KING FAISAL SPECIALIST HOSPITAL AND RESEARCH CENTRE
(General Organization)

NON-CLINICAL INTERNAL POLICY AND/OR PROCEDURE (NCIPP)

TITLE: Formation and Functions of the Animal Care and Use Committee (ACUC)			**DOCUMENT NUMBER:** NCIPP-8763 **VERSION:** 1
EFFECTIVE DATE: 21/02/2019	**REPLACES NUMBER/DATE:** Not Set	**APPLIES TO:** COMPARATIVE MEDICINE (Dpt)-R	**APPROVED BY:** ABDALLAH ASSIRI

Important Note: Printed Copies are for reference only. Please refer to Policy Management System for valid policies.

1. PURPOSE

To outline the policy and procedure of formation and functions of the Animal Care and Use Committee (ACUC) at the King Faisal Specialist Hospital and Research Centre.

2. SUMMARY

The Animal Care and Use Committee (ACUC) is established to oversee and evaluate the Animal Care and Use Program (ACUP) at KFSH&RC. Proper care, use, and humane treatment of animals used in research, testing, and teaching require scientific and professional judgment based on the knowledge of the needs of the animals and the special requirements of the research, educational programs and/or testing. Responsibility for directing the program is generally entrusted either to a veterinarian with training or experience in laboratory animal science and medicine or to another qualified professional.

3. DEFINITIONS

For the purpose of this NCIPP, the following definitions shall apply:

3.1 **"Organization"**, **"Hospital"**, or the acronym **"KFSH&RC":** Refers to, or when used interchangeably, shall mean the King Faisal Specialist Hospital and Research Centre (General Organization) and its branches.

3.2 **Animal Care and Use Program (ACUP):** An organization-wide program implemented by KFSH&RC aligned with its mission and in accordance with national laws and international standards for the care and use of animals in research, teaching and/or testing.

3.3 **Comparative Medicine Department (CMD):** A department of the Research Centre (RC) responsible for supporting ongoing research and training activities at the KFSH&RC by providing quality animal models and veterinary medical care. CMD offers an array of advanced technical and research expertise in animal modeling to elucidate animal and human diseases mechanism.

3.4 **Laboratory Animal Services (LAS):** A section under the CMD responsible for acquiring, receiving and animal acclimation and provision of daily animal care.

3.5 **Office of Research Affairs (ORA):** A section of RC responsible for managing the operational activities related to the conduct of all research at KFSH&RC and providing administrative support to RAC and its sub-committees.

3.6 **Research Advisory Council (RAC):** The standing committee of KFSH&RC accountable for reviewing and recommending plans for research as well as the continuous monitoring and review of the execution of the Council's recommendations. It reports directly to the Chief Executive Officer (CEO) and functions as an independent advisory, monitoring and oversight body.

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3.7 **Animal Care and Use Committee (ACUC):** A sub-committee of the RAC responsible for overseeing the ACUP and evaluating all research proposals involving the use of animals that are undertaken by members of, or within, KFSH&RC. The committee ensures that the acceptable national and international stands for issues related to animal care, use and rights are upheld.

3.8 **Research Centre Safety Committee (RCSC):** A standing committee of RC responsible for overseeing safety regulations pertaining to biological and chemical hazards, equipment, space, storage and waste disposal within the RC, including but not limited to, promulgation of biological, chemical, and radiological safety standards that satisfies local, national and international laws and regulations to improve work environment and safeguard RC laboratories, offices, tunnels, corridors and facilities.

3.9 **National Committee of BioEthics (NCBE):** The National committee created by Royal Decree No. (7/B/9512) dated 18/5/1422H that operate under the supervision and authority of King Abdulaziz City for Science and Technology (KACST) to implement regulations of the Law of Ethics of Research on Living Creatures.

3.10 **American Association for Laboratory Animal Science** (**AALAS**): A membership association for professionals around the world, who are dedicated to the humane care and treatment of laboratory animals, as well as the quality research that leads to scientific gains that benefit people and animals. AALAS also provides educational materials to laboratory animal care professionals and researchers, administers certification programs for laboratory animal technicians and managers, publishes scholarly journals, supports laboratory animal science research, and serves as the premier forum for the exchange of information and expertise in the care and use of laboratory animals.

3.11 **Institutional Official (IO):** An individual with overall administrative authority, responsible for allocating required resources, including staffing, space and finance to safeguard the ACUP's functionality in compliance with national laws and international standards pertinent to quality animal care and use.

3.12 **Attending Veterinarian (AV):** A qualified veterinarian who has clinical experience with used animal species at KFSH&RC and responsible for providing medical and surgical care of animals used in research, teaching and/or testing.

3.13 **The *Guide*:** An internationally accepted primary reference on animal care and use, entitled: "Guide for the Care and Use of Laboratory Animals" (8^{th} edition), which assist institutions and researchers/investigators in conducting research, teaching and/or testing using animas in accord with the highest scientific, humane and ethical principles.

3.14 **Physical Restraint**: The use of manual or mechanical means to limit some or all of the normal movements of the animal(s) for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation.

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3.15 **Humane Endpoint:** The point at which pain or distress in an experimental animal is prevented, terminated, or relieved by either euthanasia, cessation of painful procedure and/or administration of pain relieve medications.

3.16 **Principal Investigator (PI)**: Qualified group leader with enough experience to plan and supervise animal usage activities in research, teaching and/or testing. He/she is responsible for ensuring compliance with the policy and procedures of the ACUC.

3.17 **Zoonosis:** Diseases of animals that can transmit to humans.

3.18 **Occupational Health:** Identifying and controlling hazards, risks and health problems that incur during work or practice.

3.19 **Quality Information System (QIS)-Safety Reporting System (SRS) Form:** A web-based application of the Hospital to report safety incidents incurred during work.

