I. Policies, Regulations, and Standards Relating to the Care and Use of Laboratory Animals

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A. National

1. Animal Welfare Act - The Animal Welfare Act (AWA), Public Law 89-544, and its amendments regulate the transportation, purchase, sale, housing, care, handling, and treatment of animals used for research, testing or teaching, for exhibitions, and sold as pets. The Act specifically includes dogs, cats, nonhuman primates, guinea pigs, hamsters, rabbits, and any other warm-blooded animals that are being used or are intended for use for research, testing, teaching, experimentation, exhibition purposes, or as pets. Specifically exempted from the AWA are birds, rats of the genus *Rattus*, mice of the genus *Mus*, as well as horses and other farm animals used for food, or livestock and poultry used for the improvement of animal nutrition, breeding, management, or production. Recent amendments address such issues as exercise for dogs; care of nonhuman primates to ensure their psychological well-being; the composition and duties of an Institutional Animal Care and Use Committee; adequate veterinary care and responsibilities of the attending veterinarian; training of all personnel using laboratory animals in humane methods of animal maintenance and experimentation; and record keeping.

Animal Welfare Act

The Institutional Animal Care and Use Committee must be composed of at least three members to include; a veterinarian with special training in laboratory animal medicine/science, a person not affiliated with the institution other than by his/her committee membership, and one other member. This committee is responsible for review of all protocols using animals to ensure that they meet criteria listed in the AWA. In addition, the committee must conduct semiannual inspections of all animal study areas and animal facilities to ensure that the use of animals does not deviate from the approved protocol and the institution's program description. The importance of this requirement is underscored by the fact that the Chief Executive Officer of the

Institution must certify that the attending veterinarian and the Institutional Animal Care and Use Committee have the authority to enter any animal area at any reasonable time.

The AWA is administered by the United States Department of Agriculture (USDA), specifically, the Regulatory Enforcement and Animal Care (REAC) component of the Animal and Plant Health Inspection Service (APHIS). Research facilities are subject to unannounced inspections by USDA veterinarians and are required to furnish annual reports that include, in addition to other information and assurances, the common names and numbers of animals being used. These must be categorized by procedures; e.g., (a) no pain, distress or use of pain-relieving drugs; (b) pain or distress for which appropriate anesthetic, analgesic or tranquilizing drugs were used appropriately during research and testing and that the principal investigator has considered alternatives to painful procedures.

Noncompliance with the USDA standards for the humane, care, use, and transportation of animals may lead to substantial fines and/or suspension of animal research activities.

2. Public Health Service Policy on Humane Care and Use of Laboratory Animal (NIH Policy) - The Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals incorporates the changes in the Public Health Service Act (PHS Act) mandated by the Health Research Extension Act of 1985, Public Law 99-158. The PHS Policy requires that each institution receiving PHS funds for activities involving animals submit detailed information regarding the institution's program for the care and use of all live vertebrate animals to the Office of Laboratory Animal Welfare (OLAW). This information is in the form of an Animal Welfare Assurance, and it must be updated annually and completely revised every five years. Significant changes in existing Assurance status or significant problems encountered in implementing this policy must be reported immediately to the OLAW. The PHS Assurance is available for review in the UT Southwestern Medical Center IACUC office.

Institutions are required to identify an institutional official who is ultimately responsible for the institution's program for the care and use of animals, and a veterinarian qualified in

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laboratory animal medicine who will participate in the program. At the University of Texas Southwestern Medical Center, Dr. Kern Wildenthal, President, is the institutional official and Dr. William Porter Director of the Animal Resources Center (ARC), is the veterinarian. Each institution also is required to designate clear lines of authority and responsibility for those involved in animal care and use for PHS-supported activities.

The Policy clearly defines the role and responsibilities of Institutional Animal Care and Use Committees in all aspects of PHS-supported research. The committee must be composed of at least five members to include; an individual not affiliated with the institution, a veterinarian who has program responsibilities and who has training or experience in laboratory animal science and medicine, a practicing scientist experienced in research involving animals, and a member whose concerns are in a nonscientific area.

The Policy requires that the Institutional Animal Care and Use Committee review and approve those sections of PHS grant applications that relate to the care and use of animals before funds will be awarded. Institutions are required to conduct semiannual self-assessments of the institution's program. Both major and minor deficiencies in the institution's program must be identified and the institution must adhere to an approved plan and schedule for correcting major deficiencies.

An institution's failure to comply with these policies may lead to various actions including the termination of support for all grants and contracts involving animals.

3. US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training - These principles were developed by the Interagency Research Animal Committee (IRAC), and have been adopted as the basis for laboratory animal care and use by the UT Southwestern Medical Center.

I. The transportation, care and use of animals should be in accordance with the Animal Welfare Act 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

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US GOVERNMENT PRINCIPALS

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 a 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 the

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Institutional Animal Care and Use Committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

4. Guide for the Care and Use of Laboratory Animals - In 1963, NIH and the National Academy of Sciences Institute for Laboratory Resources (ILAR) published the first edition of the Guide for the Care and Use of Laboratory Animals (the Guide). The current Guide was revised in 1996. The purpose of the Guide is to assist institutions in caring for and using laboratory animals in ways to be professionally appropriate. It is a long-standing, National Institutes of Health (NIH) policy that grantees and contractors using live vertebrate animals in projects or activities supported by NIH should be guided by the recommendations in this publication. The Guide is also used by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) as a basis for its accreditation of institutions.

5. Association for the Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) is the organization for voluntary peer-review accreditation of laboratory animal care facilities and programs in North America. AAALAC judges animal care, facilities, and programs by the standards set forth in the tri-annual site visits and inspections are made by representatives of this organization to assure that the institution continues to meet these standards. The PHS, in its current policies, accepts AAALAC accreditation as the best means of demonstrating conformance with PHS requirements for animal care and use.

6. Good Laboratory Practice Regulations - The Good Laboratory Practice (GLP) regulations pertain to nonclinical laboratory studies done in support of applications for research or marketing permits for products regulated by the Food and Drug Administration (FDA).

The GLP regulations, as they apply to the use of animals, address such issues as construction and maintenance of facilities; quarantine and isolation; disease diagnosis and treatment; animal identification; caging and routine care; sanitation; and documentation requirements.

7. Controlled Substances Act - Potentially addictive or habituating drugs for human or animal use are classified under this law. Examples of controlled substances include barbiturates

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DEA

and narcotics. The Department of Justice, Drug Enforcement Administration (DEA), enforces this law and requires appropriate security and record management of these substances.

8. Policies of Various Granting Agencies - Most granting agencies have established policies for the care and use of laboratory animals. Investigators should understand fully the requirements of each agency from which they seek funds. The Office of Grants Management or the office of the Institutional Animal Care and Use Committee may be contacted for specific information.

