedural training with research animals	Veterinary services	veterinaryservices@uchc.edu
NON-COMPLIANCE ISSUES		
Non-compliance with ACC protocols	Alison D. Pohl, ACC Coordinator Joseph Lorenzo, ACC Chair	pohl@uchc.edu jlorenzo@nso2.uchc.edu
Scientific Misconduct	Leonard Paplauskas, AVP Research Adm.	paplauskas@adp.uchc.edu

Contact Websites:
The best thing about websites is that you can usually find the information you need faster and easier than what you might think! Try these websites for information:

Animal Care Committee	http://clacc.uchc.edu/ACC/Animal_Care_Committee.htm
Center for Laboratory Animal Care	http://clacc.uchc.edu
Office of Research Safety	http://ors.uchc.edu/
Biosafety	http://ors.uchc.edu/bio/biosaf1.html
Chemical Safety	http://ors.uchc.edu/ehs/ehs.html
Radiation Safety	http://ors.uchc.edu/rso/rso.html
Respirator Questionnaire	http://ors.uchc.edu/ehs/Q-resp-en.pdf
OHS information and enrollment form	http://clacc.uchc.edu/ACC/OccHealthandSafetywithAnimals.htm
ORSP (grant information)	http://resadm.uchc.edu/orsp/index.html
Employee Health Services	http://www.oehc.uchc.edu/clinser/emphealth.htm

Partial Regulatory Overview for Research at the UCHC (11/2006)