3.20 **Association for Assessment and Accreditation of Laboratory Animal Care-international (AAALAC-International):** A non-profit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs.

3.21 **Adjuvant:** A compound /agent that enhance the immune response to an antigen.

4. COMMENTS

4.1 This NCIPP is developed in compliance with the local regulations of the Saudi National Committee of Bio-Ethics and the standards stipulated in the *Guide*.

5. POLICY

5.1 The appointment of the ACUC, also referred to as "the Committee", shall be in accordance with the APP-58: Management of Hospital Committees to oversee and evaluate the ACUP of the Organization, the policies and procedures, and facilities to ensure that they are consistent with NCIPP.

5.2 The KFSH&RC shall be responsible for providing suitable orientation, background materials, access to appropriate resources, and, if necessary, specific training to assist the ACUC members in understanding and evaluating issues brought before the Committee.

5.3 All research activities conducted at the KFSH&RC, including oversight of the ACUP, funded or non-funded, irrespective of the risks, shall be under the purview of the RAC and its sub-Committees.

5.4 The RAC policies and guidelines shall be applied to all employees and non-employees of the KFSH&RC who conduct onsite or off site (nationally or internationally) research, teaching and/or testing using laboratory animals.

5.5 At least one (1) veterinarian qualified through experience or training in laboratory animal science and medicine or in the species being used must be associated with the program, who shall be appointed as the AV.

5.6 The ACUC shall report to the Chairman of the RAC.

5.7 The ORA shall serve as the liaison of the RAC, ACUC and the researchers/investigators, provide administrative support, and facilitate the application and approval process of research, teaching and/or testing using animals.

5.8 Further, the ORA shall be responsible for monitoring compliance and updating policies and procedures with current regulations pertaining to the ACUC.

5.9 Animal welfare issues or concerns shall be reported to the ACUC through the QIS-SRS Form.

5.10 This NCIPP applies to all the ACUC members, ORA, employees and non-employees of KFSH&RC and users of laboratory animals used in research, teaching and/or testing.

6. PROCEDURE

6.1 COMPOSITION AND FUNCTIONS OF ANIMAL CARE AND USE COMMITTEE (ACUC)

6.1.1 Committee Membership:

6.1.1.1 The membership shall include the following:

6.1.1.1.1 A doctor of veterinary medicine, who is certified or has training or experience in laboratory animal science and medicine or in the use of the species in question.

6.1.1.1.2 At least three (3) practicing scientists experienced in research involving animals.

6.1.1.1.3 At least one (1) member from the Hospital's Physicians with experience in use of animals in research.

6.1.1.1.4 An unaffiliated member from the community.

6.1.1.1.4.1 The unaffiliated community member may function in two roles (i.e. community member and non-scientist member, but this is not considered a requirement).

6.1.1.1.5 At least one (1) member from a non-scientific background drawn from either inside or outside the institution.

6.1.1.1.6 Additional ad hoc members can be added according to anticipated increase in research volume, nature and extent.

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6.1.2 Term of Appointment:

6.1.2.1 The term of appointment to the Committee shall be two (2) years.

6.1.3 Responsibilities:

6.1.3.1 The Committee shall be responsible for oversight and evaluation of the ACUP and its components as described in this NCIPP.

6.1.4 Functions:

6.1.4.1 Inspection of animal facilities.

6.1.4.2 Evaluation of ACUP and animal-activity areas.

6.1.4.3 Submission of reports to the responsible IO.

6.1.4.4 Review of proposed uses of animals in research, teaching and/or testing (i.e. animal usage protocols).

6.1.4.5 Establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the Institution.

6.1.4.6 Meet as a Committee as often as necessary to fulfill its responsibilities, but meet at least once every four months.

6.1.4.7 Records of Committee meetings and of results of deliberations shall be maintained as per Hospital policy.

6.1.4.8 Review the ACUP and inspect the animal facilities and activity areas at least once every year. After review and inspection, a written report, signed by a majority of the ACUC members, shall be made available to the RAC and to the responsible IO on the status of the ACUP and other activities as stated herein and as required by the Government regulations and Organizational policies.

6.2 ANIMAL CARE AND USE PROTOCOL

6.2.1 The following topics shall be considered in the preparation and review of animal care and use protocols:

6.2.1.1 Rationale and purpose of the proposed use of animals.

6.2.1.2 Description of the procedures that will be conducted on animals.

6.2.1.3 Justification of the species and number of animals requested. Whenever possible, the number of animals requested shall be justified statistically.

6.2.1.4 Availability or appropriateness of the use of less-invasive procedures, other lower species, isolated organ preparation, cell or tissue culture, or computer simulation.

6.2.1.5 Adequacy of training and experience of personnel on the procedures used.

6.2.1.6 Unusual housing and husbandry requirements.

6.2.1.7 Requirements for exemption from social housing and/or environmental enrichment.

6.2.1.8 Appropriate sedation, analgesia, and anesthesia.

6.2.1.9 Unnecessary duplication of experiments.

6.2.1.10 Descriptions of surgical procedures and justifications for conducting of multiple operative procedures on the same animal.

6.2.1.11 Impact of proposed procedures on animal wellbeing and criteria and processes for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated (i.e. determination of endpoints).

