

# **VETERINARY CARE PROGRAM**

## **Institutional Animal Care and Use Committee**



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# VETERINARY CARE PROGRAM

Veterinary care is an essential part of an Animal Care and Use Program. The primary focus of the Veterinary Care Program is to provide the policies and procedures necessary for the well-being and clinical care of animals used in research, testing, teaching and production throughout St. Cloud State University.

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# VETERINARY CARE PROGRAM

## PREAMBLE

The Animal Care and Use Program is the policies, procedures, standards, organizational structure, staffing, facilities and practices put into place by St. Cloud State University (the University) to achieve the humane care and use of animals in the laboratory and throughout the University. Veterinary care is an essential part of the Animal Care and Use Program. The primary focus of the attending veterinarian is to oversee the well-being and clinical care of animals used in research, testing, teaching and production. This responsibility is in collaboration with the animal facility manager(s) in monitoring and promoting animal well-being at all times during animal use and during all phases of the animal's life. Well-being is determined by considering physical, physiologic and behavioral indicators, which vary by species. The number, species and use of animals housed by the University influences the complexity of the Veterinary Care Program.

## 1. CLINICAL CARE AND MANAGEMENT

Healthy, well-cared-for animals are a prerequisite for good-quality animal-based science and the structure of the Veterinary Care Program fulfills the program's requirements. The attending veterinarian works in collaboration with the animal facility manager(s) and through communication, as needed, related to issues associated with animal health, behavior and well-being. Through initial review of animal use and care protocols submitted, the attending veterinarian provides guidance to principal investigators to ensure appropriate husbandry, handling, medical treatment, immobilization, sedation, analgesia, anesthesia, euthanasia, surgery programs and perioperative care involving animals. The attending veterinarian is available for consult for surgeries and perioperative care of animals and may attend surgeries with prior notification.

The attending veterinarian has familiarity with species housed and used in teaching and research activities at the University. The attending veterinarian has access to records through the animal facility manager(s), principal investigator, inspections or upon request. Follow up is facilitated through communication by the animal facility manager(s), IACUC members or the institutional official.

Review of animal care and use protocols involving blood draws from a mouse, rat, hamster, gerbil, guinea pig or chinchilla should refer to the Blood Draws Recommendations document for guidance in the review process.

### ANIMAL ABNORMALITIES OR HEALTH CONCERNS

Timely and accurate communication of any abnormalities in or concerns about animal health, behavior and well-being should be reported first to the animal facility manager who then works in collaboration with the IACUC, institutional official or the attending veterinarian. The responsibility for communicating these concerns rests with all those involved with animal care and use.

The animal facility manager or the attending veterinarian should perform an objective assessment of the animal(s) to determine the appropriate course of action related to assessment, treatment or euthanasia.

Initial triage will be assessed using appropriate pain scales (see Species – Typical Signs of Pain and Distress in Laboratory Animals) and lay person examination. If any animal shows an unanticipated pain score which exceeds mild to moderate pain/distress, difficulty breathing, distress, excessive bleeding, seizures or stupor/comatose, the animal(s) must be quarantined and the animal facility manager and/or the attending veterinarian contacted immediately.

If a catheter or stent has been removed by the animal and the animal appears stable, the attending veterinarian and the principal investigator should be contacted immediately.

Animals exhibiting non-life threatening symptoms including weakness, lameness, coughing, sneezing, minor bleeding, anorexia or cannibalism should be separated from other cage mates, examined by the animal facility manager who will make a determination as to whether the attending veterinarian needs to do an exam. If the symptoms persist longer than a reasonable timeframe for the specific species, the attending veterinarian should be notified.

Unexpected animal illness, injury or behavior should be documented in a log book and reviewed by the attending veterinarian at least semi-annually or sooner if concerns are reported. The IACUC and institutional official will be notified appropriately of problems. Notification to external agencies will be done as required by federal regulation.

