Policies, Regulations and Guidelines for Conducting Animal Research

Ministry of Public Health

Department of Research

Version 1 updated 2013

Version 2 updated 2018

Preface

The purpose of the Policies, Regulations and Guidelines for Research Involving Laboratory Animals is to assist institutions in the state of Qatar, in caring for and using animals for scientific purposes in ways judged to be scientifically, technically and humanely appropriate according to highest ethical principles.

This document is reasonably comprehensive and is stated at the level that should assist scientists, researchers and Qatar Animal Welfare Society to understand the ethics in research involving animals. The present document covers all aspects of the care and use of vertebrate animals for scientific purposes, such as but not limited to their use in research, teaching, product testing, genetically modified animals, environmental studies and the production of biological products.

The Policies, Regulations and Guidelines for Research Involving Laboratory Animals outline the responsibilities of Institutional Animal Care and Use Committees (IACUCs), staff and investigators involved in the care and use of animals for scientific purposes. Research involving animal shall comply with the Ministry of Public Health Policy. However, since science is a continuum with specific advances that may raise ethical issues, updated appendices will be added to this document as the need arises.

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1 Key Concepts

The Policies, Regulations and Guidelines for Research Involving Laboratory Animals establishes the minimum ethical, practice, and care standards for researchers and their institutions in decision making regarding the use of vertebrate laboratory animals. The present document covers all aspects of the care and use of vertebrate animals for scientific purposes, such as but not limited to their use in research, teaching, product testing, genetic modifications, environmental studies and the production of biological products.
Compliance with these regulations, policies, and standards (or subsequent revised versions) in the establishment and implementation of a program of animal care and use is discussed in Chapter 2.
The practical effect of these regulations is to establish a system of self-regulation and regulatory oversight that binds researchers and institutions using animals. Both researchers and institutions have affirmative duties of humane care and use that are supported by practical, ethical, and scientific principles. This system of self-regulation establishes a rigorous program of animal care and use and provides flexibility in fulfilling the responsibility to provide humane care. The specific scope and nature of this responsibility can vary based on the scientific discipline, nature of the animal use, and species involved, but because it affects animal care and use in every situation this responsibility requires that producers, teachers, researchers, and institutions carry out purposeful analyses of proposed uses of laboratory animals. The Ministry of Public Health Policies, Regulations and Guidelines for Research Involving Laboratory Animals is central to these analyses and to the development of a program in which humane care is incorporated into all aspects of laboratory animal care and use.

1.1 Applicability and Goals

The overall goal of the Policies, Regulations and Guidelines for Research Involving Laboratory Animals is to promote the humane care and use of laboratory animals by providing information that will enhance animal wellbeing, the quality of research, and the advancement of scientific knowledge that is relevant to both humans and animals.

The Ministry of Public Health recognizes that the use of different species in research is expanding and both researchers and institutions will face new and unique challenges in determining how to apply the regulations in these situations. In making such determinations, it is important to keep in mind that this document is intended to provide information to assist researchers, institutional animal care and use committees (IACUCs), veterinarians, and other stakeholders in ensuring the implementation of effective and appropriate animal care and use programs that are based on humane care. Throughout the Policies, Regulations and Guidelines for Research Involving Laboratory Animals scientists and institutions are encouraged to give careful and deliberate thought to the decision to use animals, taking into consideration the contribution that such use will make to new knowledge, ethical concerns, and the availability of alternatives to animal use. A practical strategy for decision making, the “Three Rs” (Replacement, Reduction, and Refinement) approach, is discussed in more detail below.

1.2 Intended Audiences and Use of the Policy

The Policies, Regulations and Guidelines for Research Involving Laboratory Animals is intended for a wide and diverse audience, including:

- the scientific community

- administrators
- IACUCs
- veterinarians
- educators and trainers
- producers of laboratory animals
- accreditation bodies
- regulators
- Qatar Animal Welfare Society
- Funding bodies
- the public

1.3 Ethics and Animal Use- General Principles

Animal use in research requires critical thought, judgment, and analysis. Using animals in research is a privilege granted by society to the research community with the expectation that such use will provide either significant new knowledge or lead to improvement in human and/or animal well-being. It is a trust that mandates responsible and humane care and use of these animals. Animal experiments should be undertaken only after due consideration of their value to human or animal health or the advancement of knowledge on biomedical research weighed against the potential effects on the welfare of the animals.
Projects involving animals must be based upon written proposals approved by an Institution Animal Care and Use Committee (IACUC), which must take into account the justification for the project, the likely value of the knowledge to be gained, and the appropriate application of what is known as the 3Rs.

The 3Rs

The approach known as the 3Rs is to be considered at all times:
(a) Replacement of animals with other methods;

Alternative methods that replace the use of animals for scientific purposes must be sought and used wherever possible.

(b) Reduction in the number of animals used;

Each project must use no more than the necessary number of animals to obtain scientific and statistical validity. The principle of reducing the number of animals used should not be implemented at the expense of greater suffering of individual animals. Scientific and teaching activities involving the use of animals must not be repeated unless essential for the purpose or design of the project.

(c) Refinement of projects, procedures and techniques to improve the welfare of animals.

Animal species chosen must be suitable for the scientific activities, taking into account their biological characteristics, including behavior, genetic constitution and nutritional, microbiological and general health status. Projects must be designed to avoid pain or distress to animals. If this is not possible, pain or distress must be alleviated. Procedures with animals that may cause more than momentary or minimal pain or distress (e.g. surgery) should only be performed with appropriate sedation, analgesia, or anesthesia. An animal that develops signs of pain or distress of a kind and degree not predicted in the proposal for the project; must have the pain or distress alleviated promptly or the animal must be killed humanely, unless a justification

for continuation is provided to and approved by the Institutional Animal Care and Use Committee (IACUC).
The planned end-point of the project must be as early as feasible to avoid or minimize pain or distress to the animals. Efforts should be made to avoid death as an end-point whenever possible. The transportation, housing, feeding and handling of animals should meet species-specific needs; including behavioral and biological needs (see Appendix I).

Key Terms-Definitions

Animal facility: any abs all buildings, rooms, area, enclosures, or vehicles, including satellite facilities, used for animal confinement, transport, maintenance, breeding, or experiments inclusive of surgical manipulation.
Animal care and use program means the policies, procedures, standards, organizational structure, staffing, facilities, and practices put into place by an institution to achieve the humane care and use of animals in the laboratory and throughout the institution.
Animal welfare Assurance or Assurance: the documentation from an institution assuring institutional compliance with this policy.
Humane care means those actions taken to ensure that laboratory animals are treated according to high ethical and scientific standards.
Institution: any government, private organization, business or agency.
Institutional Official: an individual who has the authority to represent, sign the institution Animal Welfare Assurance and make a commitment on behalf of the institution that the requirements of this policy are met.
Laboratory animals or animals: Any live, acquired, hosted or wildlife vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes.
Quorum: A majority of the members of the Institutional Animal Care and Use Committee (IACUC).
Satellite facility: Any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours.
The attending veterinarian (AV) is responsible for the health and well-being of all laboratory animals used at the institution satellite facility: Any containment outside of a core facility or centrally designated or managed area in which animals are housed for more than 24 hours.

References

1) Public Health Service Policy on Humane Care and Use of Laboratory Animals, National Institute of Health.http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf

2) Guide for the Care and Use of Laboratory Animals 7th editionInstitute of Laboratory Animal Research, Commission on Life Sciences, National Research Council – U.S.:http://www.nap.edu/openbook.php?record_id=5140

3) Guide for the Care and Use of Laboratory Animals 8th Edition – National Research Council of National Institute of Health: http://oacu.od.nih.gov/regs/guide/guide.pdf

4) Guide to the Care and Use of Experimental Animals Volume 1.Canadian Council on AnimalCare:http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/GUIDES/ENGLISH/toc_v1.htm

5) Institutional Animal Care and Use Committee Guidebook – Office of Laboratory Animal Walfare (OLAW): http://www.rw.ttu.edu/6002%20ethics/pdf/GuideBook.pdf

6) United States Department of Agriculture- National Agriculture Library:http://awic.nal.usda.gov/government-and-professional-resources/inspections-and-compliance

7) Public Health Service (PHS). 1986. Public Health Service Policy on Humane Care and Use of Laboratory Animals. Washington, D.C.: U.S. Department of Health and Human Services. (Available from: Office for Protection from Research Risks, Building 31, Room 4B09, National Institutes of Health, Bethesda, MD 20892).

8) Animal Welfare Act of 1966 (P.L. 89-544) inclusive of amendments; 1970 (P.L. 91- 579; 1976 (P.L. 94-279); 1985 (P.L. 99-198).

9) Animal Welfare Act Regulations, (9 C.F.R. 2.31) Institutional Animal Care and Use Committee.

10) Office for Laboratory Animal Welfare. Requirements for prompt reporting of problems to OLAW. OPRR Reports, January 12, 1994.

11) Academic Personnel Manual, APM – 015, The Faculty Code of Conduct

12) The Guide for the Care and Use of Laboratory Animals, Eighth Edition, National Academic Press, 2011

2 Guidance for Humanely Use of Laboratory Animal Involved in Research

2.1 Assuring Compliance with the Policy

This policy applies to all research involving the use of laboratory animals, privately or governmentally supported or otherwise subject to regulation by any department of research or research organization in the state of Qatar. This includes researches conducted or supported in collaboration with a non-Qatari institution.
The Ministry of Public Health to require institutions to establish and maintain proper measures to ensure the welfare of all animals used for scientific purposes, in the state of Qatar. The Research Division at the Ministry of Public Health is responsible for the general administration and coordination of these Guidelines, and will:

(a) Review and negotiate IACUC registration applications;
(b) Guide and instruct institutions concerning the implementation of the Guidelines;
(c) Have the authority to review and approve or disapprove exceptions to the guidelines;
(d) Monitor compliance with the Guidelines, including evaluation of IACUC reports and site visits;
(e) Work together with IACUCs to ensure the restriction or withdrawal of approval of projects in violation of the Guidelines;
(f) Suspend or withdraw approval of an institution's IACUC for serious or repeated failure to comply with the Guidelines
(g) Provide educational training, guidelines and materials for institutions and investigators.