9. American Veterinary Medical Association Panel on Euthanasia - Methods of euthanasia recommended by the American Veterinary Medical Association (AVMA) Panel of Euthanasia)are accepted by both the PHS Policy and the Animal Welfare Act as standard methods of euthanasia.

B. State and City

The state of Texas has no provisions for licensing research facilities that use laboratory animals. Research is exempted in Texas state laws concerned with cruelty to animals. Specifically, "It is a defense to prosecution under this section that the actor was engaged in bona fide experimentation for scientific research". There is no mention of pound dog use in the state laws. Municipalities have control in this area.

C. Institutional

1. Committees - The PHS Policy and the Animal Welfare Act require the establishment of a committee, referred to by the generic name of Institutional Animal Care and Use Committee (IACUC), whose function is to ensure that the care and use of animals is appropriate and humane. The Institutional Animal Care and Use Committee (IACUC) carries out the responsibilities of the IACUC at UT Southwestern Medical Center.

The membership of this committee includes a Doctor of Veterinary Medicine with experience in laboratory animal science and medicine, an individual whose primary concerns are in a nonscientific area and who is not otherwise affiliated with the Institution (the "outside

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IACUC

member"), and practicing scientists experienced in research involving animals. Members are appointed by the President of the UT Southwestern Medical Center and serve one year terms.

The committee meets at least once a month and is responsible for monitoring the Institution's animal care and use program, performing the semiannual inspection of the Institution's animal use areas, and ensuring that there are no deviations from approved animal use protocols that adversely affect animal welfare. This committee is authorized to suspend an activity involving animals if it determines that the activity is not being conducted in accordance with applicable provisions of the Animal Welfare Act, the Guide, and the PHS Policy.

This committee also reviews and approves, requires modifications in, or withholds approval of all protocols related to the care and use of animals at the UT Southwestern Medical Center. To ensure consideration of a protocol at a particular meeting, the Use of Animal Subjects Form must be submitted to the IACUC office by the 25th of the previous month.

2. Training Programs - A variety of training programs are available to personnel who care for or use laboratory animals. Lectures based on the information in this handbook are offered as needed for all personnel who use animals in research. In addition to these lectures, species specific "hands on" training is also available for personnel.

The ARC Animal Care Technicians participate in continuing education sessions as well as on-the-job training programs. Research technicians whose jobs involve animal care should participate in-house continuing education programs.

3. Reporting Deficiencies in Animal Care and Treatment - Any complaints or concerns by a UT Southwestern Medical Center employee regarding the care and use of laboratory animals at this Institution should be made to the Director of the Animal Resources Center either verbally or in writing. If the complaint is directed against the ARC, the report should be made to the Chairman of the Institutional Animal Resources Center Advisory Committee (IACUC). Confidentiality will be maintained upon request. The ARC Director (or IACUC Chairman) will keep persons expressing concerns informed of the actions taken. The IACUC subcommittee or the ARC Director will conduct an initial review of the concerns. After notification of and discussion

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with the the Chairman of the IACUC, the problem may be taken before the IACUC for full review. An investigator who is the subject of complaint will be notified in writing of concerns expressed and allowed to respond. The IACUC will maintain a file documenting the complaint, the review, and the actions taken to rectify any problem(s) identified.

4. Security - Certain security measures have been implemented to protect faculty and staff and the animals used in biomedical research at the UT Southwestern Medical Center. Cooperation in enforcing these measures is essential.

a. Entrance into Animal Housing Facilities **- Entrances into animal housing facilities are secured at all times by a magnetic card system and/or keys. The ARC will issue cards allowing entrance into specific areas at specific times based upon the investigator/technician's needs. Security Access Cards are not routinely programed to allow entrance into animal facilities after hours or on weekends. Weekend and/or after hours access requirements must be noted on the Access Card request form. Request forms for Security Access Cards may be picked up in NB2.346. Requests for room keys should be submitted on IDRs to NB2.346. All persons who require the use of Security Access cards and/ or keys must be listed on approved and active protocols. All persons who require the use of north campus facilities are required to attend a training session for the use of those facilities. Cards or keys for the north campus animal housing areas will not be issued until this training session has been completed. Individual rooms within the facilities are secured by key. Research personnel are responsible for relocking the rooms. Loans of keys may be made only with ARC permission. Security Access Cards should <u>never</u> be loaned.**

Any people or activities in the animal facilities that appear inappropriate and/or suspicious should be reported immediately to the Animal Resources Center and/or the University Police.

b. Visitors **- In an effort to protect research animals and minimize any possibility of disease transmission, visitors, including family members and especially children, are not allowed in UT Southwestern Medical Center animal facilities without prior approval by the**

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ARC Director. Tours of UT Southwestern Medical Center animal facilities are conducted by ARC personnel for interested groups. These tours must be scheduled through the Medical Information office and ARC.

***c. Photographs or Videotapes of Animals* - The use of animals in biomedical research is a very sensitive and emotional issue. Therefore, faculty members are urged to carefully consider all possible interpretations of pictures of research animals taken for documentation or publication. The ARC and Medical Information office are available to advise faculty in the development of photographic materials and to help review materials for subject matter that might be misinterpreted by the general public.**

Under no circumstances should photographic equipment be taken into UT Southwestern Medical Center animal facilities without the specific prior approval of the ARC Director.

***d. Inquiries Regarding Animal Use* - Investigators and technicians should not attempt to answer questions from individuals outside the UT Southwestern Medical Center regarding animal care and use at this Institution. All questions should be referred to the ARC Director. The Medical Information office will handle all inquires from members of the media and will clear all interviews in advance with UT Southwestern Medical Center faculty and staff. The ARC Director should be informed of all such requests for information and, when possible, provided with the name, address, telephone number, and affiliation of the individual(s) making the inquiry.**

***e. Threats Related to Animal Use* - All UT Southwestern Medical Center faculty and staff should report immediately all threats, whether written or verbal, to the University Police and the ARC Director. The University Police will advise threatened individuals on security measures and take action the Chief of Police deems appropriate.**

***f. Demonstrations* - In the event of a demonstration on the campus related to research animal use, UT Southwestern Medical Center employees should avoid the area where the demonstration is being conducted, avoid confrontation with the demonstrators, and follow the directions of the University Police.**

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THREATS

g. Break-ins **- Anyone discovering a break-in of animal housing or use areas should inform the ARC Director immediately. The area should not be cleaned or otherwise disturbed until permission is received from individuals responsible for the investigation.**

5. Pets in Animal Facilities, Laboratories, or Offices - Pet animals are not routinely allowed in animal facilities, laboratories, or offices. Housing of animals covered by the Animal Welfare Act in offices and laboratories is closely scrutinized by the USDA.

6. Removal of Animals from the Institution - Animals must not be removed from the institution without prior, specific permission of the ARC Director. See Section III.D.3 for information regarding shipment of animals to other institutions.

