MMRI
MOLECULAR MEDICINE RESEARCH INSTITUTE

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POLICY & PROCEDURE MANUAL

Care and Use of Animals in Research

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I. PURPOSE

This document presents policy regarding the approval of animal care and use protocols and the procurement, handling, and care of animals used for research.

II. DEFINITIONS. ANIMAL CARE REGULATORY AUTHORITIES

Molecular Medicine Research Institute policies on animal care and use are based on Federal government and State regulations as well as MMRI guidelines. The following describes the major public regulatory agencies and the MMRI Animal Care and Use Committee having responsibility for coordination and monitoring of animal care policies.

A. AMERICAN ASSOCIATION FOR ACCREDITATION OF LABORATORY ANIMAL CARE (AAALAC).

AAALAC certifies compliance with the provisions of the Federal Animal Welfare Act and with additional standards of animal care specified by Federal agencies. Compliance requirements include submission of an annual report that includes a census of animals used in research. MMRI is not currently AAALAC accredited.

B. ANIMAL AND PLANT HEALTH INSPECTION SERVICE (APHIS) OF THE U.S. DEPARTMENT OF AGRICULTURE (USDA).

USDA-APHIS administers the Federal Animal Welfare Act, which establishes animal care standards for all species of laboratory animals. Compliance requirements include establishment of programs of adequate veterinary care, maintenance of records of the acquisition and disposition of research animals, and submission of an annual report showing the total numbers of laboratory animals used in research, numbers of animals that receive anesthetics, analgesics, and sedatives for potential pain or distress, and numbers of animals used under conditions of unalleviated pain or distress. Periodic unannounced inspections are conducted by USDA Veterinary Services personnel. Rats of the genus *Rattus* and mice of the genus *Mus*, bred for use in biomedical research are excluded from submission of an annual report and inspections by the USDA.

C. NATIONAL INSTITUTES OF HEALTH (NIH)

A subdivision of the US Public Health Service (PHS), Department of Health and Human Services (DHHS). NIH is a major source of grants for research in the health sciences. NIH publishes the Guide for the Care and Use of Laboratory Animals (*Guide*, Ref 3), which includes standards for the construction of vivaria, the care of experimental animals, and the use of animals in research. Adherence to the Guide is mandatory for institutions either desiring AAALAC accreditation or receiving funds from NIH. PHS publishes the Public Health Service Policy on Humane Care and Use of Laboratory Animals (Ref 7). Present PHS policy requires institutional review of all research projects involving live vertebrate animals by our institute animal care and use committee (IACUC) and specifies the composition and functions of the committee; PHS will not release funds for any research project until it receives verification from the Molecular Medicine Research Institute stating that the proposal has received such committee review. PHS policy also requires MMRI to file an Animal Welfare Assurance with NIH in which the Institute agrees to comply with NIH policy.

D. CALIFORNIA DEPARTMENT OF FISH AND GAME.

This agency administers State law that regulates the importation and containment of non-indigenous wildlife species and the collection and use of California wildlife (California Administrative Code, Title 14, Sections 671-671.4).

E. CALIFORNIA OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (CAL-OSHA).

Cal-OSHA administers detailed regulations pertaining to employee occupational health and safety, including potential health hazards to persons who work with animals.

F. CALIFORNIA DEPARTMENT OF PUBLIC HEALTH.

This agency interacts with MMRI animal care Director in the investigation of reportable infectious human diseases involving possible zoonotic sources. Compliance requirements may involve such activities as posting of potentially hazardous animal areas and monitoring by the Institute's Veterinarian of zoonotic aspects of public health on this research facility.

G. MMRI ANIMAL CARE AND USE COMMITTEE (MMRI IACUC).

The Committee is composed of Chair, Veterinarian, MMRI scientific staff, non-scientist and non-affiliated public interest members and functions as the institute animal care and use committee (IACUC) required by PHS policy. MMRI IACUC is responsible for advising personnel on matters pertaining to the institute animal care, use, services and compliance with applicable State, Federal, and MMRI policies. These responsibilities include reviewing MMRI animal care and use protocols and advising scientist on the design of animal research. The committee also recommends to the MMRI Director and Chairman and to Principal Investigators alteration or suspension of research activities not in compliance with governmental and MMRI policies and regulations or not in keeping with the Institute's NIH Animal Welfare Assurance Statement. The committee may also recommend restrictions to be imposed upon investigators or scientists who ignore such policies and regulations.

H. MMRI OFFICE OF ENVIRONMENTAL HEALTH & SAFETY.

EH&S is the institute unit charged with responsibility for administering health and safety programs including accident prevention, industrial hygiene, radiation safety, environmental sanitation, and animal care. EH&S staff, under the supervision of the Veterinarian, coordinate activities pertaining to maintenance of State certification, Animal Welfare Act compliance, approval of animal facilities, animal procurement, animal and human health surveillance, and in-service training for animal care personnel.