This policy does not affect any local or foreign laws or regulations which may otherwise be applicable and which provide additional protections for laboratory animals involved in research.

2.2 Animal Care and Use Program Management

An effective program requires clearly defined roles that align responsibility with regulatory and management authority. The Ministry of Public Health regulations endorses the institutional official (IO), the attending veterinarian (AV), and the institutional animal care and use committee (IACUC) as important operating principles for all Qatari and Non-Qatari animal care and use programs. Effective leadership in and collaboration among these three components, which not only oversee but also support animal users, are necessary. In addition, interactions with regulatory and funding agencies and accreditation organizations are an integral part of the Animal Care and Use Program.
The primary oversight responsibilities in the Animal Care and Use Program rest with the IO, the AV, and the IACUC. Their roles fit in a defined organizational structure where the reporting relationships, authorities, and responsibilities of each are clearly defined and transparent. Together they establish policies and procedures, ensure regulatory compliance, monitor Program performance, and support high-quality science and humane animal use. A Program that includes these elements and establishes a balance among them has the best chance of efficiently using resources while attaining the highest standards of animal wellbeing and scientific quality.

2.2.1 Animal Care and Use Program Management

2.2.1.1 The Institutional Official

The institutional official (IO) bears ultimate responsibility for the Program, although overall Program direction should be a shared responsibility among the IO, AV, and IACUC. The IO has the authority to allocate the resources needed to ensure the Program's overall effectiveness. Program needs should be clearly and regularly communicated to the IO by the AV, the IACUC, and others associated with the Program (e.g., facilities management staff, occupational health and safety personnel, scientists). As a representative of senior administration, the IO is responsible for resource planning and ensuring the alignment of Program goals of quality animal care and use with the institution's mission.

2.2.1.2 The Attending Veterinarian

The attending veterinarian (AV) is responsible for the health and wellbeing of all laboratory animals used at the institution. The institution must provide the AV with sufficient authority, including access to all animals, and resources to manage the program of veterinary care. The AV should oversee other aspects of animal care and use (e.g. husbandry, housing) to ensure that the Program complies with the Guide. Institutional mission, programmatic goals, including the nature of animal use at the institution, and Program size will determine whether fulltime, part-time, or consultative veterinary services are needed. If a full-time veterinarian is not available on site, a consulting or part-time veterinarian should be available in visits at intervals appropriate to programmatic needs. In such instances, there must be an individual with assigned responsibility for daily animal care and use and facility management. While institutions with large animal care and use programs may employ multiple veterinarians, the management of veterinary medicine, animal care, and facility operations by a single administrative unit.

2.2.1.3 The Institutional Animal Care and Use Committee

The IACUC is responsible for assessment and oversight of the institution's Program components and facilities. It should have sufficient authority and resources (e.g., staff, training, computers and related equipment) to fulfill this responsibility.

2.2.1.4 Collaborations

Inter-institutional collaboration has the potential to create ambiguities about responsibility for animal care and use. In cases of such collaboration involving animal use (beyond animal transport), the participating institutions should have a formal written understanding (e.g., a contract, memorandum of understanding, or agreement) that addresses the responsibility for offsite animal care and use, animal ownership, and IACUC review and oversight. In addition, IACUCs from the participating institutions may choose to review protocols for the work being conducted.

2.2.2 Personnel Management

2.2.2.1 Training and Education

All personnel involved with the care and use of animals must be adequately educated, trained, and/or qualified in basic principles of laboratory animal science to help ensure high-quality science and animal well-being. Institutions are responsible for providing appropriate resources to support personnel training, and the IACUC is responsible for providing oversight and for evaluating the effectiveness of the training program. All Program personnel training should be documented.

Veterinary and *Other Professional Staff Veterinarians* providing clinical and/or Program oversight and support must have the experience, training, and expertise necessary to

appropriately evaluate the health and wellbeing of the species used in the context of the animal use at the institution. Veterinarians providing broad Program direction should be trained or have relevant experience in laboratory animal facility administration and management. Laboratory animal science and medicine are rapidly changing and evolving disciplines. The institution should provide opportunities and support for regular professional development and continuing education to ensure both that professional staff are knowledgeable about the latest practices and procedures and that laboratory animals receive high-quality care.

Animal Care Personnel caring for animals should be appropriately trained, and the institution should provide for formal and/or on-the-job training to facilitate effective implementation of the Program and the humane care and use of animals. Staff should receive training and/or have the experience to complete the tasks for which they are responsible. According to the Program scope, personnel with expertise in various disciplines (e.g., animal husbandry, administration, veterinary medical technology) may be required.

Personnel caring for laboratory animals should also regularly engage in continuing education activities and should be encouraged to participate in local and national laboratory animal science meetings and in other relevant professional organizations. On-the-job training, supplemented with institution-sponsored discussion and training programs and reference materials applicable to their jobs and the species in their care, should be provided to each employee responsible for animal care.

The institution should provide appropriate education and training to members of research teams—including principal investigators, study directors, research technicians, postdoctoral fellows, students, and visiting scientists—to ensure that they have the necessary knowledge and expertise for the specific animal procedures proposed and the species used. Training should be tailored to the particular needs of research groups; however, all research groups should receive training in animal care and use legislation, IACUC function, ethics of animal use and the concepts of the Three Rs, methods for reporting concerns about animal use, occupational health and safety issues pertaining to animal use, animal handling, aseptic surgical technique, anesthesia and analgesia, euthanasia, and other subjects, as required by statute. Continuing education programs should be offered to reinforce training and provide updates that reflect changes in technology, legislation, and other relevant areas. Frequency of training opportunities should ensure that all animal users have adequate training before beginning animal work.

It is the institution's responsibility to ensure that IACUC members are provided with training opportunities to understand their work and role. Such training should include formal orientation to introduce new members to the institution's Program; relevant legislation, regulations, guidelines, and policies; animal facilities and laboratories where animal use occurs; and the processes of animal protocol and program review. Ongoing opportunities to enhance their understanding of animal care and use in science should also be provided. For example, IACUC members may meet with animal care personnel and research teams; be provided access to relevant journals, materials, and web-based training; and be given opportunities to attend meetings or workshops.

2.2.2.2 Occupational Health and Safety of Personnel

Each institution is recommended to establish and maintain an occupational health and safety program (OHSP) as an essential part of the overall Program of animal care and use. The OHSP must be consistent with local and international regulations and should focus on maintaining a

safe and healthy workplace. The nature of the OHSP will depend on the facility, research activities, hazards, and animal species involved.

At minimum, the program must include:

(a) Pre-placement medical evaluation
(b) Orientation program
(c) Appropriate testing and vaccination
(d) Training of personnel on hazard handling and safeguard;
(e) Provisions for treating job injury
(f) Personal protective equipment (PPE)

2.2.2.3 Investigating and Reporting Animal Welfare Concerns

Safeguarding animal welfare is the responsibility of every individual associated with the Program. The institution must develop methods for reporting and investigating animal welfare concerns, and employees should be aware of the importance of and mechanisms for reporting animal welfare concerns. Responsibility for review and investigation of these concerns rests with the IO and the IACUC. Response to such reports should include communication of findings to the concerned employee(s), unless such concerns are reported anonymously; corrective actions if deemed necessary; and a report to the IO of the issue, findings, and actions taken. Reported concerns and any corrective actions taken should be documented.

Mechanisms for reporting concerns should be posted in prominent locations in the facility and on applicable institutional website(s) with instructions on how to report the concern and to whom. Multiple points of contact, including senior management, the IO, IACUC Chair, and AV, are recommended. The process should include a mechanism for anonymity, compliance with applicable whistleblower policies, nondiscrimination against the concerned/reporting party, and protection from reprisals.

Training and regular communication with employees (including personnel such as custodial, maintenance, and administrative staff, who are farther removed from the animal use) about the institution’s animal use activities may reduce potential concerns.

3 Program Oversight

3.1 Responsibilities of Institutions

Any institutions that intending to perform activities involving vertebrate animals shall comply with the Ministry of Public Health guideline by: (a) operating an animal care and use program and (b) applying to the Ministry of Public Health for IACUC registration. The ultimate responsibility for ensuring compliance with these guidelines rests with the designated Senior Administrator responsible for animal use for the institution, known as Institutional Official (IO).
Institutions responsibilities include:

1. Establishing an animal care and use program that includes-but not limited to-:

(a): a properly constructed and functioning IACUC(s).
(b): institution self-regulation and overseeing procedure manual.
(c): adequate veterinary services.
(d): personnel training program
(e): occupational health and safety program
(f): animals' environment, housing and management program.
(g): emergency program.

2. Designation of one or more Institutional Animal care and Use committees (IACUCs) established in accordance with the requirements of this policy, and for which provisions are made for meeting space and sufficient staff to support the IACUC's review and recordkeeping duties. Where there is little use of animals for scientific purposes, institutions may consider accessing an external IACUC or sharing an IACUC with another institution;

a. Ensuring, through the IACUC institutional animal Welfare Assurance Letters, that investigators and staff are aware of their responsibilities under the guidelines and that the use of animals for scientific purposes complies with the guidelines;
b. Responding promptly and effectively to recommendations from the IACUC to ensure that all care and use of animals remains in accord with the guidelines;
c. Providing the IACUC with the resources required to fulfill its Terms of Assurance and responsibilities;
d. Conducting at least twice annual review of the operation of the IACUC, including an assessment of the IACUC's Annual Report and a meeting with the IACUC chairperson
e. Ensuring a high standard of animal housing and management is maintained over weekends and holidays (see Appendix I).
f. Ensuring that there are adequate numbers of staff (a minimum of 2) to care for the animals and that those staff are appropriately trained and instructed;
g. Ensuring that the adequate veterinary services are available at all times and that there is access to diagnostic services;
h. Ensuring adequate record keeping and annual reporting.