6.2.1.12 Post procedure care.

6.2.1.13 Method of euthanasia or disposition of animal.

6.2.1.14 Proposed use of hazardous agents (i.e. infectious, chemical, physical).

6.2.1.15 Safety of work environment for personnel.

6.3 SPECIAL CONSIDERATIONS FOR ACUC REVIEW

6.3.1 Occasionally, protocols include procedures that have not previously been encountered or that have the potential to cause pain or distress that cannot be reliably controlled. Additionally, the ACUC shall consider other unique laboratory animal care and use activities. Such procedures might include:

6.3.1.1 Physical restraint

6.3.1.2 Multiple survival surgeries

6.3.1.3 Food or fluid restriction

6.3.1.4 Experimental and humane endpoints

6.3.1.5 Unexpected outcomes

6.3.1.6 Use of non-pharmaceutical-grade chemicals and other substances

6.3.1.7 Use of adjuvants

6.3.1.8 Repeated blood collection

6.3.1.9 Antibody production

6.3.1.10 Pain and/or distress

6.3.1.11 Tumor burden

6.3.1.12 Intracardiac or orbital-sinus blood sampling

6.3.1.13 Exemptions from social housing and/or environmental enrichment

6.3.1.14 Cage or pen space

6.3.1.15 The use of abnormal environmental conditions

6.3.2 Relevant objective information regarding the procedures and the purpose of the study shall be sought from the literature, veterinarians, investigators, and others knowledgeable about the effects on animals. If little is known regarding specific procedures, limited pilot studies designed to assess the effects of the procedure on the animals, conducted under the ACUC oversight might be appropriate. General guidelines for evaluation of some of those methods are provided in this section, but they might not apply in all instances.

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6.4 PHYSICAL RESTRAINT

6.4.1 Animals can be physically restrained for brief periods, usually minutes, either manually or with restraint devices. Restraint devices shall be suitable in size, design, and operation to minimize discomfort or injury to the animal. Many dogs, non-human primates (e.g. Reinhardt 1991, 1995), and other animals can be trained, through use of positive reinforcement, to present limbs or remain immobile for the brief procedures.

6.4.2 Prolonged restraint, including chairing of non-human primates, shall be avoided unless it is essential for achieving research objectives and is approved by the ACUC. Less-restrictive systems that do not limit an animal's ability to make normal postural adjustments, such as the tether system for non-human primates and stanchions for farm animals shall be used when compatible with protocol objectives. When restraint devices are used, they shall be specifically designed to accomplish research goals that are impossible or impractical to accomplish by other means or to prevent injury to animals or personnel.

6.4.3 <u>The following are important guidelines for restraint</u>:

6.4.3.1 Restraint devices shall not be considered normal methods of housing.

6.4.3.2 Restraint devices shall not be used simply as a convenience in handling or managing animals. The period of restraint shall be the minimum required to accomplish the research objectives.

6.4.3.3 Animals to be placed in restraint devices shall be given training to adapt to the equipment and personnel.

6.4.3.4 Provision shall be made for observation of the animal at appropriate intervals, as determined by the ACUC.

6.4.3.5 Veterinary care shall be provided if lesions or illnesses associated with restraint are observed. The presence of lesions, illness, or severe behavioral change often necessitates temporary or permanent removal of the animal from restraint.

6.5 MULTIPLE SURGICAL PROCEDURES

6.5.1 Major surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiological function. Whether a surgical procedure is major or minor shall be determined on a case-by-case basis as determined by the AV and ACUC. Distinguishing minor from major surgical procedures does not necessary equate with the level of pain or distress that an animal may experience. Some procedures characterized as minor by using the previous definition may induce substantial post-procedural pain or impairment and should be justified as detailed below. Alternatively some procedures that may be considered major may result in minimal post-procedural pain or distress.

6.5.2 Multiple major survival surgical procedures or other procedures that may induce substantial post-procedural pain on a single animal shall be discouraged but may be permitted if scientifically justified by the user and approved by the ACUC. For example, such procedures can be justified if they are related components of a research project, if they will conserve scarce animal resources, or if they are needed for clinical reasons.

6.5.3 If multiple major survival surgeries or procedures that may cause substantial post-procedural pain are approved, the ACUC shall pay particular attention to animal well-being through continuing evaluation of outcomes.

6.5.4 Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures.

6.6 FOOD AND FLUID RESTRICTIONS

6.6.1 When experimental situations require food or fluid restriction, at least minimal quantities of food and fluid shall be available to provide for development of young animals and to maintain long-term well-being of all animals.

6.6.2 Restriction for research purposes shall be scientifically justified, and a program shall be established to monitor physiologic or behavioral indexes, including criteria (such as weight loss or state of hydration) for temporary or permanent removal of an animal from the experimental protocol.

6.6.3 Restriction is typically measured as a percentage of the ad libitum or normal daily intake or as percentage change in an animal's body weight.

6.6.4 Precautions that shall be used in cases of fluid restriction to avoid acute or chronic dehydration include:

6.6.4.1 Daily recording of fluid intake and recording of body weight at least once a week or more often, as might be needed for small animals, such as rodents.

6.6.4.2 Special attention shall be given to ensure that animals consume a suitably balanced diet because food consumption might decrease with fluid restriction.

6.6.4.3 The least restriction that will achieve the scientific objective shall be used.

6.6.4.4 In the case of conditioned-response research protocols, use of a highly preferred food or fluid as positive reinforcements, instead of restriction, is recommended.

6.7 EXPERIMENTAL AND HUMANE ENDPOINTS

6.7.1 As detailed in the *Guide,* the experimental endpoint of a study occurs when the scientific aims and objectives have been reached. The use of humane endpoints contributes to refinement by providing an alternative to experimental end- points that result in unrelieved or severe animal pain and distress,

including death. For many invasive experiments, the experimental and humane endpoints are closely linked and shall be carefully considered during ACUC protocol review. While all studies shall employ endpoints that are humane, certain studies commonly require special consideration (e.g. tumor models, infectious diseases, vaccine challenge, pain modeling, trauma, production of monoclonal antibodies, assessment of toxicological effects, organ or system failure, and models of cardio-vascular shock, inflammation, wound healing, brain injury, etc.).