7. Transportation of Animals within the Institution - In planning the route by which animals will be transported between laboratories and the animal housing areas or other laboratories, care should be taken to minimize time spent in public areas including hallways or lobbies. Passenger elevators are not to be used. Carrying the animals in your arms or in open boxes is unacceptable. Animals should be concealed from the public during transportation in public corridors by placing a drape loosely over the cage. Call the ARC office or ask the area ARC supervisor for advice or assistance. Transportation of animals to the north campus buildings Rogers Magnetic Resonance Center, Record Crossing, or Callier Center must be scheduled through ARC. Animals are not to be transported by research personnel.

8. Animal Identification - The Animal Welfare Act (AWA) and the Guide require certain information on all animal cages for identification purposes. Cage cards supplied by the ARC have been designed to satisfy these requirements. Research or other data may be placed on a second card in the holder behind the identification card. However, the completed ARC card must be visible on all animal cages at all times.

The AWA requires that individual animals of certain species be identified either by tattoo or tag. When USDA tags are used, the tag must be retained by ARC for a period of up to one year after the animal's death.

9. Record Keeping- Each investigator is responsible for maintaining records that

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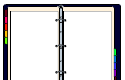
ANIMAL ID AND RECORD KEEPING



document efforts to avoid animal pain and distress during the research procedure. These records must be maintained for three years after completion of the project and are subject to inspection by the USDA, NIH site visitors, AAALAC, and the IACUC. Records for individual dogs, cats, rabbits, nonhuman primates, and farm animals and experimental groups of rodents and other small animals should include the Animal Project Number, source of the animal; date of experimental procedure; procedure performed including Animal Project Number, person(s) performing procedure; presurgical drugs, anesthetics and post-surgical care; illnesses or injuries; medical treatment during course of experiment; date of death or euthanasia; and disposition. Occasionally, it is appropriate to keep such information on individual rodents as well.

10. Experimental Procedures in Animal Housing Areas - Experimental procedures including euthanasia are not to be performed in occupied animal rooms unless justified for scientific or environmental control reasons and the investigator has obtained approval from ARC and/or the IACUC.

11. Animal Experimentation Involving Hazardous Agents - To protect the safety of animals and humans, the use of hazardous biological, chemical, or physical agents must be approved by both the Biosafety Committee and the IACUC. Animals exposed to hazardous agents must be clearly identified and housed in designated facilities; animal wastes and animal carcasses must be disposed of according to established protocols.

Animal experiments involving infectious agents of animal origin must be conducted with great care to avoid potential epizootic infection in the animal colonies. Caution also must be exercised when inoculating animals with biological material such as transplant tumors and tissue culture products that may contain infectious agents. Transplant tumors must be free of murine pathogens prior to inoculation in experimental rodents.

Facilities for housing animals exposed to biohazardous agents/organisms are available. However, arrangements for such special housing must be made with the ARC as far in advance of the study initiation as possible. After consultation with the investigator, the ARC faculty and the UT Southwestern Biosafety Officer will develop protocols for the handling and care of the animals

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HAZARDOUS AGENTS

during the study. These protocols will apply to all personnel handling or caring for the animals.

12. Waste Disposal - Animal waste is incinerated or otherwise disposed of in a safe and sanitary manner. Carcasses should be bagged and placed in walk-in freezers located in G9.300, J1.502, Y2.402 and NB.400.

Hazardous wastes must be rendered safe by sterilization, decontamination, or other appropriate measures before disposal. Questions concerning the disposal of hazardous agents should be directed to the Environmental Health and Safety (EHS) office. The ARC and EHS will coordinate the disposal of animal wastes and carcasses. It is the investigator's responsibility, however, to ensure that the ARC and EHS are aware that biohazardous agents are being used.

13. Ether - While ether provides good analgesia for surgical procedures, it is not an acceptable euthanatizing agent for animals. Its use is strongly discouraged because it is highly flammable and explosive. If ether must be used, its use must comply with the "UT Southwestern Policy on Use of Ether as an Anesthetic Agent in Animal Research".

14. Blood Collection Techniques - Aseptic procedures should be used when collecting blood in all situations. Blood collection by cardiac puncture in any species or from the retro-orbital plexus in rats and mice should be performed only on anesthetized animals.

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BLOOD COLLECTION PROCEDURES

`Scalpel incision of the ear vessels, generally, is not an acceptable technique for bleeding rabbits. Withdrawal of blood from the lateral ear vein or, for large volumes of blood, the central artery of the ear using a hypodermic needle and syringe or vacuum tube is recommended. Hemostasis should be achieved by direct pressure with gauze or a cotton pledget.`

Consult the ARC veterinary staff for recommendations on the volume of blood and frequency of bleeding for each species.

15. Animal Surgery

a. Presurgical and Postsurgical Care of Animals **- The health status of all animals used for survival surgical procedures should be evaluated prior to surgery. For rabbits**

and larger animals, determinations of heart rate, respiratory rate, body temperature, packed cell volume (PCV), and blood urea nitrogen (BUN) are considered the minimum components of a presurgical physical exam. A complete blood count and function tests of various organs, especially liver and kidneys, are very desirable. The presurgical evaluation should be performed not more than 24 hours prior to the procedure. The animal's cage should be tagged to withhold food and water overnight or longer as necessary depending upon the species and the procedure. The use of pre-surgical tranquilizers can reduce animal anxiety thus resulting in a much smoother, quieter induction and a reduced requirement for anesthetic agent. Other agents, such as atropine, should be used as needed.

The principal investigator is responsible for postoperative care of the animal with appropriate input from an ARC veterinarian. Immediate postsurgical care should include observing the animal to ensure uneventful recovery from anesthesia and surgery. The animal must be monitored and not returned to the animal housing area until it regains sternal recumbency and is capable of holding its head up. Color and capillary refill time should be evaluated frequently. The animal should be kept warm and dry and fluids, analgesics, and antibiotics, administered as required. Surgical wounds should be kept clean, bandaging as necessary. An ARC post-surgical recovery room is available for use for the larger species as well as smaller species requiring specialized care.

Subsequent care may include administering supportive fluids, analgesics, and other drugs as required; monitoring of the animal to include daily body temperatures; clinical observations for signs of pain, abnormal behavior, appetite, and excretory functions; providing adequate care for surgical incisions; and maintaining appropriate medical records.

Appropriate postoperative care for rodent species includes the administration of fluids, analgesics and other drugs as indicated; clinical observations for signs of pain, abnormal behavior, appetite, and excretory functions; and providing care for surgical incisions.

Documentation of the pre-and postsurgical care is required by the USDA Animal Welfare Act.