3.2 The Institutional Animal Care and Use Committee

3.2.1 IACUC Authority

The Ministry of Public Health mandates the existence of IACUCs to ensure, on behalf of institutions, that all care and use of animal programs are conducted in compliance with the Ministry of Public Health regulations and that the principles of the 3Rs are properly applied. The regulations require the highest operational officer, Chief Executive Officer (CEO), of an organization to appoint the IACUC, whose responsibilities is outlined in the Guideline. The institution authority is delegated through the Institutional Official (IO) to appoint the membership of the IACUC on an annual basis. The IO is given the administrative and operational authority to commit institutional resources to ensure compliance with the policy and other requirements. The IACUC has an independent authority to review and approve protocols which cannot be override by IO. However, the Institution is not obligated to conduct the research activity and may request additional institutional review. The IACUC semiannually submit reports of the Institution's compliance, deficiencies required corrections and evaluation reports of the Institution's animal use and care program, facilities, or personnel training to the IO for necessary actions and recommendations.

Each IACUC's operation must be governed by a formal Assurance Letter that includes the requirements detailed in Assurance and IACUC registration application. The institutional Assurance must be tailored to reflect and refer to the institution's program, including the members of the program and the institution's policies, practices and procedures. The Assurance must be made publicly available.

3.2.2 IACUC Constitution and Function

The responsibility of the IACUC is to oversee and routinely evaluate the Program. It is the institution's responsibility to provide suitable orientation, background materials, access to appropriate resources, and specific training to assist IACUC members in understanding their roles and responsibilities and evaluating issues brought before the committee. Committee Quorum should consist at least from five (5) members that include but not limited to the following:

- a Doctor of Veterinary Medicine either certified or with training and experience in laboratory animal science and medicine or in the use of the species at the institution
- at least one practicing scientist experienced in research involving animals
- at least one member from a nonscientific background, drawn from inside or outside the institution
- at least one public member non-affiliated with the institution to represent general community interests in the proper care and use of animals.

The committee is responsible for oversight and evaluation of the entire Program and its components. Its oversight functions include review and approval of proposed animal use (protocol review) and of proposed significant changes to animal use; regular inspection of facilities and animal use areas; regular review of the Program; ongoing assessment of animal care and use; and establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution. The committee must meet as often as necessary to fulfill its responsibilities, and records of committee meetings and results of deliberations should be maintained. After review and inspection, a written report (including any minority views) should be provided to the IO about the status of the Program.

3.2.3 Institutional Animal Care and Use Committee (IACUC) Membership

It is obligated by this policy that an IACUC comprises of at least 5 voting members. Alternate voting members and non-voting members are optional.

An IACUC must comprise the following members:

(a) The IACUC chairperson; with knowledge of ethical and humane care and use of animals possessing necessary skills to review animal involved research activities.
(b) A veterinarian, formally trained and/or with experience in laboratory animal medicine with a direct or delegated responsibility of the care and use of species.
(c) A scientist member or a teacher experienced in using laboratory animals for experimental purposes;
(d) Non-scientific member: an institutional member whose normal activities, past or present, do not depends on or involve use of animals for scientific purposes;
(e) A public member, representing general community interest, should not be laboratory animal users, affiliated in any way with the institution, or members of the immediate family of a person who is affiliated with the institution.
(f) Additional members shall be included in the IACUC in accord to the institution animal care and use program such as:
(i) Technical staff representation (e.g. an animal research technician);
(ii) Student representation (graduate or undergraduate), in the case of institutions that have programs where students use animals.

- The institution should make every effort to ensure that no IACUC consists entirely of men or entirely of women.
- Alternative member should be assigned with specific position to replace the regular member when its needed to ensure that a committee is properly constituted
- The chairperson of the IACUC shall be appointed by the Senior Administrator.
- An individual who fulfill more than one requirement detailed in (a)-(f) of this policy is prohibited from filling multiple roles in the IACUC.

A copy of the IACUC roster must be submitted to the Ministry of Public Health

3.2.3.1 Conflict of Interest

a) It is obligated by this policy that no IACUC member participates in the IACUC's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IACUC. Consultant, PIs and/or IACUC members are required to disclose any conflict of interest (COI) and hence IACUC should develop manual and templates for COI discloser to promote the objectivity of research reviewing process and to eliminate COI.

b) IACUC member conflict of interest exists whenever a member, his or her spouse, or dependent child is involved in – but not limited to -one of the following conditions:

- Involved on the protocol as a key investigator or consultant;
- Involved in a potentially competing research program;
- Involved in a situation where s member's personal biases may interfere with his or her impartial judgment;

- Involved with the sponsor or agent of sponsor by a financial agreement which leads to an economic interest.
- Is filling an officer or a director position of the sponsor or an agent of the sponsor.
- Has an equity interest in the sponsor.
- Has identified him or herself for any other reason as having a conflict of interest.

c) If an investigator believes that a potential conflict of Interest exists with an IACUC member, the investigator may request for an exclusion of the IACUC member from reviewing the submitted proposal. The Chair (or in his/her absence, the Vice-Chair) presents the declared conflict and the IACUC evaluates and decides whether a conflict exists.

d) IACUC member with conflict of interest of a proposal under review losses the privilege of voting and is not counted toward quorum. The member may attend meeting to provide information requested by the IACUC; but must leave the meeting during discussion and voting.

3.2.3.2 Confidentiality

a) Material submitted to the IACUC for review is categorized as confidential information and the members must protect the integrity of the institution and its research by assuring the confidentiality of the data;
b) IACUC members must not disclose confidential or proprietary information (protocol or investigator specific) to any non-IACUC member;
c) IACUC member must not discuss, or disclose any details of IACUC business (e.g., protocol reviews, non-compliance discussion, subcommittee investigations or reviews, etc.) to third parties without the consent of the IACUC Chair (or in his/her absence the Vice-Chair);
d) Non-IACUC member (e.g. observers, consultants, PIs) attending IACUC meeting must sign confidentiality assurance prior to attending.
e) All IACUC records and sensitive review materials must be filed in a secure location and, if required, disposed of in an appropriate manner, e.g., shredding in accordance to the Ministry of Public Health recordkeeping requirement

3.2.3.3 Quorum Requirements

Minimum of 5 of the regular IACUC voting members must be present at a convened meeting to constitute a quorum. The Chairman of the Committee votes only in the case of tie. The Ministry of Public Health prohibit proxy voting: written or telephone.

3.2.4 Functions of the IACUC

The IACUCs functions are listed below:

a. Review, at least twice annually, the institution's animal care and use program.

b. Inspect the housing and research facilities, at least twice annually, using the Guidelines and international standards (see Appendix I) as a basis for evaluation. The inspection must also cover any Qatari satellite facilities where animals are housed for more than 12 hours and in which surgical manipulations are performed.

c. Prepare and maintain reports of its semi-annual inspections. The reports shall be reviewed and signed by the IACUC chairperson with majority agreement from IACUC members and must include a description of the nature and extent of

compliance with the Guidelines and any minority viewpoints. The reports shall be made available to the Ministry of Public Health upon request.

d. Approve only those project proposals which conform to the Guidelines and carefully consider ethical and welfare aspects, including the 3Rs.

e. Suspend or withdraw approval for any on-going project if it is determined that the project is not being conducted in accordance with the protocol approved by the IACUC.

f. Make recommendations to the Senior Administrator regarding any aspects of the program, facilities, or personnel training.

g. Review and investigate concerns involving the care and use of animals including reports of non-compliance from staff or investigators.

h. Authorize the treatment or humane killing of any animal.

i. Maintain a register of approved projects.

j. Review, at least once annually, approved projects of more than 1 year duration or the maintenance of individual animals for more than 1 year.

k. Provide continuous training for scientists, animal technicians and other personnel involved in animal care, treatment and use.

l. Perform all other duties required by the Guidelines.

3.2.5 IACUC Research Proposals

3.2.5.1 Protocol Review

The IACUC is responsible for ensuring that research activities involving animals are established based on implementation of the guideline. The IACUC must facilitates compliance with Qatari and other applicable laws, regulations and policies by reviewing proposals, overseeing and evaluating all aspects of animal care and use program. IACUC Committee has the authority to approve, require modifications in, disapprove, or table (postpone until future meeting) any proposed activity. The Committee may allow the protocol to be reviewed, and approved, using the Designated Member Review (DMR) process, as described in Chapter 3.2.6.1.2 Approval of the change from FCR to DMR must be unanimous (of a quorum of members, Chapter 3.2.3.3) and is recorded in the minutes. Committee members are given the opportunity to require that the requested modification(s) be brought before the next committee meeting. Under no circumstances will animal work be permitted to initiate or resume until final IACUC approval is obtained in written.

3.2.5.1.1 Applicability

IACUC review is required in medical, biological, behavioral and agricultural testing, research and teaching activities involving vertebrate animals. The following kinds of activities involving animals are subject to review by the IACUC prior to initiation:

- Activities conducted by affiliated personnel;
- Activities performed on the institution facilities;
- Activities performed using institution facilities, animals or equipment

3.2.5.1.2 Exemptions

The following are exempt from IACUC review but must be submitted to IACUC to issue a written exemption letter:

• Use of tissues, organs or other parts of dead animals if received as such; and

• Noninvasive observation of wild animals in their natural habitat. Field studies that involve killing, trapping, banding, darting, implantation of telemetry devices, or any other invasive manipulation of free living and wildlife animals require IACUC and the Ministry of Environment approval (http://www.moe.gov.qa/Arabic/Rules/Pages/204%رقم20%قانون.pdf).

3.2.6 IACUC Protocol Review Criteria

Overview:
In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in compliance with the Ministry of Public Health guideline. An IACUC should review all procedures performed on animal, such as food and water deprivation, use of noxious stimuli, and physical restraint. The Guide provides useful guidance on these and other practices.
In case where the IACUC lack scientific and technical expertise to evaluate all aspects of a proposal, a consultant may be invited to provide information. Such consultant must sign confidentiality assurance, disclose conflict of interest with the research proposal and be excluded during voting process.