6.7.2 The study protocol shall specify study endpoints that are both humane and scientifically sound. To the extent possible, death as an endpoint shall be avoided and if considered necessary shall be strongly justified and carefully reviewed by the Committee before being approved. Determination of humane endpoints shall involve the PI, the AV, and the ACUC, and shall be defined when possible before the start of the study. Items to consider include precise definition of the humane endpoint (including assessment criteria), the frequency of animal observation, training of personnel responsible for assessment and recognition of humane endpoint, and the response required upon reaching the humane endpoint. When novel studies are proposed or information for an alternative endpoint is lacking, the use of pilot studies is an effective method for identifying and defining humane endpoints and reaching consensus among the PI, ACUC, and the AV. Use of escalating species specific animal wellbeing/pain/and distress scoring systems may be helpful to promote more consistent interpretation of observations among different individuals.

6.8 UNEXPECTED OUTCOMES

6.8.1 By its very nature research involving novel experimental variables may result in unexpected outcomes that may adversely affect animal well-being. Genetically modified animals (GMAs) may be more likely than genetically and phenotypically well-defined animals to present with phenotypic abnormalities that impact animal welfare. As recommended in the *Guide*, the first offspring of a newly generated GMA line should be carefully observed from birth into early adulthood for signs of disease, pain, or distress. Investigators may find that the phenotype precludes breeding of particular genotypes or that unexpected infertility occurs, situations that could lead to increases in the numbers of animals used and revision of the animal use protocol. When the initial characterization of a GMA reveals a condition that negatively affects animal well-being, this shall be reported to the ACUC, and more extensive analysis may be required to better define the phenotype and procedures may need to be implemented to alleviate the impact of genetic manipulation on animal health and welfare.

6.9 USE OF NON-PHARMACEUTICAL GRADE CHEMICALS AND OTHER SUBSTANCES

6.9.1 Pharmaceutical-grade substances are those that have approved by an appropriate regulatory or oversight entity (e.g. United State Department of Agriculture (USDA), Food and Drug Administration (FDA), Saudi Food and Drug Authority (SFDA), etc.) for use in humans and/or animals. 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 or result in unexpected adverse reactions when used clinically. Therefore, pharmaceutical-grade substances shall be used, when available, for all animal-related procedures. The use of non-pharmaceutical-grade chemicals or substances shall be described and justified in the animal use protocol and be approved by the ACUC. It is acknowledged that use of non-pharmaceutical-grade substances may be necessary to meet the scientific goal when pharmaceutical grade substances are not available. It is also acknowledged that even pharmaceutical grade substances may need to be modified or diluted for treatment in smaller species. In such instances, consideration shall be given to use pharmaceutical grade agents as diluents and consider, as applicable, such factors as chemical grade, purity, sterility, pH, pyrogenicity, osmolality, stability, site and route of administration, formulation, compatibility, and pharmacokinetics of the chemical or substance to be administered, as well as animal welfare and scientific issues relating to their use.

6.10 USE OF ADJUVANTS

6.10.1 Use of adjuvants may be scientifically necessary; however, the criteria for selecting immunizing adjuvants and methods for their administration to animals shall be carefully reviewed. Use of adjuvants may cause discomfort for the animals and systemic side effects as well as affect the nature of the immune response. Use of Complete Freund's adjuvant (CFA) may result in particularly severe inflammatory reactions and subsequent pain at the site(s) of injections. Undesirable and painful side effects of large inflammatory lesions or tissue necrosis may be reduced or eliminated by adequately separating injection sites and using small amounts of inoculum per site. Further, CFA is usually only necessary for the initial immunization. Incomplete Freund's adjuvant is recommended for subsequent immunizations. Non-inflammatory adjuvants, or adjuvants known to produce less intensive inflammatory responses, should be considered when deemed capable of eliciting an adequate humoral response. Additionally, foot pad injections of immunizing agents should receive more intensive scrutiny and adequately justified, reviewed, and approved by the Committee because injections at this site may cause more pronounced pain and distress that cannot be reliably controlled. If foot pad injections are required, moderating factors shall be considered (e.g. controlling the quantity of adjuvant instilled in the foot pad, using only one foot per experimental animal, providing food and water sources on the cage floor to be more easily accessible to animals and housing animals on soft bedding).

6.11 ANTIBODY PRODUCTION

6.11.1 The production of monoclonal antibodies from rodent peritoneal exudate by the intraperitoneal administration of antigen and adjuvant is a widely recognized scientific procedure for obtaining high titered reagent or monoclonal antibodies. However, if not conducted properly this procedure may cause animals to experience pain and distress. Appropriate procedures shall be implemented to reduce pain or distress that may be associated with production of monoclonal antibodies from peritoneal exudate (e.g. limit taps to two or three with the third peritoneal tap being a terminal

procedure, observe animals closely for evidence of pain or distress or inability to ambulate normally or eat or drink, provide food and water on the cage floor where it is more accessible, consider in-vitro antibody production techniques, etc.

6.12 PAIN AND DISTRESS:

6.12.1 Projects or procedures that may cause animals to experience pain shall receive special scrutiny by the Committee. As detailed in the *Guide* and other reference resources unless the contrary is known or established, it shall be considered that procedures that cause pain in humans may also cause pain in other animals. Pain is a stressor that, if not relieved can lead to unacceptable levels of animal distress that adversely affects both animal welfare and research results. For veterinary and Committee review purposes and to focus deliberations on procedures that may cause more intense animal pain or distress, procedures and protocols shall be categorized regarding the expected pain and/or distress that may be generated as follows:

Pain-Distress Assessment Categories

Category	Category Description	Examples
Category A	Animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery, but not yet used for such purposes. No pain or distress.	1. Breeding colonies. 2. Holding protocol. 3. Euthanasia via approved method for animals not used in research.
Category B	Animals where teaching, research, experiments, or tests do not involve pain, distress, or use of pain-relieving drugs or cause only momentary or slight pain or distress. Anesthetics, sedatives or tranquilizers may be used to prevent movement during a procedure.	1. Mice used for mosquito feedings. 2. Holding or weighing animals in teaching or research activities. 3. Euthanasia for tissue collection. 4. Blood collection or nonsurgical catheter implantation via superficial vessels. 5. Immunizations that do not cause pain/distress. 6. Administration of oral medications. 7. Animal identification procedures related to research use. 8. Observation of animal behavior. 9. Feeding studies, which do not result in clinical health problems. 10. Administration of anesthetics and sedatives for restraint purposes to perform procedures that do not cause pain/distress (i.e. anesthesia for imaging, bio sample collection, etc.). 11. Minimally invasive manipulative procedures producing no or only momentary or slight pain (i.e. blood collection, oral gavage, palpations, skin scraping, radiography).

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Category C	Animals where experiments, teaching, research, surgery, or tests involve accompanying pain or distress to the animal and **appropriate anesthetic, analgesic, or tranquilizing drugs are used.** This may also include procedures that may cause pain or distress that can be **ameliorated through supportive care and provisions for timely euthanasia.** **NOTE: Scientific justification is required for procedures in this category. Use of (CFA) is considered category C for animals and a health hazard for humans. Accidental splashes or injections can cause severe inflammation. Eye protection is required and extreme caution should be employed to prevent accidental exposures. Post-immunization site monitoring in animals should be described.**	1. Survival or non-survival surgical procedures. 2. Any post procedural outcome resulting in evident pain, discomfort or distress such as that associated with decreased appetite/activity level, adverse reactions, to touch, open skin lesions, abscesses, lameness, conjunctivitis, corneal edema and photophobia 3. Terminal cardiac blood collection and/or exsanguination under anesthesia. 4. Induced infections or antibody production with appropriate anesthesia and post-op/post-procedure analgesia, other treatment or euthanasia when necessary to relieve pain or distress. 5. Systemic or local neoplasia induction with established endpoints prior to severe debilitation or death. 6. Procedures involving irradiation and bone marrow reconstitution. 7. Use of complete Freund's adjuvant. 8. Ascites production.
Category D	Animals where teaching, experiments, research, surgery, or tests involve accompanying pain or distress to the animals and the use of appropriate anesthetic, analgesic, tranquilizing drugs or other agents are withheld because use of such agents would adversely affect the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests (unrelieved pain or distress). **Justification to withhold agents that would relieve pain or distress must be provided**.	1. Toxicological or microbiological testing or infectious disease research that requires continuation until development of markedly debilitating clinical signs or death occurs (e.g. LD50 studies involving death as an endpoint). 2. Food or water deprivation beyond that necessary for ordinary pre-surgical preparation. 3. Prolonged restraint. 4. Procedures for which needed analgesics, tranquilizers, sedatives, or anesthetics would normally be administered, but must be withheld for justifiable study purposes. 5. Use of paralyzing or immobilizing drugs for restraint. 6. Paralysis or immobility in a conscious animal. 7. Procedures involving extensive irradiation. 8. Euthanasia by procedures not approved by the AVMA. 9. Endpoints such as nonresponsive to external stimuli and death as an endpoint.

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6.13 TUMOR BURDEN

6.13.1 Allowing injected tumor cells to create large subcutaneous on systemic tumors may cause animals to experience excessive pain or distress. Subcutaneous tumor masses shall not be allowed to exceed 20 mm (2 cm) in mice or 40 mm (4 cm) in rats as total individual or combined mass. Animals with ulcerated tumors shall be euthanized regardless of tumor size. Animals with internal tumors shall be monitored for body condition and overall ability to maintain its nutrition, hydration and self-grooming. Tumor burdens should not interfere with normal movement.

6.14 INTRACARDIAC OR ORBITAL-SINUS BLOOD SAMPLING

6.14.1 Intracardiac blood collection shall only be performed on adequately anesthetized animals and shall be a terminal non-recovery procedure. Collection of blood from the orbital sinus shall only be conducted on mice. Staff must be properly trained and competency verified before being allowed to collect blood from the orbital sinus without supervision. It is recommended that animals be anesthetized when collecting blood from the orbital sinus.

6.15 EXEMPTIONS FROM SOCIAL HOUSING AND/OR ENVIRONMENTAL ENRICHMENT

6.15.1 It is the AAALAC International position that social animal species must be socially housed unless otherwise justified based on social incompatibility resulting from inappropriate behavior, veterinary concerns regarding animal well-being, or scientific necessity approved by the ACUC (or comparable oversight body). (Please refer http://www.aaalac.org/accreditation/positionstatements.cfm#social for more information). When necessary, single housing of social animals shall be limited to the minimum period necessary and, where possible, visual, auditory, olfactory and, depending on the species, protected tactile contact with compatible conspecifics shall be provided. In the absence of other animals, additional enrichment shall be offered, such as safe and positive interaction with the animal care staff, as appropriate to the species of concern; periodic release into larger enclosures; supplemental enrichment items; and/or the addition of a companion animal in the room or housing area. The institution's policy and exceptions for single housing shall be reviewed on a regular basis and approved by the ACUC and/or veterinarian.

6.16 CAGE OR PEN SPACE

6.16.1 The *Guide*'s space recommendations (page 55-63, Table 3.2, 3.3, 3.4, 3.5, 3.6) shall be utilized as a basis for addressing space needs while always recognizing that performance standards also must be met.

6.17 ABNORMAL ENVIRONMENTAL CONDITIONS

6.17.1 Animal maintained in abnormal environmental conditions (e.g. hyperbaric chambers, partial hypoxia, hypo, or hyperthermia, mazes, etc.) must be closely monitored and endpoints established

before initiation of studies. Use of remote physiological monitoring of animals in these conditions, where applicable, shall be considered.