Signs will be posted in each facility where animals are currently housed instructing animal users to report animal illness or injury to the animal facility manager immediately. For animals on research protocols, the animal facility manager, IACUC members, institutional official or the attending veterinarian should make every effort to discuss any problems with the principal investigator to jointly determine the most appropriate course of treatment or action. The attending veterinarian and animal facility manager are authorized to treat, relieve pain and/or euthanize animals as needed for the humane treatment of animals.

## **2. ANIMAL PROCUREMENT AND TRANSPORTATION/PREVENTIVE MEDICINE**

All animals will be acquired lawfully and the University will ensure all procedures involving animal procurement are conducted in a lawful manner. Through the animal care and use protocol review process, the IACUC will review the source of animals provided and if there are sufficient facilities and expertise to house and manage the species being acquired. The protocol must be approved before animals can be ordered.

The ISELF vivarium currently maintains multiple strains of mice and outbred rats. In most cases, animals are produced for an approved animal use protocol by breeding individuals within existing colonies. Breeding colonies are established based on need and managed according to principles of animal reduction such as cryopreservation for rodent stocks or strains. Animals to be housed in the University's vivarium may be ordered by contacting the vivarium manager. Animals may only be ordered from vendors who can provide animal health status reports, which must include results of routine health surveillance of animal colonies and tests of the environments in which animal models are housed prior to shipment. For most strains of mice and outbred rats, The Jackson Laboratory (Bar Harbor, Maine) or Charles River Laboratories are preferred vendors who can provide such reports and with whom the University has an established business relationship. If other animal facility managers are involved, the procurement of animals process will be reviewed as part of the protocol review.

### **NIH FUNDING FOR USE OF DOGS**

For awards issued on or after October 1, 2014, institutions are prohibited from using National Institutes of Health (NIH) funds to procure or support the use of dogs from Class B dealers. Dogs used in NIH-supported research may only be from U.S. Department of Agriculture Class A dealers or other approved legal sources. Class A dealers or licensees are those individuals who deal only in animals that they breed and raise.

### **NON-NIH FUNDING FOR USE OF DOGS**

If dogs or cats are obtained from random sources, such as shelters or pounds, for non-NIH funded research, the animals should be inspected for tattoos or identification devices such as subdermal transceivers or subcutaneous communicators; such identification might indicate that an animal was a pet and, if so, ownership should be verified. Access to a microchip scanner is available through the attending veterinarian.

### **CERTAIN NON-COMMERCIAL SOURCED ANIMALS**

For non-commercial sourced animal other than fish or amphibians, the attending veterinarian must review the housing protocol prior to arrival of the animal(s) and health of the animal(s) upon arrival. If any animals are found to have health concerns, the principal investigator and the attending veterinarian will be notified and the animal(s) isolated and entered into the log book. Attention should be given to the population status of the species under consideration, the threatened or endangered status of species as updated annually by the Fish and Wildlife Service.

Appropriate records and other forms of documentation will be maintained for a reasonable timeframe when vertebrate animals are acquired by the University for use in basic science and biomedical research or teaching activities.

### **ANIMAL TRANSFERS**

The transfer of animals from other institutions (non-vendors) to the University will require IACUC approval. Should animals need to be transported, the University will ensure compliance with relevant statutes and other animal transportation requirements which must be met for animals to cross international boundaries. Careful planning for all types of transportation should occur to ensure animal safety and well-being in the transportation, loading and unloading facilities, and environment at the receiving site. Movement of animals should be planned and coordinated with the principal investigator or the animal facility manager to minimize animal transit times or delays in receipt.

Movement of animals between or out of the University's facilities, in situations not covered by the disaster plan, must be coordinated by the animal facility manager and the principal investigator. If not previously addressed in the protocol, IACUC approval is needed prior to movement. Planning must address time, limiting access to people other than the principal investigator, students involved in the protocol, animal care workers and IACUC members, limiting access/contact with other animals, weather conditions if the transport requires animals to be outside, comfort of the animals, documentation of which animals are involved, contact information for those involved (principal investigator, animal facility manager, attending veterinarian), animal health and reproductive status, possibility of zoonotic disease.