3.2.6.1 Protocol Review Procedures
The Institution may develop its own meeting Standard Operating Procedures (SOP) as long as the procedures are in compliance with the requirements of the MOPH guidelines.
The following pertains to review of initial protocols as well as to review of proposed significant changes in previously approved protocols

3.2.6.1.1 Full Committee Review (FCR)
Applicability:

- Initial applications
- Triennial review of proposals completing three years
- Request of major changes in approved protocols, when substantive modifications are required in a protocol to secure approval, the resubmitted protocol must be reviewed using either FCR or DMR

  IACUC approval of “proposed animal activities” or “major changes” to previously approved animal activities is granted after FCR or DMR.
  - “major changes” must be approved by one of the valid IACUC approval methods FCR or DMR, including changes:
    - from non-survival to survival surgery;
    - resulting in greater pain, distress, or degree of invasiveness;
    - in housing and or use of animals in a location that is not part of the animal program overseen by the IACUC;
    - in species;
    - in study objectives;
    - in Principal Investigator (PI); and
    - that impact personnel safety

- The specific major changes may be handled administratively according to IACUC-reviewed and -approved policies in consultation with a veterinarian authorized by the IACUC.

  The veterinarian is not conducting DMR in this case, but is serving as a subject matter expert to verify that compliance with the IACUC-reviewed and -approved policy is appropriate for the animals in this circumstance.

  Consultation with the veterinarian must be documented. The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the parameters of the IACUC-reviewed and -approved policies.

  This includes changes in:

  - anesthesia, analgesia, sedation, or experimental substances;
  - euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals; and
  - duration, frequency, type, or number of procedures performed on an animal

- Changes that may be handled administratively without IACUC-approved policies, consultations, or notifications include:
  - correction of typographical errors;
  - correction of grammar;
  - contact information updates; and
  - change in personnel, other than the PI. (There must be an administrative review to ensure that all such personnel are appropriately identified, adequately trained and qualified, enrolled in occupational health and safety programs, and meet other criteria as required by the IACUC.)

- Protocol involving breeding and holding colony procedures.
- Protocols with procedures involving pain or distress with relieved with anesthetics, analgesics and/or tranquilizer drugs or other methods for relieving pain or distress (Appendix I)
- Protocol involving breeding and holding colony procedures.
- Protocols with procedures involving pain or distress not relieved with anesthetics, analgesics and/or tranquilizer drugs or other methods for relieving pain or distress (Appendix I)

Outline of procedure:

1. Prior to IACUC review, each member of the Committee shall be provided with a list of proposed activities to be reviewed.
2. Written descriptions of all proposed activities that involve the care and use of animals shall be available to all IACUC members, and any member of the IACUC may obtain, upon request, full Committee review of those activities.

3. If full Committee review is not requested, at least one member of the IACUC, designated by the chairman and qualified to conduct the review (DMR), shall review those activities, and shall have the authority to approve, require modifications in (to secure approval), or request full Committee review of any of those activities.
4. If FCR is requested for a proposed activity, approval of that activity may be granted only after review, at a convened meeting of a quorum of the IACUC, and with the approval vote of a majority of the quorum present.
5. No member may participate in the IACUC review or approval of an activity in which that member has a conflicting interest (e.g., is personally involved in the activity), except to provide information requested by the IACUC, nor may a member who has a conflicting interest contribute to the constitution of a quorum;
6. The IACUC may invite consultants to assist in the review of complex issues arising out of its review of proposed activities. Consultants may not approve or withhold approval of an activity, and may not vote with the IACUC unless they are also members of the IACUC;
7. The IACUC shall notify principal investigators and the research facility in writing of its decision to approve or withhold approval of those activities related to the care and use of animals, or of modifications required to secure IACUC approval.
8. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the PI an opportunity to respond in person or in writing.
9. The IACUC may reconsider its decision, with documentation in Committee minutes, in light of the information provided by the PI.

Full committee review of protocols must be held in a convened meeting of a quorum of the members and a majority vote of the members present is required for approval. Proposals being submitted must be distributed among all IACUC members, including alternate and non-voting member(s) at least three (3) business days prior to a meeting. Proposals are assigned a primary reviewer, who has the task of orally presenting the protocol to the rest of the committee for review and discussion. Primary reviewers may contact or invite an investigator for additional information. The investigator must be excluded during discussion and voting stages. To evaluate if the proposed activity causes more than momentary or slight pain or distress to animals, the protocols must be assigned to a veterinarian to conduct an in-depth review of the protocol.

3.2.6.1.2 Designated Member Review (DMR)

Applicability:

- General Amendment Requests
- Administrative Protocols: such as addition or deletion of personnel, change in study title, change in location, are reviewed and approved by IACUC administrative staff members under delegated authority.
- Protocol involving breeding and holding colony procedures.
- Protocols with procedures involving no more than momentary or slight distress or pain and no usage of pain-relieving drugs(Appendix 3)
- Revised protocols that were reviewed by the Full Committee and categorized as Modifications Required to Secure Approval.
- Urgent Reviews: Under certain rare circumstances the IACUC Chair may designate a reviewer for urgent reviews. The investigators must provide compelling reasons for these types of reviews

Outline of procedure:

DMR is part of the general review procedure as mentioned above in the comments.

- For DMR to occur committee members are provided access to the protocol, and then polled to acquiesce to DMR.

- All members have 3 business days to respond to the request. Members who do not respond by the end of 3 business days are deemed to have acquiesced to DMR.

- After the 3 business days have passed, at least one suitably qualified member is appointed by the IACUC Chair to conduct DMR.

- The members assigned DMR may ask questions regarding the protocol without calling it to FCR.

- IACUC members that acquiesce to DMR may also submit comments for the PI to address during the review process, without calling to FCR.

All IACUC members must be provided with protocol documents to evaluate the proposal and vote for FCR or DMR. If one member voted for FCR, the protocol shall be scheduled for next committee meeting to conduct the Full committee review. Failure to respond is considered as voting for DMR.
At least one qualified IACUC member is assigned by the Chairperson (or designee) to conduct the review. These designated member(s) have authority to approve, require modifications in, or request full committee review. A designated reviewer may not withhold approval; this action may only be taken if the review is conducted using the full committee method of review.

3.2.7 Institution Animal Welfare Assurance (Assurance)

1) Each institution engaged in use and care of animal shall provide written Assurances satisfactory to the Ministry of Public Health of the state of Qatar from the institution head, on behalf of the institution, and IACUC members that they will comply with the requirements set forth in this policy.
2) Under no conditions the institutions shall conduct or support researches covered by this policy prior to receiving a written approval on the institution Assurance, and a certification of Institutional Animal Care and Use Committee (IACUC) from the Ministry of Public Health.
3) The institution Assurance letter shall be signed by the Institutional official with the institution logo as header and must include:
    3.1) A statement of principles governing the institution in the discharge of its responsibilities for providing humane care and use of animals for research, testing and teaching purposes. This requirement does not preempt provisions of this policy applicable to institution-supported or regulated research and need not be applicable to any research exempted or waived.
    3.2) A description of the institution's animal care and use program;
    3.3) A list of every branch and major component inside or outside the institution covered by the Assurance;
    3.4) A statement of authority and responsibility of the appointed IACUC to audit and ensure compliance of animal care and use program with this Policy;

3.5) An Institutional Animal Care and Use Committee(s) (IACUC s) membership list established in accordance with the requirements set forth in (chapter 3.2.3) of this guideline; identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, sufficient to describe each member's chief anticipated contributions to IACUC deliberations; and any employment or other relationship between each member and the institution.

Changes in IACUC membership shall be reported to the Institution head, and to the Department of Research, Ministry of Public Health, or any successor office.

3.6) An evidence of training in the humane and ethical practice on applying the 3Rs principles offered to all personnel involved in animal care and use program;

3.7) An occupational health and safety program for animal laboratory personnel and all personnel in contact with animals;

3.8) Details of animal facility including: (i) the number of facilities and laboratories to be used by the registered institution; (ii) the gross square footage of each animal facility (including satellite facilities), the number and type of rooms and the average daily inventory, by species, of animals in each facility; (iii) USDA category (appendix 1) of all species housed in all institution facilities.

3.9) Written procedures which the IACUC will follow for (i) conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (ii) determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IACUC review; and (iii) ensuring prompt reporting to the IACUC of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IACUC approval has already been given, may not be initiated without IACUC review and approval except when necessary to eliminate apparent immediate hazards to the animals.

3.10) Written procedures for ensuring prompt reporting to the IACUC, appropriate institutional officials and oversight bodies, sponsor and the Ministry of Public Health, if needed of: (i) any unanticipated problems involving risks to animals or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IACUC; and (ii) any suspension or termination of IACUC approval.

A Semi-annual evaluation report (for Ministry of Public Health certified IACUC) prepared by the institution IACUC or accrediting body of the institution's animal care and use programs and facilities (including satellite facilities).

3.11) Any other important information requested by the Ministry of Public Health officials.

a. The Assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this policy and shall be filed in such form and manner as the institutional head prescribes.
b. The Institutional head (the person who officially authorized to represent and speaks on behalf of the institution) will evaluate all Assurances submitted in accordance with this policy through such officers and employees of the institution. The institutional head's evaluation will take into consideration the adequacy of the proposed IACUC in light of the anticipated scope of the research activities and the types of subject populations likely to be involved, the

appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution.

c. On the basis of this evaluation, the institutional head may approve or disapprove the Assurance, or enter into negotiations to develop an approvable one. The institutional head may limit the period during which any particular approved Assurance or class of approved Assurances shall remain effective or otherwise condition or restrict approval.
d. An institution with an approved Assurance shall certify that each application or proposal for research covered by the Assurance and by this Policy has been reviewed and approved by the IACUC. Such certification should be submitted with the application or proposal or by such later date as may be prescribed by the institution to which the application or proposal is submitted. Under no condition shall research covered by the Policy be supported or conducted prior to receipt of the certification that the research has been reviewed and approved by the IACUC.
e. The Assurance is valid for 3 years.