6.18 VETERINARY CARE

6.18.1 Adequate veterinary care shall be provided, including veterinarian access to all animals for evaluation of their health and well-being. KFSH&RC's mission, programmatic goals, and size and scope of the ACUP will determine the need for full-time, part-time, and/or consultative veterinary services. Ethical, humane, and scientific considerations sometimes require the use of sedatives, analgesics, or anesthetics in animals. The AV shall give research personnel advice that ensures humane needs are met and are compatible with accepted veterinary practices and scientific requirements. The AV shall have the authority to oversee the adequacy of other aspects of animal care and use. These can include animal husbandry and nutrition, sanitation practices, zoonosis control, and hazard containment.

6.19 PERSONNEL QUALIFICATIONS AND TRAINING

6.19.1 The KFSH&RC ensures that employees caring for or using animals are qualified and properly trained to do so. The number and qualifications of personnel required to conduct and support animal care and use shall be sufficient to provide adequate quality services. The following practices shall be enforced:

6.19.1.1 Personnel caring for animals are trained appropriately.
6.19.1.2 KFSH&RC provides formal or on-the-job training to facilitate effective implementation of the program and humane care and use of animals.
6.19.1.3 According to the program scope, personnel will be required with expertise in other disciplines, such as animal husbandry, administration, laboratory animal medicine, surgery and pathology, occupational health and safety, behavioral management, genetic management, and various other aspects of research support.
6.19.1.4 Employees are encouraged and assisted to partake in non-degree training, with certification programs for laboratory animal technicians and technologists, prepared by the AALAS and may use commercially available training materials that are appropriate for self-study.
6.19.1.5 Personnel using or caring for animals are instructed to participate regularly in continuing-education activities relevant to their responsibilities.
6.19.1.6 They are encouraged to be involved in local and national meetings of Laboratory Animal Science professional organizations.
6.19.1.7 On-the-job training is a part of every technician's job and is supplemented with Hospital sponsored discussions and training programs and with reference materials applicable to their jobs and the species with which they work.
6.19.1.8 Investigators, technical personnel, trainees, and visiting investigators who perform animal anesthesia, surgery, or other experimental manipulations must be qualified through training

or experience to accomplish these tasks in a humane and scientifically acceptable manner.

6.20 PERSONNEL OCCUPATIONAL HEALTH AND SAFETY

6.20.1 The Occupational Health and Safety Program (OHSP) of the KFSH&RC applies to the overall ACUP.

6.20.1.1 The program is consistent with the Government regulations and the focus is on maintaining a safe and healthy workplace.

6.20.1.2 The program depends on the facility, research activities, hazards, and animal species involved. An effective program relies on strong administrative support and interactions among several functions or activities of the Organization, including the research program (as represented by the investigator), the ACUP (as represented by the AV and the ACUC), the environmental health and safety program, occupational-health services, and administration (e.g., human resources, finance, and facility maintenance personnel).

6.20.1.3 Operational and day-to-day responsibility for safety in the workplace, however, resides with the laboratory or facility supervisor (e.g., PI, facility director, or veterinarian) and depends on performance of safe work practices by all employees.

6.20.2 Hazard Identification and Risk Assessment:

6.20.2.1 KFSH&RC's professional staff who conduct and support research programs that involve hazardous biological, chemical, or physical agents (including ionizing and non-ionizing radiation) are qualified to assess dangers associated with the programs and to select safeguards appropriate to the risks.

6.12.1.1 The OHSP ensures that the risks associated with the experimental use of animals are reduced to acceptable levels.

6.12.1.2 Potential hazards such as animal bites, chemical cleaning agents, allergens, and zoonoses that are inherent in or intrinsic to animal use are also identified and evaluated.

6.12.1.3 Health and safety specialists with knowledge in appropriate disciplines are involved in the assessment of risks associated with hazardous activities and in the development of procedures to manage such risks.

6.12.1.4 The extent and level of participation of personnel in the OHSP are based on the hazards posed by the animals and materials used; on the exposure intensity, duration, and frequency, on the susceptibility of the personnel and on the history of occupational and/or non-occupational related illness and injury in the particular workplace.

6.20.3 Personnel Training:

6.20.3.1 Personnel with potential exposure to laboratory animals or associated tissues or agents are provided with clearly defined procedures for conducting their duties, shall understand the hazards involved, and shall be proficient in implementing the required safeguards. The staff shall be educated and trained on:

6.20.3.1.1 Zoonoses
6.20.3.1.2 Chemical safety
6.20.3.1.3 Microbiologic and physical hazards (including those related to radiation and allergies)
6.20.3.1.4 Unusual conditions or agents that might be part of experimental procedures (including the use of genetically engineered animals and the use of human tissue in immunocompromised animals)
6.20.3.1.5 Handling of waste materials
6.20.3.1.6 Personal hygiene and other considerations (e.g. precautions to be taken during female personnel pregnancy, illness, or decreased immunocompetence) as appropriate to the risk imposed by their workplace.

6.20.4 Personal Hygiene:
6.20.4.1 It is essential that all personnel maintain a high standard of personal cleanliness.
6.20.4.2 Clothing suitable for use in the animal facility and laboratories are supplied and laundered by the KFSH&RC laundry services using universal practices precautions to reduce risks to laundry staff.
6.20.4.3 Appropriate arrangements are made to decontaminate clothing exposed to potential hazards.
6.20.4.4 Appropriate personal protective equipment (e.g. applicable use of disposable gloves, masks, head covers, eye protection, coats, gowns, or coveralls, and/or shoe covers) may be required as appropriate.
6.20.4.5 Personnel are instructed to wash their hands and change clothing as often as necessary to maintain personal hygiene.
6.20.4.6 Outer garments worn in the animal rooms are not worn outside the animal facility.
6.20.4.7 Personnel are not permitted to eat, drink, use tobacco products, or apply cosmetics within the designated animal vivarium area (e.g. animal rooms, sanitation areas, corridors, procedure rooms, surgery rooms, necropsy rooms, etc.).