I. MMRI VETERINARIAN.

The Institute's Veterinarian, is responsible for supervision of animal care and for liaison between research and animal service units and the various public regulatory agencies. USDA regulations hold the Institute's Veterinarian, directly responsible for the supervision of animal disease control and prevention, euthanasia, appropriate use of pain-relieving drugs, and other aspects of veterinary care specified in the Animal Welfare Act. The Institute's Veterinarian is responsible to IACUC as that committee discharges its duties regarding the review and approval of animal care and use protocols.

III. GENERAL POLICY

The Molecular Medicine Research Institute recognizes the importance of the use of animals in its research programs. Animals are vital both for understanding basic biological processes and in developing treatment for human and animal diseases. The Institute, committed to maintaining high standards for the care and use of animals in research, therefore adopts as its own principles the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (Ref 7 Pg. 4-5). The Institute, including its investigators and

scientists, accepts responsibility for determining that research and teaching involving the use of animals fulfill these principles.

IV. ANIMAL CARE AND USE PROTOCOLS

A. REQUIREMENTS

1. Each investigator in charge of any research activity involving live vertebrate animals shall prepare and submit a Protocol Application for Animal Care and Use as described below. No research activity involving live vertebrate animals may be initiated until such protocol has been approved.

2. Animals shall not be obtained for any research activity without an approved Protocol for Animal Care and Use.

3. Many funding agencies, such as NIH, and others, require that funding proposals submitted to them be reviewed and approved by the IACUC prior to the award date for the proposal. Investigators are responsible for familiarizing themselves with the requirements of the agencies from which they seek funding. It is MMRI's responsibility to ensure that the research described in the grant application is congruent with any corresponding protocols approved by the IACUC.

B. EXEMPTIONS

The following activities are exempt from the requirement for a Protocol for Animal Care and Use:

1. Use of dead animals.

2. Routine husbandry procedures that are incidental to maintenance of the animals and not part of an experiment per se (such as vaccinations, medical or surgical procedures performed for the animal's benefit).

Although such operations are not subject to committee review, they must be registered with the Institute's Veterinarian, in order that they may be included in such census reports and inspections as are required by outside agencies. Individual scientists using these animals on research projects are not exempt from submitting a Protocol for Animal Care and Use.

C. PROCEDURE

1. The investigator will route the completed Protocol for Animal Care and Use to the IACUC for review. Kayla Vuong, IACUC Coordinator, serves as contact for IACUC Protocol review (kvuong@mmrx.org) and will keep the author updated during the review process.

2. The Committee will conduct an initial review by MMRI Committee members only, providing guidance to the investigator and requesting changes/modifications to the protocol. The review will include (but is not limited to):

   (a) Review the document for completeness
   (b) Verify that the proposed activity has scientific merit
   (c) Verify that the personnel are qualified by training and experience to conduct the activity proposed.
   (d) Verify that the type and amount of any analgesic, anesthetic, or tranquilizing drugs shown are appropriate to the procedure and the species
   (e) Verify that the number of animals requested is justified.

3. After initial revisions are made, the protocol will be sent to the full IACUC committee, including the Veterinarian Consultant and non-affiliated member. The IACUC will review the protocol and will approve, withhold approval, or require modifications to secure approval in accordance with IACUC's policies. Individual protocols may be approved for one to three years, at IACUC's discretion.

4. Notification of approval and a copy of the approved protocol will be sent via e-mail to all IACUC members and all personnel approved to perform studies under the protocol. A letter of verification can be issued to the investigator upon request. The investigator can then forward the letter to any funding agency as evidence that the project has been reviewed and approved by a properly constituted institutional committee.

D. CRITERIA FOR REVIEW OF PROTOCOLS

IACUC will fulfill the duties of an institutional animal care and use committee as defined in the PHS Policy on Humane Care and Use of Laboratory Animals (Ref 7) and in the MMRI Animal Welfare Assurance to NIH. IACUC shall confirm the following for each Protocol for Animal Care and Use:

1. That the proposed activities are in compliance with Federal, State, and Institute policies.

2. That the activity is consistent with the *Guide* (Ref 3), unless acceptable justification for a departure is presented.

3. That procedures will avoid or minimize discomfort, distress, and pain to the animals consistent with sound research design.

4. That procedures causing more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator.

5. 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.

6. That the living conditions of the animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and non-medical care of the animals will be directed by a trained and experienced associate in the proper care, handling, and use of the species being maintained or studied.

7. That medical care for animals will be available and provided as necessary by the Institute's veterinarian.

8. That personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures.

9. That methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia (Ref 4), unless a deviation is justified for scientific reasons in writing by the investigator.

V. ANIMAL PROCUREMENT

1. Animals shall not be procured for investigators who lack an approved protocol. Contact Kayla Vuong, IACUC Coordinator (kvuong@mmrx.org) to determine if proposed work is already approved under an existing protocol, an amendment to an approved protocol is required, or a new protocol must be written and approved.