3.2.8 Responsibilities of the Institution's Staff and Investigators

3.2.8.1 Liability

Under the Qatari Policy, the primary responsibility for meeting applicable law and guideline rests with the research facility and awardee institution. The Institutional Official (IO) is the individual held responsible on behalf of the research facility for ensuring compliance. Failure to comply with the Ministry of Public Health guideline and the state of Qatar Policy could result institution's Animal Welfare Assurance and IACUC Certification withdrawal, thereby making the institution ineligible to use, conduct, or receive funds for activities involving animals.

3.2.8.2 Staff

Staff working with animals should be appropriately trained and instructed in their duties in the care and use of the animals. Staff should be instructed in how to recognize at an early stage, changes in animal behavior and health.

3.2.8.3 Staff in charge

The Staff member with overall supervision of general animal care at the institution is the Staff-in charge. The Staff-in-charge must have appropriate veterinary or animal care qualifications or experience. The Staff-in-charge should be responsible for:

(a) Managing the day-to-day care of animals in holding and breeding facilities;

(b) Supervising the work of personnel in the facility;

(c) Liaising between investigators, teachers and facility personnel; and

(d) Communicating with the IACUC on management of the facility and any adverse incidents.

The Staff-in-charge should be knowledgeable about signs of pain, distress and illness specific to each animal species kept and ensure that the wellbeing of all animals is regularly assessed.
After animals are allocated to a project, investigators and teachers have primary responsibility for ensuring adequate monitoring of animal wellbeing. The Staff-in-charge must be familiar with the Guidelines and with the institution's animal care policies and procedures.
Written procedures must be established for the management and care of animals. These procedures should take into account the requirements of the species and the experiments being

conducted. For detailed standards, see Appendix I. The Staff-in-charge must maintain adequate records to allow effective management of the breeding stock including the detection of the origin and spread of disease.

Daily Records maintained must be made available to Investigators, IACUCs and the Ministry of Public Health.

3.2.8.4 Investigators

Investigators have an ethical and professional obligation to follow all the requirements of the Guidelines and to ensure the welfare of the animals under their control.
They should ensure that the extent of supervision is compatible with the level of competence of staff and the responsibilities they are given. Protocols must be in place for the Staff-in-charge to effectively communicate with the Investigator regarding animal welfare and research concerns.
Investigators should consult with the veterinarian or their designee whenever adverse effects occur, to ensure that veterinary care and treatment regimes are promptly implemented.

3.2.9 Special Considerations for IACUC review

Certain animal use protocols include procedures or approaches that require special consideration during the IACUC review process due to their potential for unrelieved pain or distress or other animal welfare concerns. The topics below are some of the most common requiring special IACUC consideration. For these and other areas the IACUC is obliged to weigh the objectives of the study against potential animal welfare concerns. By considering opportunities for refinement, the use of appropriate non animal alternatives, and the use of fewer animals, both the institution and the principal investigator (PI) can begin to address their shared obligations for humane animal care and use.

3.2.9.0 Cooperative research

Cooperative research projects are those projects covered by this policy which involve collaborations between more than one institution. This collaboration is governed by legal written agreement, contract or memorandum of understanding addressing that each institution is responsible for health and welfare of animals and for complying with this policy. With the approval of the department or institutional head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another registered IACUC, or make similar arrangements for avoiding duplication of effort.

Research collaboration with foreign institutions must provide IACUC approval from the foreign institution as well as IACUC approval from the Qatari institution to the funding body.

3.2.9.1 Experimental and Humane Endpoints

The experimental endpoint of a study occurs when the scientific aims and objectives have been reached. The humane endpoint is the point at which pain or distress in an experimental animal is prevented, terminated, or relieved. The use of humane endpoints contributes to refinement by providing an alternative to experimental endpoints that result in unrelieved or severe animal pain and distress, including death. The humane endpoint should be relevant and reliable. For many invasive experiments, the experimental and humane endpoints are closely linked and should be carefully considered during IACUC protocol review. While all studies should employ endpoints that are humane, studies that commonly require special consideration include those that involve tumor models, infectious diseases, vaccine challenge, pain modeling, trauma, production of monoclonal antibodies, assessments of toxicologic effects, organ or system failure, and models of cardiovascular shock.

The PI, who has precise knowledge of both the objectives of the study and the proposed model, should identify, explain, and include in the animal use protocol a study endpoint that is both humane and scientifically sound. The identification of humane endpoints is often challenging, however, because multiple factors must be weighed, including the model, species (and sometimes strain stock), animal health status, study objectives, institutional policy, regulatory requirements, and occasionally conflicting scientific literature. Determination of humane endpoints should involve the PI, the veterinarian, and the IACUC, and should be defined when possible before the start of the study.
Information that is critical to the IACUC's assessment of appropriate endpoint consideration in a protocol includes precise definition of the humane endpoint (including assessment criteria), the frequency of animal observation, training of personnel responsible for assessment and recognition of the humane endpoint, and the response required upon reaching the humane endpoint. An understanding of preemptive euthanasia, behavioral or physiologic definitions of the moribund state (ibid.), and the use of study specific animal assessment records can aid the PI and IACUC when considering or developing proposed endpoints. 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, IACUC, and veterinarian. A system for communication with the IACUC should be in place both during and after such studies. Numerous publications address specific proposals for the application and use of humane endpoints.

3.2.9.2 Unexpected Outcomes

Unexpected outcomes fundamental to scientific research is the investigation of novel experimental variables. Because of the potential for unexpected outcomes that may affect animal well-being when highly novel variables are introduced, more frequent monitoring of animals may be required. Condition that negatively affects animal well-being should be reported to the IACUC, and more extensive analysis may be required to better define the phenotype.

3.2.9.3 Restrain Guidance

The following are important guidelines for restraint:
• Restraint devices should not be considered a normal method of housing, and must be justified in the animal use protocol.
• Restraint devices should not be used simply as a convenience in handling or managing animals.
• Alternatives to physical restraint should be considered.
• The period of restraint should be the minimum required to accomplish the research objectives.
• Animals to be placed in restraint devices should be given training (with positive reinforcement) to adapt to the equipment and personnel.
• Animals that fail to adapt should be removed from the study.
• Provision should be made for observation of the animal at appropriate intervals, as determined by the IACUC.
• Veterinary care must be provided if lesions or illnesses associated with restraint are observed. The presence of lesions, illness, or severe behavioral change often necessitates the temporary or permanent removal of the animal from restraint.
• The purpose of the restraint and its duration should be clearly explained to personnel involved with the study.

3.3 Monitoring of Approved Protocols

3.3.1 Continuing Review: The Annual Review

3.3.1.1 IACUC Recordkeeping requirements

The Institution's Senior Administrator shall maintain:

a. Copy of the Assurance which has been approved by the Ministry of Public Health;
b. Minutes of IACUC meetings, including records of attendance, decisions, recommendations;
c. Records of other aspects of the IACUC's operation.
d. Records of semi-annual IACUC reports and recommendations.

All records and reports shall be maintained for at least three years beyond the project's duration. All records that relate directly to a project shall be maintained for the duration of the project and for an additional three years after completion of the project. Records can be maintained in an electronic format.

All records shall be available for inspection and copying by the Ministry of Public Health.

3.3.2.1 IACUC Reporting Requirements

3.3.2.1 Prompt Report to the Ministry of Public Health

The institutional official is obligated to promptly report in written- no more than 30 days - to the Ministry of Public Health any of the followings:

a. Changes in the institution's program or facilities which would place the institution in a different category than specified in its Assurance;
b. Changes in the IACUC membership and
c. Serious or continuing non-compliance with the *guideline.*
d. Suspension of an activity by the IACUC.

3.3.2.2 Annual reporting to the Ministry of Public Health

At least once every 12 months the Senior Administrator shall report in writing to the Ministry of Public Health on the use of animals for scientific purposes at the facility, including the following:

a. Demonstrate that the Guidelines, including the principles of 3Rs, are being complied with by the IACUC, investigators and staff;
b. Details of any exceptions to compliance with Guidelines and the reasons for noncompliance;
c. The names and qualifications of all IACUC members;
d. The name(s) of Attending Veterinarian(s) and whether they are engaged on a full-time or part-time basis;
e. The location of all facilities where animals are housed, used or held for scientific activities;
f. The common names and numbers of animals used for scientific activities at each facility during the prior 12 month period;

g. The common names and numbers of animals being bred, conditioned, or held for scientific activities at each facility but not yet used for procedures;

h. The dates of facility reviews and inspections conducted by the IACUC;

i. Any significant deficiencies identified in the annual program reviews and facility inspections conducted by the IACUC, and whether the actions taken to correct these deficiencies were implemented as described in the IACUC reports;

3.3 Post-approval Monitoring (PAM)

Continuing IACUC oversight of animal activities is required by the Ministry of Public Health regulations, and policies. A variety of mechanisms can be used to facilitate ongoing protocol assessment and regulatory compliance. Post approval monitoring (PAM) is considered here in the broadest sense, consisting of all types of protocol monitoring after the IACUC's initial protocol approval. PAM helps ensure the well-being of the animals and may also provide opportunities to refine research procedures. Methods include continuing protocol review; laboratory inspections (conducted either during regular facilities inspections or separately); veterinary or IACUC observation of selected procedures; observation of animals by animal care, veterinary, and IACUC staff and members; and external regulatory inspections and assessments. The IACUC, veterinary, animal care, and compliance staff may all conduct PAM, which may also serve as an educational tool.