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ANIMAL SURGERY

b. Survival Surgery in Nonrodent Mammals **- Survival surgery is defined as any surgery from which the animal recovers consciousness for any period of time. Individuals performing survival surgical procedures must be knowledgeable about aseptic surgical techniques and have adequate training and skills to conduct the procedure without causing undue postsurgical distress to the animal. Aseptic techniques must be used for all survival surgical procedures. Major surgical procedures on non-rodent mammalian species must be conducted in surgical facilities approved by the IACUC.**

The classification of "major" or "minor" for each proposed surgical procedure will be determined by the IACUC. The guidelines used by the committee to make this determination are described in the current edition of the Guide.

Minor survival surgery does not expose a body cavity and causes little or not physical impairments of the animal. Wound suturing, peripheral vessel cannulation, pump implantation in subcutaneous tissue, castration and dehorning in farm animals, etc. are examples of minor survival surgery.

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Minor surgical procedures may be performed in a suitably located and equipped laboratory setting using appropriate aseptic technique. This includes a clean work area, preparation of the surgical site including clipping of the hair, disinfecting of the skin and draping of the surgical site with sterile drapes; the use of sterile supplies and instruments; and the use of sterile gloves and a surgical mask by the surgeon and any assistants working in the surgical field.

Major survival surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions of the animal. Laparotomy, thoracotomy, craniotomy, joint replacement, limb amputation, etc. are examples of major survival surgery.

All major survival surgical procedures on non-rodent species must be conducted in facilities intended for that purpose. The functional components of the facility include surgical support, animal preparation, surgeon's scrub, operating room, and postoperative recovery. These facilities must be constructed, maintained and operated to ensure a level of sanitation appropriate for aseptic surgery, and directed and staffed by trained personnel. The operating room(s) must be

uncluttered and contain only standard surgical equipment and supplies and essential special equipment required to support current research and teaching protocols. Use of the operating room(s) should be limited to aseptic procedures and must not be used for general storage or officing personnel. A separate area must be provided for clipping hair from the operative site although the final surgical preparation of the skin may be conducted in the surgery room. An area equipped with surgical scrub sinks should be apart from the operating room(s) and the animal preparation area. Other necessary surgical support functions require facilities for cleaning and sterilizing instruments and storing instruments and sterile supplies; a dressing area for personnel to change into surgical attire; and an area for intensive care and supportive treatment of the animals postsurgically. Although it is desirable, it is not necessary for support areas to be contiguous with the surgery room, with the exception of the surgical scrub sinks.

Aseptic technique must be used. This includes wearing sterile surgical gloves, gowns, caps, and face masks; using sterile supplies and instruments; and aseptically preparing the surgical field.

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RODENT SURGERY

***c. Surgery in rodent species* - All procedures on rodent species may be conducted in a laboratory. For major survival surgical procedures appropriate aseptic techniques including a clean work area; preparation of the surgical site including removal of the hair, disinfection of the skin and draping of the surgical site with sterile drapes; use of sterile supplies, instruments and suture materials; and use of sterile gloves and a surgical mask by the surgeon and any assistants working in the surgical field should be used. (See the "UT Southwestern Policy for Aseptic Survival Surgery on Rodents".)**

***d. Non-survival Surgery* - If the animal will not regain consciousness postoperatively, major surgical procedures on non-rodent species may be conducted in a suitably located and equipped laboratory.**

***e. Multiple Survival Surgeries* - Multiple-survival surgical procedures on a single animal are discouraged. Under special circumstances, such as if the procedures are essential related components of the research projects, more than one major surgical procedures on a single**

animal may be permitted with the approval of the IACUC. Occasionally, unanticipated additional surgeries to correct complications that arise following the primary surgical procedures may be done so long as it is approved by an ARC veterinarian and does not cause an inordinate degree of pain or distress to the animal. Multiple- survival surgical procedures for teaching protocols are not to be done. Cost alone is not an adequate justification for performing multiple-survival surgical procedures on an animal.

16. Paralytic Agents - The use of paralytic agents is discouraged, particularly in surgical experimentation. It is recognized, however, that their use for certain applications has merit. If such agents must be used, written justification must be provided to the IACUC. Under no circumstances are paralytic agents to be used for surgery without appropriate anesthesia. The protocol must specifically note, in detail, how an appropriate level of anesthesia will be maintained throughout the time that the animal is under the influence of the paralytic agent.

17. Prolonged Physical Restraint - Prolonged physical restraint may be stressful to the animal and should be avoided unless justified as essential to the research objectives. All physical restraint for periods longer than one hour must be specifically justified in the protocol for consideration and approval by the IACUC. Convenience alone is not adequate justification for the use of prolonged physical restraint.

When prolonged physical restraint is required, animals should be conditioned to the equipment by gradually increasing times of restraint until the required restraint time is reached. The period of restraint must be limited to the minimum required to accomplish the research objectives. For comfort and safety of the animal, certain kinds of restraint equipment, such as slings for dogs, require that the animals be attended throughout the period of restraint. For each situation, the IACUC will make a determination regarding the intensity of the attention required. Generally, chairing of nonhuman primates for periods longer than 24 hours is discouraged. When a reasonable alternative to prolonged chair restraint is not possible, the animals must be removed from the chair for exercise periods as long and as frequently as possible. Attention must be given to the possible development of lesions or illnesses associated with restraint,

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including contusions, decubital ulcers, dependent edema, and weight loss. If these or other problems occur, prompt veterinary care must be provided. This may require temporary or permanent removal of the animal from the restraint device. If the health problem is considered serious by the ARC clinical veterinarian tending the animal, the well-being of the animal must take priority over the experimental objectives.

18. Immunization of Research Animals - Because there are diverse opinions and techniques associated with animal immunization, protocols that propose to use procedures contrary to the following policies will be considered by the IACUC upon receipt of written justification and documentation. If appropriate documentation is lacking, it may be necessary to conduct a study designed to provide appropriate documentation.

a. Complete Freund's Adjuvant **- Many of the classical adjuvants, especially Freund's Complete Adjuvant (FCA), cause local inflammation and often chronic pain. When draining skin granulomas form and tissue is sloughed, the antigen-adjuvant emulsion may be lost.**

FCA should be used only in the primary injections. It should be prepared as a 1:1 suspension with the antigen solution and injected aseptically at scattered sites over the back and flank of the rabbit. Subcutaneous injections from 0.05-0.5 ml total per site or 0.5 - 1 ml total per site intramuscular injections in the thigh are recommended. If intradermal injections must be used, the volume per site should be reduced to 0.05 ml - 0.1 ml to prevent necrosis or drainage.

FCA is used only for the primary inoculation, as secondary inoculation with FCA produces a severe and painful hypersensitivity reaction. Booster doses may be given as antigen in Freund's Incomplete Adjuvant (FIA) or an aqueous vehicle such as saline after a suitable priming period.

Laboratory personnel using FCA should be cautioned about inadvertent self-injection on needle tips. This results in painful and long-lasting inflammation in humans.