All animal orders for the ISELF vivarium should identify the ISELF loading/delivery zone as the space in which animals are to be received and include the name and contact information of the vivarium manager who will oversee receipt of the animals. Upon receipt in the vivarium, all animals will be

housed in the quarantine room, ISELF 311, for no less than two weeks. During this period, animals will be checked daily and monitored for evidence of illness or disease. If no evidence of illness or disease is detected, animals will be incorporated into existing animal housing systems and housed per established procedures as approved in the animal use or holding protocol.

For research conducted under the supervision of Dr. Heiko Schoenfuss, fish deliveries only happen on days the Biology Office is open (typically 7:30AM to 4:30PM). The biology office is given delivery notice a day in advance and the principal investigator or responsible student will pick the fish up from the office shortly after arrival. Fish deliveries typically ship FedEx Priority overnight so that fish arrive during a narrow window between 8:30 and 10AM. Once the fish arrive, the principal investigator/student will bring the fish into the fish room (WSB-9 or WSB-32), open the package and check temperature (fish are usually shipped at much lower temperatures than holding temps to reduce stress). The student/principal investigator then records the temperature, adds air stones to the package and slowly adds temperate lab water to the fish container (to reduce the chance for osmotic shock). Once the fish are at the regular 21C holding temp and once 50% water has been added to the package (usually within 3hrs of arrival or a bit longer in the winter), the fish are transferred into their aquaria and some "Stress Coat" is added to the water to help the fish rebuild their protective slime coat. Fish will not be shipped when air temps are forecasted to be >90F or <20F. This procedure has worked extremely well over the past decade with <1% mortality across shipments. In most instances, all fish arrive alive and well with no mortality in the first 72hrs.

#### **PREVENTIVE MEDICINE**

All animals are observed daily or more frequently per individual protocols for signs of illness, injury or abnormal behavior. Any concerns are recorded in the log book and appropriate people notified and appropriate steps taken to resolve the problem. Access to diagnostic lab testing is available through the attending veterinarian.

Oversight of animal care is to be provided by the attending veterinarian or his/her designee. If the principal investigator or animal facility manager cannot be reached related to emergency care of animals, the attending veterinarian or his/her designee has the authority to treat, remove, relieve pain or distress or euthanize.

Clean and soiled cages shall not be stored together to reduce transfer of disease. All bedding and food will be purchased from reputable vendors. Pest control in animal and food storage areas will be monitored and addressed in a timely manner.

Quarantine is employed for all newly acquired animals and any ill animals to decrease the risk of introductions of pathogens, to reduce the risk of spread of pathogens and to reduce the risk of zoonotic disease transmission. New animals are quarantined for a timeframe appropriate for the species or as defined in the approval animal use protocol plus any additional acclimation time needed based on species specific behavior or needs, intended use or travel. Ill or injured animals not euthanatized are quarantined for a timeframe appropriate for the species beyond clinically normal status as determined by attending veterinary exam.

The animal facility manager will review all paperwork from newly acquired animals.

If illness or injury occurs in an animal or group of animals related to a specific protocol, the protocol and procedures will be reviewed by some IACUC members. Recurrent health problems will be reported to the IACUC for review or others as deemed appropriate.

Physical separation of different species is maintained to decrease disease transmission, decrease stress and decrease behavioral changes by use of different rooms in the animal facility. Fish can be separated by utilizing different tanks and visual barriers within the same room. This same procedures may be followed for amphibians.

To prevent the introduction, establishment or spread of disease in animal colonies, standard practice is to remove sick, injured or diseased animals from the colonies through humane methods of euthanasia (e.g, carbon dioxide asphyxiation of rodents, immersion of aquatic vertebrates in a 3-gram/L solution of MS-222). The protocol for this method, as employed in the vivarium, is described in detail in the addendum entitled Euthanasia Guidelines and it is posted clearly next to the CO<sub>2</sub> chamber in the ISELF surgical suite. Further reference is provided in the addendum entitled NIH Guidelines for the Euthanasia of Rodent Fetuses and Neonates.