Continuing protocol review typically consists of an annual update or review as well as the triennial review required by The Ministry of Public Health. The depth of such reviews varies from a cursory update to a full committee review of the entire protocol. Annual review may be used as an opportunity for the investigator to submit proposed amendments for future procedures, to provide a description of any adverse or unanticipated events, and to provide updates on work progress.

The Ministry of Public Health guidelines and institution assurance require the IACUC to inspect animal care and use facilities, including sites used for animal surgeries, every 6 months. As part of a formal PAM program some institutions combine inspection of animal study sites with concurrent review of animal protocols. Based on risks to animals and their handlers, other study areas may require more or less frequent inspections. Examples of effective monitoring strategies include:

• examination of surgical areas, including anesthetic equipment, use of appropriate aseptic technique, and handling and use of controlled substances
• review of protocol-related health and safety issues
• review of anesthetic and surgical records
• regular review of adverse or unexpected experimental outcomes affecting the animals
• observation of laboratory practices and procedures and comparison with approved protocols.

Institutions may also consider the use of veterinary staff and/or animal health technicians to observe increased risk procedures for adverse events (e.g., novel survival surgeries, pain studies, tumor growth studies) and report their findings for review by the IACUC. The level of formality and intensity of PAM should be tailored to institutional size and complexity, and in all cases should support a culture of care focusing on the animals' well-being. Regardless of the methods used or who conducts and coordinates the monitoring, PAM programs are more likely to succeed when the institution encourages an educational partnership with investigators

3.4 Disaster Planning and Emergency Preparedness

Animal facilities may be subject to unexpected conditions that result in the catastrophic failure of critical systems or significant personnel absenteeism, or other unexpected events that severely compromise ongoing animal care and well-being. Facilities must therefore have a disaster plan. The plan should define the actions necessary to prevent animal pain, distress, and deaths due to loss of systems such as those that control ventilation, cooling, heating, or provision of potable water. If possible the plan should describe how the facility will preserve animals that are necessary for critical research activities or are irreplaceable. Knowledge of the geographic locale may provide guidance as to the probability of a particular type of disaster.
Disaster plans should be established in conjunction with the responsible investigator(s), taking into consideration both the priorities for triaging animal populations and the institutional needs and resources. Animals that cannot be relocated or protected from the consequences of the disaster must be humanely euthanized. The disaster plan should identify essential personnel who should be trained in advance in its implementation. Efforts should be taken to ensure personnel safety and provide access to essential personnel during or immediately after a disaster. Such plans should be approved by the institution and be part of the overall institutional disaster response plan that is coordinated by the IO or another senior-level administrator.

All institution must include in the manual a section that describes actions taken when unexpected conditions that could jeopardize the health and welfare of animals and personnel take place. Disaster and emergency plan must define:

(a) Actions needed to prevent animal pain, distress and death
(b) replaceable animal facility and resources
(c) Measures to ensure personal safety and security

4 Environment, Housing and Management

This chapter provides guidelines for the environment, housing, and management of laboratory animals used or produced for research, testing, and teaching both terrestrial and aquatic. The design of animal facilities combined with appropriate animal housing and management are essential contributors to animal well-being, the quality of animal research and production, teaching or testing programs involving animals, and the health and safety of personnel.

4.1 Terrestrials Animals

4.1.1 Terrestrial Environment

The *microenvironment* of a terrestrial animal is the physical environment immediately surrounding it i.e. the primary enclosure such as the cage, pen or stall. It contains all the resources with which the animals come directly in contact and also provides the limits of the animals' immediate environment. The microenvironment is characterized by several factors, including illumination, noise, vibration, temperature, humidity, and gaseous and particulate composition of the air. *Evaluation of the microenvironment* of small enclosures can be difficult. Evaluation criteria are the temperature, humidity, and concentrations of gases and particulate matter.

4.1.1.1 Temperature and Humidity

Maintenance of body temperature within normal circadian variation is necessary for animal well-being. Animals should be housed within temperature and humidity ranges appropriate for the species, to which they can adapt with minimal stress and physiologic alteration. Dry-bulb temperatures in animal rooms should be set below the animals' lower critical temperature (LCT) to avoid heat stress. This, in turn, means that animals should be provided with adequate resources for thermoregulation (nesting material, shelter) to avoid cold stress.

Environmental temperature and relative humidity can be affected by husbandry and housing design. Factors that contribute to variation in temperature and humidity between and within enclosures include housing design; construction material; enrichment devices such as shelters and nesting material; use of filter tops; number, age, type, and size of the animals in each enclosure; forced ventilation of enclosures; and the type and frequency of contact bedding changes. Exposure to wide temperature and humidity fluctuations or extremes may result in behavioral, physiologic, and morphologic changes, which might negatively affect animal well-being and research performance as well as outcomes of research protocols.

In climates where it is difficult to provide a sufficient level of environmental relative humidity, animals should be closely monitored for negative effects such as excessively flaky skin, ecdysis (molting) difficulties in reptiles, and desiccation stress in semiaquatic amphibians

4.1.1.2 Ventilation and Air Quality

The primary purpose of ventilation is to provide appropriate air quality and a stable environment for animals. The successful operation of any heating, ventilation and air-conditioning system requires regular preventive maintenance and evaluation, including measurement of its function at the level of the secondary enclosure. Such measurements should include supply and exhaust air volumes, fluctuation in temperature and relative humidity, and air pressure differentials between spaces as well as critical mechanical operating parameters.

4.1.1.3 Illumination

Light can affect the physiology, morphology, and behavior of various animals. Numerous factors can affect animals' needs for light and should be considered when an appropriate illumination level is being established for an animal holding room. These include light intensity and

wavelength as well as the duration of the animal's current and prior exposure to light, and the animal's pigmentation, circadian rhythm, body temperature, hormonal status, age, species, sex, and stock or strain.
In general, lighting should be diffused throughout an animal holding area and provide sufficient illumination for the animals' well-being while permitting good housekeeping practices, adequate animal inspection including for the bottom-most cages in racks, and safe working conditions for personnel.

4.1.1.4 Noise and Vibration

Noise produced by animals and animal care activities is inherent in the operation of an animal facility and noise control should be considered in facility design and operation. Assessment of the potential effects of noise on an animal warrants consideration of the intensity, frequency, rapidity of onset, duration, and vibration potential of the sound and the hearing range, noise exposure history, and sound effect susceptibility of the species, stock, or strain.

4.1.2 Terrestrial Housing

Appropriate housing strategies for a particular species should be developed and implemented by the animal care management, in consultation with the animal user and veterinarian, and reviewed by the IACUC. Housing should provide for the animals' health and well-being while being consistent with the intended objectives of animal use. Expert advice should be sought when new species are housed or when there are special requirements associated with the animals or their intended use (e.g., genetically modified animals, invasive procedures, or hazardous agents). Objective assessments should be made to substantiate the adequacy of the animal's environment, housing, and management. Whenever possible, routine procedures for maintaining animals should be documented to ensure consistency of management and care.

4.1.2.1 Environmental Enrichment

Enrichment programs should be reviewed by the IACUC, researchers, and veterinarian on a regular basis to ensure that they are beneficial to animal well-being and consistent with the goals of animal use. They should be updated as needed to ensure that they reflect current knowledge. Personnel responsible for animal care and husbandry should receive training in the behavioral biology of the species they work with to appropriately monitor the effects of enrichment as well as identify the development of adverse or abnormal behaviors.

4.1.2.2 Space

Space allocations should be assessed, reviewed, and modified as necessary by the IACUC considering the performance indices (e.g., health, reproduction, growth, behavior, activity, and use of space) and special needs determined by the characteristics of the animal strain or species (e.g., obese, hyperactive, or arboreal animals) and experimental use (e.g., animals in long-term studies may require greater and more complex space).

4.1.3 Terrestrial Management

Animal Activity typically implies motor activity but also includes cognitive activity and social interaction. Animals' natural behavior and activity profile should be considered during evaluation of suitable housing or behavioral assessment. Social Environment Appropriate social interactions among members of the same species (conspecifics) are essential to normal development and wellbeing. Single housing of social species should be the exception and justified based on experimental requirements or veterinary-related concerns about animal well-being. In these cases, it should be limited to the minimum period necessary, and where possible, visual, auditory, olfactory, and tactile contact with compatible conspecifics should be provided. In the absence of other animals, enrichment should be offered such as positive

interaction with the animal care staff and additional enrichment items or addition of a companion animal in the room or housing area. The need for single housing should be reviewed on a regular basis by the IACUC and veterinarian.

4.2 Aquatic Animals

The variety of needs for fish and aquatic or semiaquatic reptiles and amphibians is as diverse as the number of species considered. This section is intended to provide facility managers, veterinarians, and IACUCs with basic information related to the management of aquatic animal systems.

4.2.1 Aquatic Environment

The microenvironment of an aquatic animal is the physical environment immediately surrounding it—the primary enclosure such as the tank, raceway, or pond. It is characterized by the water quality, illumination, noise, vibration, and temperature.

Water Quality

Water quality is essential to aquatic animal wellbeing. Water quality parameters and life support systems for aquatic animals will vary with the species, life stage, the total biomass supported, and the animals' intended use. Characteristics of the water that may affect its appropriateness include temperature, pH, alkalinity, nitrogen waste products (ammonia, nitrite, and nitrate), phosphorus, chlorine/bromine, oxidation-reduction potential, conductivity/salinity, hardness (osmolality/dissolved minerals), dissolved oxygen, total gas pressure, ion and metal content, and the established microbial ecology of the tank.

Standards for acceptable water quality, appropriate parameters to test, and testing frequency should be identified at the institutional level and/or in individual animal use protocols depending on the size of the aquatic program. Staff managing aquatic systems need to be trained in biologically relevant aspects of water chemistry, how water quality parameters may affect animal health and well-being, how to monitor water quality results, and how water quality may affect life support system function.