Use of alternate adjuvants which produce less detrimental side effects is strongly encouraged.

b. Footpad Injection **- Footpad injections must be approved by the IACUC. FCA**

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ANTIBODY PRODUCTION

inoculated into the footpad produces swelling, ulceration, and necrosis, therefore it should be given by this route only when justified for scientific reasons.

Adjuvants should be inoculated into only one of the animal's feet and, for rodents, a hindfoot should be used.

***c. Post Injection Care* - Animals given aqueous solutions of antigens after sensitization should be observed for signs of anaphylactic shock. Appropriate treatment should be administered if an acute reaction occurs.**

Inflammatory reactions at injection sites should be reported to an ARC veterinarian for examination and treatment if indicated.

***d. Ascites Production* - Animals are primed with 0.2 ml pristane intra peritoneally. Intraperitoneal injections of pristane induces granulomatous reactions and interferes with peritoneal fluid drainage. Large volumes (>0.2 ml) of pristane are associated with weight loss, hunched appearance, and lethargy. Volumes of 0.1-0.2 ml pristane produce minimal distress to the animal yet yield ascites producing tumors equivalent to those produced in mice using higher doses of pristane.**

The rate of ascites fluid production is extremely variable, therefore, animals must be observed daily and the peritoneal fluid drained as necessary to prevent excessive accumulation. Ascites can cause discomfort, pain and, respiratory distress. The following general guidelines should be followed: the ascites fluid should be collected when the abdomen is approximately the proportion of a near-term pregnant animal; collections should be made using a 21g or 22g needle, preferably on an anesthetized animal; and animals should be euthanatized if their condition begins to deteriorate (their hair coats become rough, they become thin, they become lethargic or have difficulty moving, etc.). The volume of ascites fluid removed should not exceed 3ml per collection. Administration of saline subcutaneously or intra peritoneally after collection of ascites may help prevent hypovolemic shock.

19. Unavoidable Pain or Distress - Every effort must be made to avoid or minimize discomfort, distress or pain to experimental animals, consistent with sound research design.

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Procedures that may cause more than momentary or slight pain or distress must be justified for scientific reasons in writing by the investigator. To minimize distress to the animals, the earliest possible end point to the study must be defined and used. Whenever possible, this should be prior to death of the animal. The protocol must justify and clearly state the end point to be used.

20. Euthanasia - The euthanasia guidelines provided by the ARC are based on recommendations of the American Veterinary Medical Association Panel on Euthanasia and the experience of the ARC veterinary staff in this Institution. Any deviations from these guidelines must be justified in writing and approved by the IACUC.

21. Personnel Health Surveillance Program - The Occupational Health Program for animal care personnel and professional and technical personnel working with animals is monitored by the Office of Environmental Health and Safety.

22. Animal Bites or Other Animal Related Injuries. - In the event of an animal bite or other animal related injury, administer first aid and promptly report the injury to the designated person (supervisor, instructor, employer, etc.). Go to a clinic/hospital if additional treatment is necessary. Complete the "Workers Compensation Worksheet for First Report of Injury" form and submit it to the designated person, and contact the UT Southwestern Workers Compensation/Benefits office.

In the event of a dog, cat, or wild animal bite, call the ARC Animal Health Technologists. If the animal is still alive it will be examined by an ARC Veterinarian and isolated for the required observation period. If the animal is dead, tissues will be collected and submitted to the proper authorities for rabies evaluation. Under most circumstances, rodents and rabbits do not need to be isolated and observed. Contact the Environmental Health and Safety office for information regarding the immunization status of anyone bitten by an animal.

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OCCUPATIONAL HEALTH PROGRAM

II. Humane Methods of Animal Maintenance and Experimentation

Laboratory animal care and use at UT Southwestern Medical Center is based on the US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, the recommendations of the Guide for the Care and Use of Laboratory Animals, and the requirements of the Animal Welfare Act and its amendments.

A. Animal Care - Animals are housed in cages designed to provide a physical and social environment that contributes to the well-being of the animals while minimizing variables that can modify an animal's response during experimentation. Environmental factors such as temperature and humidity ranges, air exchange rates, lighting, and noise levels are considered in housing the various species. Palatable, uncontaminated, and nutritionally adequate food and fresh, potable, uncontaminated drinking water are provided to meet the particular requirements of each species. Bedding, if used, is absorbent and free of toxic chemicals. Cage and equipment-cleaning schedules and methods are designed to keep animals clean and dry and eliminate pathogenic organisms while providing minimal interference with normal physiological requirements of each species.

The veterinary care program consists of observing all animals daily to assess their health and welfare; using appropriate methods to prevent, control, diagnose, and treat diseases and injuries; providing guidance to users regarding handling, immobilization, anesthesia, analgesia, and euthanasia; and monitoring surgery programs and postsurgical care.

Personnel caring for animals are trained in laboratory animal husbandry through formal courses and closely supervised on-the-job experience. They are taught to detect and report variations in normal function or behavior of the animals. Personnel learn to handle the animals in a calm, confident manner that minimizes stress and ensures the safety of both the handler and the animal.

B. Animal Experimentation - It is the responsibility of any investigator using animals in research to ensure that he/she and their employees, both professional and technical, know how to handle and care properly for the species being used. They also should be knowledgeable about the animal model and the techniques used. The veterinary staff should be consulted if there are

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any questions. In addition, information regarding the basic needs of each species is readily available from reference sources in the library of the Animal Resources Center. Investigators should try whenever possible to reduce the number of animals used, refine techniques to minimize pain or distress suffered, and replace animals with alternative or adjunctive methods.

1. Reduction - The numbers of animals used in research can be reduced in a variety of ways.

***a. Literature Review* - No experiment using animals should be performed without a thorough review of the literature to eliminate the possibility of needless repetition and to determine the most appropriate model to answer a particular research question. Through the inter-library loan system, the UT Southwestern Medical Center library has access to literature concerning all aspects of animal experimentation. Specific information may be sought using a variety of databases including AGRICOLA which is maintained by the National Agricultural Library. Consult the UT Southwestern Medical Center library staff for assistance with searches.**

***b. Use Based on Requirements to Achieve Statistical Significance* - All experiments should be planned to provide sufficient data points to determine statistical significance. Using insufficient numbers of animals may require a repetition of the experiment and, therefore, may be as undesirable as using too many animals. Formula for estimating the number of animals needed for a particular experiment may be found in biostatistical publications or consult one of the biostatisticians in Academic Computer Services.**

***c. Disease-Free Animals* - While the cost of disease free animals, sometimes called SPF (Specific Pathogen Free), is greater initially, the long term benefits of using such animals usually far outweigh the initial cost. For example, it makes little sense to inject a rabbit carrying *Pasteurella multocida*, an organism that can produce significant disease or death in this species, with an antigen that is very costly to prepare.**

***d. Sharing Animals or Tissues* - In some cases, the organs, tissues, antibodies, etc., may be commercially available. Several investigators sharing the organs of a single animal reduces the number of animals necessary and the cost to the investigator.**

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THE 3 R'S

REDUCE
REFINE
REPLACE

2. Refinement - Whenever possible, investigators should design experiments so that death is not the end point. Minor modifications of the approach to the experimental problem may allow euthanasia of an animal before it suffers significant discomfort or anxiety. Along the same lines, when passing tumors or growing tumors *in vivo*, efforts should be made to collect tissues or evaluate effects prior to the time that the animal is incapacitated.