### **3. SURGERY**

Successful surgical outcomes require appropriate attention to pre-surgical planning, personnel training or expertise, anesthesia, aseptic and surgical technique, assessment of animal well-being, appropriate use of analgesics and animal physiologic status during all phases of a protocol involving surgery and postoperative care. The individual impact of these factors varies according to the complexity of procedures involved and the species of animal used. Proposed surgical procedures are to be assessed during the IACUC review of the animal use protocol to ensure the appropriate procedures are to be followed and timely corrective changes are instituted. In the case of emergency complications, pain, distress or illness immediately post-operative, surgical outcomes will be reviewed without delay. Modification of standard techniques may be needed in aquatic or field surgery but should not compromise the well-being of the animals.

Researchers conducting surgical procedures must have the appropriate training and expertise to ensure good surgical technique is practiced. Principal investigators are responsible to ensure all co-investigators, other investigators or students involved with the research have completed the appropriate level of training prior to their involvement with the animals. Training is provided as a standard through the Collaborative Institutional Training Initiative (CITI) or customized through instruction by the principal investigator.

Pre-surgical planning is done in conjunction with the attending veterinarian and typically discussed prior to IACUC protocol review. This planning will include discussion of location, surgeon, anesthetist, technique(s), equipment and supplies, perioperative assessment, anesthetic doses, analgesic doses, intraoperative monitoring, post-surgical monitoring, post-surgical care, recordkeeping and post-surgical cleaning of facilities. Aseptic surgery is conducted in dedicated facilities or spaces, unless the exception is sufficiently justified and approved by the IACUC. Per the animal care and use protocol, all surgeries are categorized as minor or major and survival or non-survival.

#### **4. PAIN, DISTRESS, ANESTHESIA AND ANALGESIA**

An integral component of veterinary medical care is prevention and alleviation of pain associated with procedural and surgical protocols. Pain is a complex experience which typically results from stimuli that damage or have the potential to damage tissue; such stimuli prompt withdrawal and evasive action. A description of species typical pain should be posted in the applicable animal holding facility. Pain is a stressor and, if not relieved, can lead to unacceptable levels of stress and distress in animals. Therefore, the proper use of anesthetics and analgesics in research and teaching animals is an ethical and scientific imperative. Distress may be defined as an aversive state in which an animal fails to cope or adjust to various stressors with which it is presented. Distress may not induce an immediate and observable pathologic or behavioral alteration which makes it difficult to monitor and evaluate the animal's state when it is present. Both the duration and intensity of the state are important considerations when trying to prioritize attention to and treatment of animal distress.

##### **CITI TRAINING ON ASSESSMENT AND CATEGORIZATION OF PAIN**

Utilizing the Collaborative Institutional Training Initiative (CITI) modules, principal investigators are required to complete training on the guidelines for assessment and categorization of pain, distress and animal well-being per the U.S. Department of Agriculture classifications. The classifications are also clearly defined in the animal care and use protocol in the Pain or Distress Classification and Considerations section. For more information, review the CITI module entitled USDA Pain/Distress Categories.

Additional CITI training is available with the Reducing Pain and Distress in Laboratory Mice and Rats – Lab Animal Research course related to systematically monitoring, detecting clinical signs and alleviation of pain and distress in mice and rats. See attached for overview of this CITI course.

##### **APPROPRIATE ANALGESICS AND ANESTHETICS**

During the animal care and use protocol review process, the attending veterinarian ensures the selection of appropriate analgesics and anesthetics reflects professional veterinary judgment as to which best meets clinical and humane requirements and the needs of the teaching or research protocol. Loss of animal consciousness occurs at a light plane of anesthesia, before antinociception (lack of response to noxious stimuli) and is sufficient for purposes of restraint or minor, less invasive procedures, but painful stimuli can induce a return to consciousness. Antinociception occurs at a surgical plane of anesthesia and will be ascertained before surgery, as outlined in the protocol.