Life Support system

Life support system refers to the physical structure used to contain the water and the animals as well as the ancillary equipment used to move and/or treat the water. There are three general categories: recirculating systems where water (all or part) is moved around a system, flow through systems where water is constantly replaced, or static systems where water is stationary and periodically replenished or replaced

5 Veterinary Care

The primary focus of the veterinarian is to oversee the well-being and clinical care of animals used in research, testing, teaching, and production. This responsibility extends to monitoring and promoting animal well-being at all times during animal use and during all phases of the animal's life. The number, species, and use of animals housed in an institution may influence the complexity of the veterinary care program, but a veterinary program that offers a high quality of care and ethical standards must be provided, regardless of the number of animals or species maintained. An adequate veterinary care program consists of assessment of animal well-being and effective management of

- Facilities, personnel and equipment
- Animal procurement and transportation
- Animal quarantine and surveillance
- Preventive medicine (including quarantine, animal biosecurity, and surveillance)
- Clinical disease, disability, or related health issues
- Protocol-associated disease, disability, and other sequelae
- Pre-operative, Surgery and post-operative care
- Pain and distress
- Anesthesia and analgesia
- Euthanasia

The veterinary care program is the responsibility of the attending veterinarian (AV), who is certified or has training or experience in laboratory animal science and medicine or is otherwise qualified in the care of the species being used. Some aspects of the veterinary care program can be conducted by persons other than a veterinarian, but a mechanism for direct and frequent communication should be established to ensure that timely and accurate information is conveyed to the responsible veterinarian about issues associated with animal health, behavior, and well-being, and that appropriate treatment or euthanasia is administered. The AV should provide guidance to investigators and all personnel involved in the care and use of animals to ensure appropriate husbandry, handling, medical treatment, immobilization, sedation, analgesia, anesthesia, and euthanasia. In addition, the AV should provide guidance and oversight to surgery programs and perioperative care involving animals.

5.1 Animal Procurement and Transportation

5.1.1 Procurement

Before procuring animals, the principal investigator should confirm that there are sufficient facilities and expertise to house and manage the species being acquired. Procurement of animals should be linked to the prior approval of animal use and number by the IACUC (see Chapter 1, Protocol Review). Potential vendors should be evaluated for the quality of animals they supply. As a rule, vendors of purpose-bred animals regularly provide information that describes the genetic and pathogen status of their colonies or individual animals and relevant clinical history (e.g., vaccination status and anthelminthic administration). The use of purpose-bred and preconditioned animals is therefore preferable when consistent with the research, teaching, and testing objectives. Attention should also be given to the population status of the species under consideration; the threatened or endangered status of species is updated annually by the Fish and Wildlife Service. Appropriate records and other forms of documentation should be maintained for animals acquired by an institution for its investigators.

5.1.2 Transportation

Animal transportation is governed by the Ministry of Environment (MOE) according to Veterinary quarantine law and the international standards [i.e. International Air Transport Association (IATA)] for interstate and export/import transportation of regulated species.;
Any institution intent to import or export any type of animals they should contact the Department of Animal Resources at MOE to issue importation/exportation certificates.
(http://www.moe.gov.qa/English/SitePages/PublicServices.aspx).

5.2 Preventive Medicine

Disease prevention is an essential component of comprehensive veterinary medical care and biosecurity programs. Preventive medicine programs consist of policies, procedures, and equipment related to quarantine and stabilization and the separation of animals by species, source, and health status.
All animals should be observed for signs of illness, injury, or abnormal behavior by a person trained to recognize such signs. As a rule, such observation should occur at least daily, but more frequent observations may be required, such as during postoperative recovery, when animals are ill or have a physical deficit, or when animals are approaching a study endpoint. Professional judgment should be used to ensure that the frequency and character of observations minimize risks to individual animals and do not compromise the research for which the animals are used.
Appropriate procedures should be in place for disease surveillance and diagnosis. Unexpected deaths and signs of illness, distress, or other deviations from normal in animals should be reported promptly and investigated, as necessary, to ensure appropriate and timely delivery of veterinary medical care. Animals that show signs of a contagious disease should be isolated from healthy animals. If an entire room or enclosure of animals is known or believed to be exposed to an infectious agent (e.g., Mycobacterium tuberculosis in nonhuman primates), the group should be kept intact during the process of diagnosis, treatment, and control.
Healthy, well-cared-for animals are a prerequisite for good-quality animal-based science. The structure of the veterinary care program, including the number of qualified veterinarians, should be appropriate to fulfill the program‘s requirements, which will vary by institution, species used, and the nature of the animal use. To be effective in providing clinical care, the veterinarian should be familiar with the species and various uses of animals in the institutional research, teaching, testing, or production programs and have access to medical and experimental treatment records.
For animals on research protocols, the veterinarian or veterinarian’s designee should make every effort to discuss any problems with the principal investigator or project director to jointly determine the most appropriate course of treatment or action. Standard operating procedures (SOPs) may be developed for recurrent health conditions to expedite treatment. Recurrent or significant problems involving experimental animal health should be communicated to the IACUC, and all treatments and outcomes should be documented.

5.3 Clinical Care and Management

There should be a timely and accurate method for communication of any abnormalities in or concerns about animal health, behavior, and wellbeing to the veterinarian or the veterinarian’s designee. The responsibility for communicating these concerns rests with all those involved with animal care and use. Reports should be triaged to ensure that animals most in need receive priority attention, and the veterinarian or veterinarian’s designee should perform an objective assessment of the animal(s) to determine an appropriate course of action.

Well-planned experiments with clearly delineated scientific and humane endpoints will help to ensure that a contingency plan is in place for problems that may arise during the study (see Chapter 2, Experimental and Humane Endpoints). For animals on research protocols, the veterinarian or veterinarian's designee should make every effort to discuss any problems with the principal investigator or project director to jointly determine the most appropriate course of treatment or action. Standard operating procedures (SOPs) may be developed for recurrent health conditions to expedite treatment. Recurrent or significant problems involving experimental animal health should be communicated to the IACUC, and all treatments and outcomes should be documented (USDA).

Procedures must be in place to provide for emergency veterinary care both during and outside of regularly scheduled hours. Such procedures must enable animal care and research staff to make timely reports of animal injury, illness, or death. A veterinarian or the veterinarian's designee must be available to expeditiously assess the animal's condition, treat the animal, investigate an unexpected death, or advise on euthanasia. In the case of a pressing health problem, if the responsible person (e.g., investigator) is not available or if the investigator and veterinary staff cannot reach consensus on treatment, the veterinarian must have the authority, delegated by senior administration (see Chapter 2, Institutional Official and Attending Veterinarian) and the IACUC, to treat the animal, remove it from the experiment, institute appropriate measures to relieve severe pain or distress, or perform euthanasia if necessary.

Medical records are a key element of the veterinary care program and are considered critical for documenting animal well-being as well as tracking animal care and use at a facility. A veterinarian should be involved in establishing, reviewing, and overseeing medical and animal use records. All those involved in animal care and use must comply with federal laws and regulations regarding human and veterinary drugs and treatments. Drug records and storage procedures should be reviewed during facility inspections.

5.4 Surgery

Surgical outcomes should be continually and thoroughly assessed to ensure that appropriate procedures are followed and timely corrective changes are instituted. Modification of standard techniques may be required (for instance, in aquatic or field surgery), but should not compromise the well-being of the animals. In the event of modification, close assessment of outcomes may have to incorporate criteria other than clinical morbidity and mortality. Such assessments rely on continuing communication among technical staff, investigators, veterinarians, and the IACUC.

Researchers conducting surgical procedures must have appropriate training to ensure that good surgical technique is practiced. The IACUC, together with the AV, is responsible for determining that personnel performing surgical procedures are appropriately qualified and trained in the procedures.

Pre-surgical planning should specify the requirements for postsurgical monitoring, care, and recordkeeping, including the personnel who will perform these duties. The investigator and veterinarian share responsibility for ensuring that postsurgical care is appropriate.

Unless an exception is specifically justified as an essential component of the research protocol and approved by the IACUC, aseptic surgery should be conducted in dedicated facilities or spaces.

5.5 Pain and Distress

An integral component of veterinary medical care is prevention or alleviation of pain associated with procedural and surgical protocols. Pain is a complex experience that typically results from

stimuli that damage or have the potential to damage tissue; such stimuli prompt withdrawal and evasive action.
Pain is a stressor and, if not relieved, can lead to unacceptable levels of stress and distress in animals. Furthermore, unrelieved pain may lead to “wind-up,” a phenomenon in which central pain sensitization results in a pain response to otherwise non painful stimuli. For these reasons, the proper use of anesthetics and analgesics in research animals is an ethical and scientific imperative. Recognition and Alleviation of Pain in Laboratory Animals (NRC 2009a) is an excellent source of information about the basis and control of distress and pain (see also Appendix 3, Anesthesia, Pain, and Surgery).

5.6 Anesthesia and Analgesia

The selection of appropriate analgesics and anesthetics should reflect professional veterinary judgment as to which best meets clinical and humane requirements as well as the needs of the research protocol. The selection depends on many factors, such as the species, age, and strain or stock of the animal, the type and degree of pain, the likely effects of particular agents on specific organ systems, the nature and length of the surgical or pain-inducing procedure, and the safety of the agent, particularly if a physiologic deficit is induced by a surgical or other experimental procedure. Preemptive analgesia (the administration of preoperative and intraoperative analgesia) enhances intraoperative patient stability and optimizes postoperative care and well-being by reducing postoperative pain. Analgesia may be achieved through timely enteral or parenteral administration of analgesic agents as well as by blocking nociceptive signaling via local anesthetics (e.g., bupivacaine).
Some classes of drugs such as sedatives, anxiolytics, and neuromuscular blocking agents may not provide analgesia but may be useful when used in combination with appropriate analgesics and anesthetics to provide balanced anesthesia and to minimize stress associated with perioperative procedures. Neuromuscular blocking agents (e.g., pancuronium) are sometimes used to paralyze skeletal muscles during surgery in which general anesthetics have been administered; because this paralysis eliminates many signs and reflexes used to assess anesthetic depth, autonomic nervous system changes (e.g., sudden changes in heart rate and blood pressure) can be indicators of pain related to an inadequate depth of anesthesia. It is imperative that any proposed use of neuromuscular blocking drugs be carefully evaluated by the veterinarian and IACUC to ensure the well-being of the animal. Acute stress is believed to be a consequence of paralysis in a conscious state and it is known that humans, if conscious, can experience distress when paralyzed with these drugs. If paralyzing agents are to be used, the appropriate amount of anesthetic should first be defined on the basis of results of a similar procedure using the anesthetic without a blocking agent.