2. Vendors shall not provide animals to the Institute's users without first confirming that the project is covered by an approved protocol.

3. Laboratory animals may be procured only through the Institute's Purchasing Department and must be from reputable vendors that are approved by MMRI IACUC and Attending Veterinarian.

VI. HOUSING, CARE, AND HANDLING OF ANIMALS

1. MMRI practices in the housing and care of animals shall conform to the *Guide* (Ref 3). This document sets forth detailed guidelines for animal care and use in research.

2. Animals shall be housed only in MMRI animal facility. Animals can be removed from the animal facility for research purposes (e.g. laboratories) and returned to the holding facility at the end of the working day only if specified in an approved protocol.

3. Animals used for research are the responsibility of the Molecular Medicine Research Institute. No animal or animal carcass shall be removed from or brought onto MMRI property except in accordance with established Institute's procedures or with prior approval of the Institute's Veterinarian.

4. Laboratory animal carcasses shall be bagged in a manner consistent with current MMRI standard operating procedure ANP003: Animal Carcass Disposal requirements. All dead animals are to be discarded into a biohazard bag, then sealed and placed into a secondary biohazard bag which is also sealed before placing in the disposal freezer to await pickup by the disposal company. Disposal of all biohazardous wastes shall be conducted in accordance with MMRI Safety Guidelines (contact Bhaumik Patel for additional information, bpatel@mmrx.org).

5. The Institute's Veterinarian is responsible for monitoring animal care and use practices and for providing advice and assistance to investigators in the correction of any deficiencies with respect to conformance with applicable policies, laws, and regulations. Any issues of disagreement between animal users and the Institute's Veterinarian shall be referred to IACUC for review and recommendation.

VII. TRAINING, SUPERVISION, AND MEDICAL SURVEILLANCE OF ANIMAL CARE PERSONNEL

1. All persons having significant contact with animals shall participate in a medical surveillance program as outlined in the MMRI Animal Care Facility – Laboratory Animal Occupational Health Surveillance document.

2. Supervisors of persons involved in the care of animals shall be responsible for providing adequate supervision and training to ensure conformance with occupational safety practices, animal care regulations, and accepted experimental techniques.

VIII. FURTHER INFORMATION

Contact the following MMRI staff for information and assistance with compliance questions or problems.

Bhaumik Patel, bpatel@mmrx.org
Kayla Vuong, kvuong@mmrx.org
Dr. Puja Ravikumar, pravikumar@mmrx.org

IX. RESOURCES AND REFERENCES

1. Animal Welfare Act. U.S.Code of Federal Regulations, Title 9, Subchapter A. https://www.law.cornell.edu/cfr/text/9/chapter-I/subchapter-A

2. National Institutes of Health, Office of Laboratory Animal Welfare https://olaw.nih.gov/home.htm

3. Guide for the Care and Use of Laboratory Animals (*Guide*), 8th Edition, National Academy Press, Washington DC, 2011 https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf

4. AVMA Guidelines for the Euthanasia of Animals: 2020 Edition, American Veterinary Medical Association
https://www.avma.org/sites/default/files/2020-01/2020-Euthanasia-Final-1-17-20.pdf

5. Public Health Service Policy on Humane Care and Use of Laboratory Animals, U.S. Department of Health and Human Services, National Institute of Health, Office of Laboratory Animal Welfare, 2015
https://olaw.nih.gov/sites/default/files/PHSPolicyLabAnimals.pdf

6. Institutional Animal Care and Use Committee Guidebook, 2nd Edition, Applied Research Ethics National Association, Office of Laboratory Animal Welfare, 2002
https://grants.nih.gov/grants/olaw/guidebook.pdf

7. Biosafety in Microbiological and Biomedical Laboratories 5th Edition, U.S. Department of Health and Human Services, Public Health Service. Centers for Disease Control and Prevention, National Institutes of Health, Revised December 2009
https://www.cdc.gov/labs/pdf/CDC-BiosafetyMicrobiologicalBiomedicalLaboratories-2009-P.PDF

8. Information Resources on the Care and Welfare of Rodents, U.S. Department of Agriculture, Agriculture Research Service, National Agricultural Library, Animal Welfare Information Center, Beltsville, MD, 2006
https://pubs.nal.usda.gov/sites/pubs.nal.usda.gov/files/Rodents2006.pdf

9. Training resources from Office of Intramural Research (NIH)
https://oacu.oir.nih.gov/training-resources

10. Journal of Visualized Experiments
https://www.jove.com/

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X. ACKNOWLEDGEMENT OF POLICIES AND PROCEDURES

I, the undersigned, acknowledge reading and understanding the regulations and standards applicable to the Molecular Medicine Research Institute.

Company Name (print): _____

Name (print):_____

Signature: _____ Date:_____