Anesthetic, analgesic, or tranquilizing agents should be administered for any procedure potentially causing more than minimal pain or distress to the animal. (Exceptions must be justified and approved by the IACUC.) The principal investigator should be alert to, and recognize signs of, pain or distress in the species with which he/she is working. Changes in dietary or grooming habits or changes in body temperament may indicate that an animal is in pain or distress. If the investigator or research technician has any questions or needs assistance, an ARC Veterinarian should be consulted.

3. Replacement

***a. Teaching New Techniques* - New techniques should be demonstrated or practiced on models or cadavers. Videotapes and slide-tape presentations should be developed and used as much as possible in training programs.**

***b. Alternative or Adjunctive Methods* - While an intact biological system may be required to answer some research questions, tissue culture, or other *in vitro* techniques, including computer or mathematical modeling may provide satisfactory alternative or adjunctive methods.**

III. Animal Resources Center (ARC)

The Animal Resources Center (ARC) is responsible for establishing and providing appropriate facilities for the care and use of animals; professional and technical expertise, consultation and service in all phases of laboratory animal care and use; health care programs for laboratory animals, including diagnostic services; and continuing education in the care and use of animals for ARC staff.

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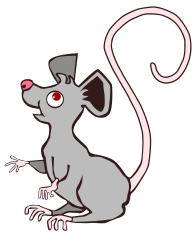
ARC



A. Veterinarians and Staff - The veterinarians and staff of the ARC provide expertise in the biology, diseases, and pathology of laboratory animals and techniques associated with the use of these animals in research. Veterinarians are usually board certified in laboratory animal medicine and/or veterinary pathology.

The technical staff providing animal care is encouraged to be certified by AALAS, and are carefully supervised during on-the-job training. The veterinary support staff are trained in animal health technology and veterinary assistance.

B. Organization - The ARC is an academic service department responsible to the President of UT Southwestern Medical Center through the Associate Dean for Research.

The Director of the ARC coordinates and directs operations of animal health programs, animal care programs, business operations and teaching programs within the ARC.

Clinical Veterinarians are responsible for the veterinary care and treatment of all animals housed at UT Southwestern Medical Center. Animal Health Technologists (AHTs) assist the veterinarians and are available to provide surgical or other technical support to investigators.

Animal Care Supervisors organize and direct the daily operation of the animal facilities. They also assist in planning facility renovations, training technicians and evaluating services.

The ARC Diagnostic Laboratory, consisting of clinical pathology and anatomic pathology components, is responsible for the evaluation of specimens as they relate to animal health. The Laboratory performs bacteriologic, hematologic, parasitologic, clinical chemistry, and histopathologic procedures.

The ARC administrative offices coordinate the daily operation of the different ARC units, orders animals and supplies, bills investigators for animal care, supplies, as well as requested assistance. Moreover, other issues relating to the finances of the ARC and communications between the ARC and other departments within the UT Southwestern Medical Center are directed from the administrative offices.

C. Description of Facilities - The animal resources facilities consist of approximately 140,000 net square feet of animal housing and support areas located on various floors of twelve

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FACILITIES

campus buildings. Specialized space includes: cage washing areas, autoclave areas, refrigerated food storage, bedding storage, diet kitchens, sterile surgical suites, radiology facilities, intensive care units, postoperative care rooms, necropsy rooms, and a diagnostic laboratory.

D. Animal Procurement - All animal orders must be processed by ARC in order for the correct paperwork and backup documentation to be completed. Animals are generally not shipped after Wednesday of each week so they will not arrive on a weekend.

1. Ordering - No orders will be processed without an Animal Project Number indicating approval of the animal use by the IACUC. All orders for animals (commercial or otherwise) must be processed through ARC.

Orders for animals from commercial vendors or from other institutions should be placed by completing an Animal Purchase Requisition and delivering it to room NB2.346. ARC personnel will assign a purchase order number to the requisition, order the animals, and arrange for the delivery of the animals to UT Southwestern Medical Center. The shipper's address and phone number and instructions for housing at UT Southwestern Medical Center must be included on the requisition.

If the shipper pays all costs, provide the ARC Animal Purchasing Agent will coordinate with the shipper the shipping date, the air carrier to be used and the type of housing requirements for the animals upon arrival at UT Southwestern Medical Center. There may be exceptions to this routine for animals that are shipped from a foreign country. In this situation, the UT Southwestern investigator should contact the ARC purchasing agent to determine what information is required and what procedures are to be followed.

2. Receiving - Animals are received at the ARC by an animal receiving clerk and checked for order specifications and any obvious signs of illness. The animals are then identified in an appropriate manner. The animal receiving clerk ensures that the animals are housed in the appropriate animal room and notifies the investigator of the animal's arrival and location. If by mistake, animals are delivered directly to an investigator and bypass receiving procedures, ARC should be notified immediately. If an investigator requires animals to be delivered directly to a

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ANIMAL ORDERS AND SHIPPING

laboratory for immediate use, the requirement should be noted on the purchase requisition.

3. Shipping - All shipment of animals to other institutions, regardless of whether or not they are to be returned, must be coordinated through the ARC to ensure that proper Health Certificates required by the USDA are completed. ARC personnel will assist in making the necessary shipping arrangement.

4. Sources of Animals - The staff of the ARC is knowledgeable regarding the sources and availability of animals for use in research and should be consulted especially if special strains are required.

The ARC receives periodic health assessment reports for laboratory animals available from various sources. Recommendations regarding use of these animals is made based on their health status. Request to obtain animals from an unapproved vendor must be approved by an ARC clinical veterinarian.

***a. Commercial Vendors* - Commercial vendors, selected on the basis of consistent good health of their animals and on dependable delivery and service, are used most frequently as a source of research animals. Animals generally not considered acceptable or with limited acceptability due to known disease problems may be purchased if required for a particular study; however, the investigator must realize that these animals will have to be housed and handled in such a way that they do not jeopardize the health of any other animals or humans.**

***b. Other Institutions* - The ARC must be notified if animals are to be acquired from other institutions. ARC veterinarians will inquire about the health status of these animals so that they may be shipped and housed in a manner that protects them from infection and prevents infection of resident animals.**

E. Animal Care

1. Routine Animal Care - ARC personnel check all animals daily, including weekends and holidays, for signs of illness and to ensure that adequate food and water are available. Rooms are cleaned daily and air filters are changed as needed. Cages and litter pans

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are changed on a regular basis depending upon the animal species. The schedule for animal room work and cage changing is posted on the door of each animal room.