Issues (What you want to do in research)	**Biohazards &** Use of non-exempt **rDNA** host/vector/ DNA of interest systems	Use of vertebrate **animals** in research, or in testing or training of students	Use of **humans**, identifiable human products or identifiable information in research.	Procurement of all **hESC lines** for *in vitro* and animal studies and Clinical trials	Procurement and Use of **Radioactive Materials, Xrays and Lasers**	Procurement and use of **Hazardous Chemicals**
What you have to do before you do what you want to do. Note: Compliance to some of these things is prerequisite to funding, especially continuations.	For funding, a PI must follow the NIH rDNA Guidelines as well as the rules to the right. For Sect. III-D experiments get registration approval. See http://ors.uchc.edu/bio/ibc/ibc.html . For work with non rDNA human or infectious materials;OSHA Bloodborne Pathogen Standard or CT DPH registration respect-tively. Trainings required.	In order to use animals in experiments at the UCHC, you need to have an approved ACC protocol and have training.	In order to use humans or identifiable human products or information in your experiments you need to have an approved IRB protocol and have training.	In order to use hESC & receive state hESC funding, some or all of the approvals to the left as well as ESCRO approval are needed. For human use development, FDA's GLP/GMP may be needed. http://www.escro.uconn.edu	In order to use radioactive materials and radiation producing instruments you need to be licensed with the Office of Radiation Safety and have training. http://ors.uchc.edu	Adhere to Chemical Hygiene Plan Policies http://www.ors.uchc.edu/ehs/CHP-index.html and participate in Laboratory Safety Training
Whom to contact: UCHC Oversight Committee (UCHC Name) & Contact	UCHC Institutional Biosafety Committee (**IBC**); IBC Coordinator/Biological Safety Officer: Ron Wallace; rwallace@adp.uchc.edu; x3781;	UCHC Animal Care Committee (ACC); **ACC** Coordinator: Alison Pohl; pohl@uchc.edu; x4129	UCHC Institutional Review Board (IRB); **IRB** Coordinators – see web: http://resadm.uchc.edu/hspo/index.html	UConn & UCHC **ESCRO** Committee; contact Dr. Hiskes: anne.hiskes@uconn.edu (860) 486 2215	UCHC Radiation Safety Committee (**RSC**); Asst. Rad. Safety Officer: James Fomenko; fomenko@adp.uchc.edu ; x3817	Office of Research Safety (ORS); Chem. Hygiene Officer: Steve Jacobs;Jacobs@adp.uchc.edu ; x2723
Consequences of non-compliance.	*Institutional*: Freeze PI's funding; *Federal*: Sanctions against the PI and their funding OR the Institution and its funding. OSHA fines. *State*: ConnOSHA fines. Shutdown by the CT Department of Public Health (CT DPH).	*Institutional*: Protocol suspension; permanent withdrawal of animal use privileges. *Federal*: Loss of funding; Loss of Institution PHS Assurance; Loss of AAALAC accreditation; Suspension/ withdrawal of USDA Facility Registration	*Institutional*: Protocol suspension; permanent withdrawal of human research privileges. *Federal*: Loss of funding; Loss of Institution PHS Assurance; Loss of AAHRPP accreditation; Suspension	Legal sanctions against researchers who research with non-approved hESC lines using federal funding.	Sanctions up to and including suspension of privileges; Fines against the Institution.	Institutional Sanctions; Fines against the Institution.
Federally Mandated Local Oversight by Committee (Federal Name) or Institutional Office	Institutional Biosafety Committee (IBC)	Institutional Animal Care and Use Committee (IACUC)	Institutional Review Board (IRB)	Embryonic Stem Cell Research Oversight (ESCRO) committee [but not fed. Mandated]	UCHC Radiation Safety Committee & the Office of Research Safety	Office of Research Safety
Authority	NIH rDNA Guidelines (nihG); Biosafety in Microbiol. and Biomed. Labs (BMBL) OSH Act and UCHC Policy	Animal Welfare Act, Public Health Service Policy on Humane Care and Use of Laboratory Animals and UCHC Policy	Department of Health and Human Services Regulation – Protection of Human Subjects 45CFR 46	Involvement of all of the mechanisms to the left and right, State Statute and Institutional Policy.	Nuclear Regulatory Agency (NRC); Food and Drug Admin. (FDA); CT Dept. of Envir. Protection (CT DEP)	OSHA HazComm & Lab Std. 29CFR 1910.1200 & ~.1450; EPA RCRA 40CFR… ; CT State Statutes
Federal Oversight Agency(ies)	NIH Office of Biotechnology Activities (NIH OBA);	Office of Laboratory Animal Welfare (OLAW); USDA Animal and Plant Health Inspection Service (APHIS)	DHHS Office for Human Subject Protections, Division of Compliance Oversight (DCO), FDA	Same as all those to the left.	NRC; FDA	Environmental Protection Agency (EPA)
State Oversight Agencies	CT DPH; ConnOSHA	CT DPH – for use of dogs	NA	NA (yet)	CT DEP	ConnOSHA CT DEP

IX. References

1. *The Guide for the Care and Use of Laboratory Animals*, National Academy Press, Institute of Laboratory Animal Resources, 1996.

2. 9 CFR Chapter I – Animal Welfare Regulations, 2003.

3. 21 CFR Chapters 291, 1207, 1391— Controlled Substances, 2003.

4. *Public Health Service Policy on Humane Care and Use of Laboratory Animals*, Office of Laboratory Animal Welfare, 2002.

5. Animal Care Resource Guide, United States Department of Agriculture, 2000.

6. Hume, C.W. 1957. Introductory paper to UFAW Symposium on Humane Techniques in the Laboratory, May, 1957, London.

7. NASA Principles for the Ethical Care and Use of Animals, 1997.

8. Notes from "IACUC 101" attended March 28-30, 2004, Boston, Massachusetts.

9. OneVoice, Cordis News Service, 2003.

10. Hawk, C.T. and Leary, S.L. *Formulary for Laboratory Animals*, ACLAM, 1995.

11. Silverman, J., Suckow, M. and Murphy, S. *The IACUC Handbook*, CRC Press, 2000.

12. Occupational Health and Safety in the Care and Use of Research Animals, National Research Council, 1997.

13. "Working with the IACUC: Writing an Animal Protocol", American Association for Laboratory Animal Science, 2002.