##### **NON-PHARMACEUTICAL GRADE COMPOUNDS**

The use of pharmaceutical-grade chemicals and other substances ensures that toxic or unwanted side effects are not introduced into studies conducted with experimental animals. Therefore, pharmaceutical-grade compounds should be used when available for all animal-related procedures. The use of non-pharmaceutical-grade chemicals or substances must be described and justified in the animal care and use protocol and are subject to approval by the IACUC. Further information can be found in the attached Policy for Use of Non-Pharmaceutical Grade Compounds in Research Involving Live Vertebrate Animals.

Tribromoethanol (TBE) is an injectable anesthetic agent used in rodents. Since this product is no longer commercially available, principal investigators who wish to use TBE as an anesthetic must make their



own solutions from a non-pharmaceutical grade chemical. See the attached Guidelines for Use of Tribromoethanol (TBE) in Rodents.

## **5. EUTHANASIA**

Euthanasia is the act of humanely killing animals by methods that induce rapid unconsciousness and death without pain or distress. Unless a deviation is justified for scientific or medical reasons and approved by the IACUC, methods of euthanasia will be consistent with the *AVMA Guidelines for the Euthanasia of Animals*. Review criteria may include the ability to induce loss of consciousness and death with no or only momentary pain, distress or anxiety; reliability; irreversibility; time required to induce unconsciousness; appropriateness for the species and age of the animal; compatibility with research objectives; and the safety of and emotion effect on personnel. Death to be confirmed through monitoring for absence of movement, lack of corneal reflex and lack of response to toe pinch.

Standard training on euthanasia and endpoint criteria through the Collaborative Institutional Training Initiative (CITI) modules is required for principal investigators before their animal care and use protocol will be approved. Training modules are provided on appropriate methods for each species and considers psychological stress to personnel.

The protocol for euthanasia as employed in the ISELF vivarium is described in detail in the addendum entitled Euthanasia Guidelines and it is posted clearly next to the CO<sub>2</sub> chamber in the ISELF surgical suite. Further reference is provided in the addendum entitled NIH Guidelines for the Euthanasia of Rodent Fetuses and Neonates. In addition, the vivarium manager may review these procedures with anyone who performs euthanasia on the rodents or *Xenopus* to ensure understanding of how to perform the techniques described. Euthanasia of other animal species will be reviewed by the IACUC as part of the protocol review process.

## **6. DRUG STORAGE AND CONTROL**

Medical records are a key element of the Veterinary Care Program and are considered critical for documenting animal well-being and tracking animal care and use at the University. All those involved in animal care and use must comply with federal laws and regulations regarding human and veterinary drugs and treatments. Agents that provide anesthesia and analgesia must be used before their expiration dates and will be acquired, stored, their use recorded and disposed of legally and safely. Drug records relative to the storage, dispensing and end use of controlled substances are reviewed during semiannual facility inspections and must be stored securely with the related controlled substances.

Individuals conducting research and/or teaching activities involving the use of controlled substances must be either the registrant on a current Drug Enforcement Agency (DEA) controlled substance registration (DEA registration) or an authorized user listed on the Authorized Users Signature Log of a current DEA registration (see list of forms below). To obtain a DEA registration for use of controlled substances at the University, an individual must be an employee of the University and have sufficient

authority, as delegated by the head of his/her department, college or other administrative unit, to assume full responsibility for ordering, storing, using, recording and disposing of controlled substances. To be an authorized user on a DEA registration, an individual must be an employee of the University and either apply for such status as part of the application procedures of a prospective registrant or obtain permission from a current registrant to be added as an authorized user to his/her DEA registration. Application procedures are described at <http://www.deadiversion.usdoj.gov/drugreg/index.html>.