6.20.5 Facilities, Procedures and Monitoring:
6.20.5.1 Facilities required to support occupational health and safety concerns associated with the ACUP will vary.
6.20.5.2 Because a high standard of personal cleanliness is essential, facilities and supplies for meeting this obligation shall be provided.
6.20.5.3 Washing and showering facilities appropriate to the program must be available.
6.20.5.4 Facilities, equipment, and procedures are designed, selected, and developed to provide for ergonomically sound operations that reduce the potential of physical injury to personnel (such as might be caused by the lifting of heavy equipment or animals and the use of repetitive movements).
6.20.5.5 Safety equipment shall be properly maintained and routinely calibrated.

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6.20.5.6 The selection of appropriate animal-housing systems requires professional knowledge and judgement and depends on:
- 6.20.5.6.1 The nature of the hazards in question;
- 6.20.5.6.2 The types of animals used;
- 6.20.5.6.3 The design of the experiments; and
- 6.20.5.6.4 Experimental animals shall be housed so that potentially contaminated food and bedding, feces, and urine can be handled in a controlled manner. Facilities, equipment, and procedures are provided for appropriate bedding disposal.

6.20.5.7 Appropriate methods shall be used for assessing exposure to potentially hazardous biologic, chemical, and physical agents where the possibility of exceeding permissible exposure limits (PELs) exists (CFR 1984b).

6.20.6 Animal Experimentation Involving Hazards:

6.20.6.1 The Research Centre Laboratory Safety Manual policies (2003 edition) governing experimentation with hazardous biologic, chemical, and physical agents shall be followed. An oversight process (such as use of a safety committee) shall be developed to involve personnel who are knowledgeable in the evaluation of hazards and safety issues. Because the use of animals in such studies requires special considerations, the procedures and facilities to be used should undergo review for specific safety concerns.

6.20.6.2 Formal safety programs should be established to assess the hazards, determine the safeguards needed for their control, ensure that the staff has the necessary training and skills, and ensure that the facilities are adequate for the safe conduct of the research. Technical support shall be provided to monitor and ensure compliance with policies of the Organization.

6.20.6.3 The Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) publication "Biosafety in Microbiological and Biomedical Laboratories (BMBL)" (5th ed., 2007) recommend practices and procedures, safety equipment, and facility requirements for working with hazardous biologic agents and materials. Facilities that handle agents of unknown risk shall consult with appropriate hospital safety committee, infection control and/or CDC personnel about hazard control and medical surveillance.

6.20.6.4 In selecting specific safeguards for animal experimentation with hazardous agents, careful attention should be given to:
- 6.20.6.4.1 Procedures for animal care and housing
- 6.20.6.4.2 Storage and disbursement of the agents
- 6.20.6.4.3 Dose preparation and administration
- 6.20.6.4.4 Body-fluid and tissue handling
- 6.20.6.4.5 Waste and carcass disposal
- 6.20.6.4.6 Personal protection

6.20.6.4.7 Special safety equipment shall be used in combination with appropriate management and safe practices

6.20.6.4.8 As a general rule, safety depends on trained personnel who rigorously follow safe practices

6.20.6.5 Special facilities and safety equipment are needed to protect the following from exposure to hazardous biologic, chemical and physical agents used in animal experimentation:

6.20.6.5.1 The animal-care and investigative staff

6.20.6.5.2 Other occupants of the facility

6.20.6.5.3 The public

6.20.6.5.4 Animals

6.20.6.5.5 The environment

6.20.6.6 Facilities used for animal experimentation with hazardous agents shall be:

6.20.6.6.1 Separated from other animal housing and support areas, research and clinical laboratories, and patient care facilities

6.20.6.6.2 Shall be appropriately identified

6.20.6.6.3 Access to them shall be limited to authorized personnel

6.20.6.6.4 Such facilities shall be designed and constructed to facilitate cleaning and maintenance by mechanical systems

6.20.6.6.5 A properly managed and used double corridor facility or barrier entry system is an effective means of reducing cross contamination

6.20.6.6.6 Floor drains should always contain liquid or be sealed effectively by other means

6.20.6.6.7 Automatic trap priming can be provided to ensure that traps remain filled

6.20.6.7 Hazardous agents shall be contained within the environment:

6.20.6.7.1 Control of airflow (such as through the use of biologic-safety cabinets) that minimizes the escape of contaminants is a primary barrier used in the handling and administration of hazardous agents and the performance of necropsies on contaminated animals (7)

6.20.6.7.2 Special features of the facility such as airlocks, negative air pressure, air filters, and redundant mechanical equipment with automatic switching and secondary barriers shall be aimed at preventing accidental release of hazards outside the facility and work environment

6.20.6.7.3 Exposure to anesthetic waste gases shall be limited. This is usually accomplished using various scavenging techniques. Use of ether shall be strongly discouraged. If ether is used, it must be scientifically justified in the protocol and, personnel safety shall be ensured by proper use of signs and by using equipment and practices to minimize risks associated with its explosiveness

6.20.7 Personal Protection:

6.20.7.1 Personal protective equipment (PPE) shall be provided, and other safety measures shall be adopted when needed.

6.20.7.2 Animal-care personnel shall wear appropriate Institution-issued protective clothing, shoes or shoe covers, and gloves. Closed toed shoes shall be warn in animals housing and use areas and laboratories.