Each day Animal Care Technicians tag cages containing sick animals and remove any animals that died overnight. The reports of sick and dead animals are submitted daily to the ARC clinical staff for further action.

2. Special Care Requirements - Animals receiving special care (i.e., special diet, fasting, etc.) are identified through the use of color coded tags attached to the animal's cage. A supply of these tags is available in each animal room or can be provided by animal care personnel. Care should be taken to select the most appropriate tag and complete it properly prior to attaching it to the animal's cage.

Other special requirements such as altered lighting cycles or temperature, isolation, etc. or special care for large groups of animals may be arranged with the ARC supervisor.

3. Standard and Special Diets - Standard dry diets are fed ad libitum in self-feeders to all animals unless otherwise specified. Special diets are not provided by the ARC but ARC personnel can assist investigators in locating sources for them. Dietary supplements are provided when necessitated by disease problems or dietary requirements.

4. Environmental Control - Each animal room has a minimum of 10-15 changes per hour of non-recirculated air. Biohazard and conventional facilities are maintained with a negative air pressure relative to the corridor. Barrier rooms are maintained with a positive air pressure. "Conventional" rooms may be positive or negative, dependant on the building location. Relative humidity and temperature are periodically monitored as appropriate. All rooms are on individual time-controlled lighting systems set for 12 hours dark (6PM-6AM CST) and 12 hours light (6AM-6PM CST) unless deviations are required by the research protocol.

To assure USDA and Guide standards are met, animals should be housed only in facilities approved by ARC. Housing animals in laboratories for periods longer than 12 hours must be approved by the IACUC.

5. Vermin Control - ARC personnel perform all vermin control tasks in animal

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DAILY ANIMAL CARE

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facilities. Animal rooms are treated with a boric acid based powder on a regular basis. Pyrethrins, carbamates and organophosphates are used occasionally, but only after approval by investigators to ensure that ongoing studies will not be adversely affected. Live Traps are used to control escaped rodents.

6. Disposition of Carcasses or Animal Wastes - After ensuring that the animal is dead, the carcass should be placed in an opaque plastic bag at least 2.5-3 mill thick and placed in the dumpsters in the G9.300, J1.502, Y2.402, or NB3.400 freezers. Radioactive carcasses and animal wastes should be bagged in the same manner and placed in the Radiation Safety refrigerators. Infectious carcasses or animal wastes should be incinerated after autoclaving. Call the ARC or Environmental Health and Safety to discuss arrangements.

7. Other Support Services - ARC personnel are trained to provide a variety of specialized animal care support functions including establishment and maintenance of animal breeding colonies. Call the ARC office for information or assistance.

8. Per Diem Charges - The ARC must recover all costs for the care of animals housed within its facilities through per diem rates charged to investigators for the care of their research animals . These rates are established through a cost analysis performed according to guidelines established by the NIH. Rates are implemented only after review and approval by the budget office, IACUC and the UT Southwestern Medical Center administration. Faculty members applying for grants may contact the ARC Director to obtain information concerning any anticipated increases.

F. Animal Health

1. Routine Health Care - Animal health reports and information on animals that died during the previous 24 hour period are reviewed by a clinical veterinarian at 9AM daily. The clinical veterinarian may request necropsies on animals that died overnight. The veterinarians with the assistance of the animal health technologists (AHT) perform preliminary physical examinations as needed. Animals are treated only after approval of the investigator except in emergency situations. Animals may be treated during rounds or the veterinarian may

first request that various samples be collected and submitted to the ARC Diagnostic Laboratory.

2. Emergency Health Care - If the individual(s) who were designated by the principal investigator as an emergency contact can not be reached within a reasonable length of time, an ARC veterinarian will provide supportive care to his/her professional judgement. In the event the animal must be euthanatized, every effort will be made to save tissues needed for the research protocol. The investigator or his designee will be notified as soon as possible of any action taken.

3. Reporting Sick Animals - An animal observed to be ill or exhibiting abnormal behavior should be reported to the ARC as soon as possible so that it may be examined by a veterinarian. Inconsistent laboratory results of experimental animals may suggest an underlying disease problem in the research animals used. If all other possibilities for the inconsistencies have been eliminated, please consult with the ARC veterinary staff for assistance.

4. Quarantine Procedures - As determined by a clinical veterinarian, animals will be quarantined upon arrival at UT Southwestern Medical Center for a period dependent upon the species, source, and health status.

5. Zoonotic Disease - When people handle animals, the potential always exists for contracting zoonotic diseases such as rabies, toxoplasmosis, or LCM (lymphocytic choriomeningitis); however, this potential can be almost eliminated by purchasing only disease-free animals from reliable vendors and by practicing good hygiene.

G. Surgery and Radiology - A surgical suite for survival surgery is located in the ARC. The suite consists of a pre-op room, four sterile surgical rooms, two scrub areas, a recovery/intensive care room, and locker and shower rooms. The facility is maintained and operated to ensure its cleanliness. Appropriate emergency equipment including EKG is available. The facility is staffed by appropriately trained personnel. There is a fee for the use of specialized areas, equipment, supplies, or technical assistance.

A radiology facility is maintained for use by ARC veterinary staff for diagnostic purposes; however, it may be used for a limited number of research projects by special

arrangement with ARC.

H. Diagnostic Laboratory and Necropsy - The Diagnostic Laboratory has full anatomic and clinical pathology capabilities, including parasitology, microbiology, hematology, and clinical chemistry. Samples submitted by the clinical medicine staff are analyzed and a report returned promptly to assist in timely clinical decisions and responses.

Investigators needing to necropsy animals as part of a research protocol may reserve time and a table in the necropsy room.

I. Technical Assistance - All requests for surgery and/or technical assistance must be submitted to the ARC on UT Southwestern Medical Center "Request for Surgery and/or Technical Assistance" form. These forms are available in the ARC. NB2.346 and J9.502.

Requests for use of the surgery rooms, surgical/anesthetic equipment, or surgical/anesthetic assistance should be submitted as soon as possible and preferably no later than 5PM on the Thursday preceding the week in which the surgery is to be performed. Every effort will be made to accommodate all requests. Whenever possible, plan surgeries to finish by 4PM so that the rooms may be cleaned for the next day's use.

Requests for blood collection also should be submitted by 5PM on the Thursday preceding the week the sample is actually needed. Indicate on the form if the animal to be bled is pathogen free or has been injected with radioactive or biohazardous materials. In addition, specify the time(s) the blood is needed.

Requests for veterinary assistance on weekends or holidays must be submitted by noon on Friday or by noon of the day preceding the holiday to ensure ARC has the drugs requested for treatment and that the animal to be treated is correctly identified.