The application process usually takes between two and six months to complete and, in some cases, will require that an applicant obtain a controlled substance registration from the Minnesota Board of Pharmacy (MNBP) before obtaining a DEA registration. Applicants are strongly encouraged to contact both the DEA and MNBP before applying for either registration.

All applicants must become familiar with the five controlled substance schedules currently in use by the DEA for the purpose of identifying all applicable ordering and recordkeeping requirements for the controlled substances they intend to use in research or teaching. Information regarding DEA schedules is available at <http://www.deadiversion.usdoj.gov/schedules>. Additionally, all applicants must become familiar with the various forms required for purchasing, keeping inventory, recording disposition and disposing of controlled substances. These forms are described below and accessible on the University's IACUC webpage.

#### **DEA FORM 222**

A registrant is required to obtain this form directly from the DEA and use it to purchase any substances in DEA schedules I and II. Information and frequently asked questions regarding this form can be found at <http://www.deadiversion.usdoj.gov/faq/dea222.htm>.

#### **AUTHORIZED USERS SIGNATURE LOG**

Only a DEA registrant or authorized users indicated on a DEA registration may access, dispense or administer controlled substances. All authorized users must be listed on and sign an Authorized Users Signature Log in order to use controlled substances.

#### **CONTROLLED SUBSTANCE INVENTORY RECORD**

An inventory of all controlled substances obtained, used and stored under a single DEA registration must be performed by the registrant in March and September of each year and recorded on this form. Additionally, all newly obtained controlled substances must be recorded on this form immediately upon receipt.

#### **RESEARCH CONTROLLED SUBSTANCE DISPOSITION RECORD**

The disposition of every quantity of a controlled substance withdrawn from a container must be recorded on this log. For Schedule II controlled substances, each quantity must be recorded on a separate row. For Schedule III, IV or V controlled substances, the cumulative amount of the substance withdrawn from a container during a single day or for a single use activity (e.g., surgical procedure involving multiple animals) may be recorded on a single row.

### **CONTROLLED SUBSTANCE SINGLE DRUG DISPOSITION RECORD**

A record of each dose of a controlled substance administered to an animal subject(s) must be entered onto this form. The form is intended to track the use of a single container or set of containers within the same original package (e.g., 10 10-mL vials of ketamine HCl packaged within a single box) and also serves as part of the veterinary records kept for animals used in research or teaching.

### **CONTROLLED SUBSTANCES DISPOSAL FORM**

Each quantity of a controlled substance placed into a slurry bottle (waste container), as well as any expired or excess controlled substances that are in their original container, must be recorded on this form. When the substances listed on this form are ready for disposal, this form must be submitted to Jeff Stobb in the Department of Chemistry, who will coordinate pick-up by an agent of the University of Minnesota's Department of Environmental Health and Safety (DEHS) for hazardous waste disposal. A record of the transfer of the controlled substances to DEHS custody will be provided to the DEA registrant named on this form once this transfer has been completed. DEA registrants must review their inventory of controlled substances for waste containers and any expired or excess drugs on a regular basis. These items must be identified and purged from a controlled substance inventory at least once annually.

DEA controlled substances may be purchased *only* by a registrant on a current DEA registration. Registrants are encouraged to check with the Student Health Services Pharmacy in Hill Hall prior to purchasing controlled substances, as selected anesthetics and analgesics used commonly in laboratory animal use activities may be obtained there, often at highly competitive prices. Immediately upon receipt of a controlled substance, the registrant must record the quantity and initial volumes or masses of all containers on a Controlled Substance Inventory Record. All controlled substances must be stored in either a wall safe or a floor safe bolted to the floor, along with all documentation associated with their storage and disposition. The combination or other means of accessing a safe in which controlled substances are stored must not be provided to anyone not indicated on a DEA registration.

DEA controlled substances may be accessed, dispensed, administered or prepared for disposal only by individuals named on a DEA registration or an employee of the University whose official duties include handling and disposal of chemical hazardous wastes.