6.20.7.3 Clean protective clothing shall be provided as often as necessary.

6.20.7.4 If it is appropriate, personnel shall shower when they leave the animal-care, procedure, or dose-preparation areas. Protective clothing and equipment shall not be worn beyond the boundary of the hazardous-agent work area or the animal facility.

6.20.7.5 Personnel with potential exposure to hazardous agents shall be provided with PPE appropriate to the agents (CFR 1984c). For example, personnel exposed to non-human primates shall be provided with such protective items as gloves, arm protectors, masks, and face shields.

6.20.7.6 Hearing protection shall be provided in high-noise areas.

6.20.7.7 Personnel working in areas where they might be exposed to contaminated airborne particulate material or vapors should be provided with suitable respiratory protection.

6.20.8 Medical Evaluation and Preventive Medicine for Personnel:

6.20.8.1 Development and implementation of a program of medical evaluation and preventive medicine shall involve input from trained health professionals, such as occupational-health physicians and nurses. Confidentiality and other medical and legal factors must be considered in the context of appropriate Governmental regulations.

6.20.8.1.1 A health history evaluation before work assignment is advisable to assess potential risks for individual employees.

6.20.8.1.2 Periodic medical evaluations are advisable for people in some risk categories. An appropriate immunization schedule shall be adopted.

6.20.8.1.3 It is important to immunize animal-care personnel against tetanus. In addition, pre-exposure immunization shall be offered to people at risk of infection or exposure to such agents as rabies or hepatitis B virus.

6.20.8.1.4 Vaccination is recommended if research is to be conducted on infectious diseases for which effective vaccines are available.

6.20.8.1.5 Specific recommendations can be found in the CDC and NIH publication Biosafety in Microbiological and Biomedical Laboratories (BMBL) (5th ed., 2007[6]).

6.20.8.1.6 Pre-employment or pre-exposure serum collection is advisable only in specific circumstances as determined by an occupational health and safety professional. In such cases, identification, traceability, retention, and storage conditions of samples should be considered, and the purpose for which the serum samples will be used must be consistent with applicable government laws and regulations.

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6.20.9 Zoonosis:

6.20.9.1 Zoonosis surveillance shall be a part of the OHSP. Personnel shall be instructed to notify their supervisors of potential or known exposures and of suspected health hazards and illnesses. Clear procedures shall be established for reporting all accidents, bites, scratches, and allergic reactions.

6.20.9.2 Non-human primate diseases that are transmissible to humans can be serious hazards. Additionally humans can transmit diseases to nonhuman primates and jeopardize the health of the animals and the integrity of the research.

6.20.9.2.1 Animal technicians, clinicians, investigators, students and postdoctoral trainees, research technicians, consultants, maintenance workers, security personnel, and others who have contact with non-human primates or have duties in non-human-primate housing areas shall be routinely screened for tuberculosis.

6.20.9.2.2 KFSH&RC does not use macaque species. However, if macaques were used, because of the potential for Macacine herpesvirus I (formerly Herpes B, Herpesvirus simiae, or Cercopithecine herpesvirus I) exposure personnel who work with macaques should have access to and be instructed in the use of bite and scratch emergency-care stations (Holmes and others 1995).

6.20.9.2.3 KFSH&RC has an established procedure for ensuring medical care for bites and scratches.

7. EQUIPMENT/MATERIALS

7.1 Personal Computer
7.2 Printer, Photocopier, Scanner
7.3 Microsoft Office Applications
7.4 Hospital web applications

8. RESPONSIBILITY

The responsibility of implementing and ensuring compliance with this NCIPP lies with CMD and the ACUC.

The responsibility of updating and archiving with this NCIPP rests with CMD and the ACUC.

9. ATTACHMENTS

9.1 Animal Care And Use Committee (ACUC) Application Form
9.2 ACUC and Facility Inspection Checklist

10. REFERENCES

10.1 "Guide for the Care and Use of Laboratory Animals", 8th edition, National Research Council, The National Academies Press, 2011.

10.2 Reinhardt,V. 1991 Training Male Adult Rhesus Monkey To Actively Cooperate During In-Homecage Venipuncture, Anim. Technol. 42(1) 11-17. & Reinhardt, V.1995. Restraint Methods Of Laboratory Non-Human Primates: A Critical Review. Animal Welfare, 4:221-238.

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10.3 American Association for Laboratory Animal Science, 9190 Crestwyn Hills Drive, Memphis, Tennessee 38125, USA. e-mail: info@aalas.org or http://www.aalas.org
10.4 The Research Centre Laboratory Safety Manual, 2003.
10.5 CFR (Code of Federal Regulations), 1984b, Title 29 Part 1910, Occupational Safety and Health Standards; Subpart G, Occupational Health and Environmental Control, and Subpart Z, Toxic and Hazardous Substances. Washington, D.C. Office of the Federal Register.
10.6 CDC (Centers for Disease Control and Prevention and NIH (National Institute of Health), 2007, Biosafety in Microbiological and Biomedical Laboratories, 5th edition. HHS Publication No. (CDC) 93-8395. Washington, D.C.: U.S. Government Printing Office.
10.7 CDC (Centers for Disease Control and Prevention and NIH (National Institute of Health), 2007, Primary Containment of Biohazards: Selection, Installation and Use of Biological Safety Cabinets, 3rd edition Washington, D.C.: U.S. Government Printing Office.
10.8 CFR (Code of Federal Regulations), 1984c, Title 29 Part 1910, Occupational Safety and Health Standards; Subpart I, Personal Protective Equipment. Washington, D.C. Office of the Federal Register.
10.9 Holms, G.P. et al and the B-Virus Working Group. 1995. Guidelines for Prevention and Treatment of B-virus Infections in Exposed Persons, Clin. Infect. Dis. 20:421-439.
10.10APP-58: Management of Hospital Committees