J. ARC Billing Procedure - The ARC must recover all of its operating costs from charges for services rendered. Charges for services, assistance, supplies, and/or animal care are itemized on a monthly bill submitted to each investigator. Most charges fall into one of three categories as follows: 1.) routine daily care of laboratory animals , 2.) services performed by ARC personnel, such as bleeding or euthanatizing animals at an investigator's request, that are not a part of

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normal animal care activities; and 3.) supplies sold to the investigator. Charges are based upon technician time; cost of supplies plus the overhead resulting from ordering, inventorying, and storage.

IV. Grant and Manuscript Preparation

A. Preparing NIH Grant Applications - The Public Health Service Policy requires that the use of all vertebrate animals in research be governed by the Principles for Use of Animals and also, in the case of warm-blooded vertebrates, the Guide for the Care and Use of Laboratory Animals. No PHS award involving the use of animals is made unless an Assurance (see Section I.A.2.) has been approved by the Office for Protection from Research Risks (OLAW).

Several sections of the application require information about the proposed animal use. Failure to supply the requested information may delay consideration or jeopardize funding. These sections are:

Face page - 5. Vertebrate Animals: Indicate the IACUC (IACUC) approval date. Enter "pending" if IACUC review is delayed beyond the submission date of the application. The UT Southwestern Medical Center Animal Welfare Assurance Number is A3472-01.

Page 4 - Supplies: State the number of animals to be used, their unit purchase cost (actual cost of animal + shipping + box charges), and their unit care cost.

Page 5 - Supplies: Include the full initial cost of the animals and an inflationary increase of 4-10% per year for each succeeding year. Although 4% inflation is the maximum allowed on most grants, higher rates may be accepted if it can be documented.

Resources and Environment - Animal: UT Southwestern Medical Center animal facilities encompass approximately 140,000 sq. ft. including specialized areas such as a sterile surgery suite, intensive care unit, radiology, necropsy, a diagnostic laboratory, a diet kitchen, and storage areas. Animal care is provided by a staff of veterinarians and technical personnel. The program is closely monitored by an institutional animal care and use committee (the Institutional

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Animal Care and Use Committee).

Research Plan - F. Vertebrate Animals: Provide a detailed description of the proposed use of the animals in the work outlined in the experimental design and methods section. Identify the species, strain, ages, sex, and numbers of animals to be used.

Justify the use of vertebrate animals, the choice of species, and numbers used. If the animals are in short supply, costly, or to be used in large numbers, provide a specific rationale for their selection and their numbers.

Describe the procedures for adequate maintenance and veterinary care of the animals involved. Reviewers will wish to know if the living conditions of animals will be appropriate for the species and contribute to their health and comfort and if medical care for animals will be available and provided as necessary by a qualified veterinarian. The following general statement may be used if the proposed work will necessitate no special care. "Housing and day-to day care for the animals are consistent with the standards of the Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act. All animals are observed daily and appropriate veterinary care provided by the veterinary medical staff of the Animal Resources Center. This staff consists of veterinarians with training and experience in laboratory animal medicine and science and technicians certified by AALAS."

Describe the procedures to avoid unnecessary discomfort, pain, or injury to the animals. Reviewers will specifically try to determine that procedures will avoid or minimize discomfort, distress and pain to the animals, consistent with sound research design; procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons by the investigator; personnel conducting procedures are qualified and trained in those procedures; and that animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly sacrificed at the end of the procedure or, if appropriate, during the procedure.

Describe methods of euthanasia to be used and reasons for selection. Justification based

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ANIMAL USE

on scientific reasons must be provided if methods of euthanasia used are not consistent with the recommendations of the American Veterinary Medical Association Panel on Euthanasia

B. UT Southwestern Medical Center Application for Use of Animal Subjects Form - Investigators are urged to submit the Application for Use of Animal Subjects forms 2 months prior to the grant deadline to ensure no delays in approval and subsequent notification of the granting agency. Lack of timely receipt by NIH of the verification of approval can delay consideration and jeopardize funding. It is the investigator's responsibility to submit a completed Application for Use of Animal Subjects Form to the Institutional Animal Care and Use Committee (IACUC), MC 9107, NB2.332 for each new proposal, competitive renewal, modification of ongoing grant, grant supplement, or noncompetitive continuation involving animals, regardless of funding source; any pilot project and modifications in approved animal use protocols; and any educational project in which vertebrate animals are used. Protocols using vertebrate animals must be approved prior to beginning the project.

Submit the original with 18 copies of the completed Use of Animal Subjects Form directly to the IACUC Office. The investigator will be notified in writing of the decision of the IACUC. Upon approval, one copy of the Use of Animal Subjects Form will be filed in the IACUC office. Appropriate notification will be provided to Office of Grants Management and the granting agency. The assigned Animal Project Number (APN) must be indicated on all orders for animals to be used on that protocol.

IACUC approval is valid for one year only. Requests for study continuations must be submitted by the investigator to the IACUC on an annual basis. Approximately two months prior to a projects approval expiration, the IACUC office will mail out annual renewal notifications. It is the investigator's responsibility, however, to assure all ongoing projects are submitted for annual review. All new and competitive renewals require the submission of full and complete Application for Use of Animal Subjects form.

C. Manuscript Preparation - Publications of work based on animal studies should provide a complete and accurate description of the animals used including common name; genus

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and species; strain, stock, or breed; source; age and/or weight; sex; method of identification; and microbiologic status. The animals' environment - kind of caging; stocking density; room temperature, humidity, ventilation, and lighting; diet and water; and husbandry routines - should be defined for duplication of experimental results. Other information that should be provided includes time of sampling; where and how the samples were obtained; all drugs and dosages used; and the euthanasia method employed.

V. Drugs and Other Medications

A. Obtaining Controlled Drugs for Use in Animal Studies - The Environmental Health and Safety (EHS) office is the registered agent on behalf of individual investigators at UT Southwestern Medical Center. Completed requisition forms should be submitted directly to EHS rather than to Purchasing. EHS will attach the required Drug Enforcement Administration (DEA) forms. The requested drugs will be delivered to EHS which will promptly notify the originating department or investigator for pickups.

B. Obtaining Noncontrolled Drugs and Other Medical Supplies for Use in Animal Studies - Small quantities of antibiotics or other noncontrolled drugs and medical or disposable surgical supplies may be purchased from the ARC Animal Health Technologists (J9.502). No IDR is needed.

C. Guidelines for Selecting Species Appropriate Anesthetic, Analgesic, and Tranquilizing Agents and Methods of Euthanasia - The Animal Welfare Act requires that institutional veterinarians provide research personnel with guidelines detailing the use, species, and appropriate doses of to the tranquilizers, anesthetics, analgesics, and euthanatizing agents recommended for use by the facility.

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