5.7 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, methods should be consistent with the AVMA Guidelines on Euthanasia. In evaluating the appropriateness of methods, some of the criteria that should be considered are 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 emotional effect on personnel.
Euthanasia may be planned and necessary at the end of a protocol or as a means to relieve pain or distress that cannot be alleviated by analgesics, sedatives, or other treatments. Criteria for euthanasia include protocol-specific endpoints (such as degree of a physical or behavioral

deficit or tumor size) that will enable a prompt decision by the veterinarian and the investigator to ensure that the endpoint is humane and, whenever possible, the scientific objective of the protocol is achieved (see Chapter 2). Standardized methods of euthanasia that are predictable and controllable should be developed and approved by the AV and IACUC. Euthanasia should be carried out in a manner that avoids animal distress. Automated systems for controlled and staged delivery of inhalants may offer advantages for species killed frequently or in large numbers, such as rodents. Special consideration should be given to euthanasia of fetuses and larval life forms depending on species and gestational age.

It is essential that euthanasia be performed by personnel skilled in methods for the species in question and in a professional and compassionate manner. Special attention is required to ensure proficiency when a physical method of euthanasia is used. Death must be confirmed by personnel trained to recognize cessation of vital signs in the species being euthanized. A secondary method of euthanasia (e.g., thoracotomy or exsanguination) can be also used to ensure death. All methods of euthanasia should be reviewed and approved by the veterinarian and IACUC.

Euthanizing animals is psychologically difficult for some animal care, veterinary, and research personnel, particularly if they perform euthanasia repetitively or are emotionally attached to the animals being euthanized. When delegating euthanasia responsibilities, supervisors should be sensitive to this issue.

6. Animal Research Non-Compliance

To determine whether an issue should be classified as non-compliance, the IACUC shall initiate an investigation involving the Principal Investigator (PI), the investigative staff, and the Laboratory Animal Research Center (LARC), if appropriate. If the activity in question is determined to be non-compliant, it will be categorized based on its severity. A Compliance Report will be presented to the IACUC, and necessary corrective actions will be taken.

6.1 Minor non-compliance

Minor non-compliance typically arises in instances where protocol has been violated but the risk of harm to researchers or animals is minimal and the IACUC authority or function has not been compromised. Minor non-compliance can often be corrected at the institutional level.

Examples of Minor non-compliance include, but are not limited to:

- Not informing the IACUC of the addition of personnel;
- Not maintaining surgical and post-operative care records per IACUC policy and/or protocol requirements;
- Failure to respond to a “Health Check” card and address the problem or failure to monitor the animals adequately following invasive procedures;
- Use of an unapproved procedure area resulting in failure of the IACUC to inspect this area as required by law or policy;
- Failure to observe approved timeframe for animals to be in off-site areas (i.e. laboratories);
- Personnel not attending training within the required time frame or not maintaining updated occupational health forms;
- Personnel accessing facilities without authorization;

- Inadequate controlled substance logs or controlled substance storage;
- Unapproved transfer of animals from one protocol to another;
- Improper or unapproved animal transportation;
- Not following safety procedures when working in BSL-2 or lower such as not wearing appropriate personal protective equipment;
- Housing animals in a lab without approval or over the time limit approved in the protocol;
- Inadequate housing conditions, e.g. overcrowded cages, weaning delays, or failure to separate aggressive animals as required;
- Minor protocol deviation which does not significantly compromise animal welfare.
- Use of or failure to dispose of expired drugs;
- Use of expired medical materials without IACUC approval.

Consequences and Resolution of Minor Incidents

- First notification: The PI will be required to provide a written response regarding how the incident occurred, how it was corrected and how it will be prevented in the future. This response will be reviewed by the IACUC, and the IACUC may also require additional steps including retraining of investigative staff member(s).

- Second notification: Possible revocation of animal ordering or facility access privileges depending upon the circumstances and the response of the PI. The PI may be required to appear before the IACUC or a subcommittee of the IACUC.

- Third notification: The Non-compliance may be reclassified as significant. If reclassified, it may result in any potential consequences of significant non-compliance.

6.2 Significant non-compliance

Significant non-compliance indicates a serious breach of national regulations, or university policy which comprises the function of the IACUC or puts researchers or animals at risk of undue harm.

Examples of Significant non-compliance include, but are not limited to:

- Acquiring animals for research or performing unapproved procedures without the IACUC approval
- Performing a procedure in such a manner that animals endure pain or suffering that is not addressed by the approved protocol
- Performing a procedure with improper technique or safeguards which puts either the staff or animals at risk
- Failure to adhere to proper aseptic technique for survival surgery
- Repeated or willful incidents of minor non-compliance
- Failure to provide adequate anesthesia or analgesia according to protocol

Consequences and Resolution of Significant Incidents

1. If an occurrence of non-compliance directly results in a significant negative impact to animal welfare, the Attending Veterinarian or the IACUC Chair or their designate(s) have the authority to immediately stop all procedures necessary to protect the health and welfare of the animals. The PI will be contacted as soon as possible and the matter will be referred to the IACUC and Institutional Official for further investigation.
2. An IACUC subcommittee may recommend a corrective action, and a majority vote by a quorum of IACUC members will decide on a corrective action and may vote on protocol suspension, revocation of research privileges, or other sanctions.

3. If the IACUC votes for protocol suspension, all procedures and ordering privileges encompassed by that protocol must cease during the period of suspension.

4. If a protocol is suspended, the PI and his/her department chair will be contacted as soon as possible and a letter will be sent to the PI from the IACUC that requires a response regarding corrective action and future preventive measures.

5. The PI also may be asked to meet with the IACUC, the IACUC Chair and/or the Institutional Official as a condition of reinstatement. Animals housed under Suspended protocols will be transferred to the LARC holding protocol.

6. A majority vote of the IACUC with a quorum present, in consultation with the Institutional Official, may lift a suspension only after it has been determined that the protocol's activities can be accomplished in full compliance.

6.3 Governmental Reporting of Non-Compliance

In the event of an incident of significant non-compliance, during the initial investigation the IACUC will determine the extent of the non-compliance. Incidents of significant non-compliance that are deemed serious or continuing or represent a serious deviation from the provisions of the Policy, including suspensions, will require reporting to MOPH through the Institutional Official and may be reported to the funding agency supporting the activity.

7 Animal Facility

A properly maintained and managed facility is an important element of humane animal care and use. The design and size of an animal facility depend on the scope of institutional research activities, the animals to be housed, the physical relationship to the rest of the institution, and the geographic location. Animal facilities as well as modular units (such as custom-designed trailers or prefabricated structures) should be designed and constructed in accord with all applicable building codes and comply with construction guidelines.

7.1 Location

Quality animal management and human comfort and health protection require separation of animal facilities from personnel areas, such as offices and conference rooms. Careful planning should make it possible to place animal housing areas next to or near research laboratories but separated from them by barriers, such as entry locks, corridors, or floors. Additional

considerations include the impact of noise and vibration generated from within the facility and from surrounding areas of the building, as well as security of the facility.
Animals should be housed in facilities dedicated to or assigned for that purpose, not in laboratories merely for convenience. If animals must be maintained in a laboratory to satisfy the scientific aims of a protocol, that space should be appropriate to house and care for the animals and its use limited to the period during which it is required. If needed, measures should be taken to minimize occupational hazards related to exposure to animals both in the research area and during transport to and from the area.

7.2 Functional Areas

The size, nature, and intensity of an institutional Program (see Chapter 2) will determine the specific facility and support functions needed.
Space is required for the following:
• animal housing, care, and sanitation
• Receipt, quarantine, separation, and/or re-derivation of animals
• separation of species or isolation of individual projects when necessary
• storage.

Most multipurpose animal facilities may also include the following:

• specialized laboratories or space contiguous with or near animal housing areas for such activities as surgery, intensive care, necropsy, irradiation, preparation of special diets, experimental procedures, behavioral testing, imaging, clinical treatment, and diagnostic laboratory procedures
• containment facilities or equipment, if hazardous biologic, physical, or chemical agents are to be used
• barrier facilities for housing of SPF rodents, especially valuable genetically modified animals, or irreplaceable animal models
• receiving and storage areas for food, bedding, pharmaceuticals, biologics, and supplies
• space for washing and sterilizing equipment and supplies and, depending on the volume of work, machines for washing cages, bottles, glassware, racks, and waste cans; a utility sink; a sterilizer for equipment, food, and bedding; and separate areas for holding soiled and clean equipment
• space for storing wastes before incineration or removal
• space for cold storage or disposal of carcasses
• space for administrative and supervisory personnel, including space for staff training and education
• showers, sinks, lockers, toilets, and break areas for personnel
• security features, such as card-key systems, electronic surveillance, and alarms
• areas for maintenance and repair of specialized animal housing systems and equipment.

7.3 Construction Guidelines

7.3.1 Corridors

Corridors should be wide enough to facilitate the movement of personnel and equipment; a width of 6 to 8 feet can accommodate the needs of most facilities. Floor-wall junctions should be designed to facilitate cleaning. Protective rails or bumpers are recommended and, if provided, should be sealed or manufactured to prevent vermin access. In corridors leading to dog or swine housing facilities, cage-washing facilities, and other high-noise areas, double-door entry vestibules or other noise traps should be considered. Similar entries are advisable for areas

leading to nonhuman primate housing as a means to reduce the potential for escape. Double-door entry vestibules also permit air locks in these and other areas where directional airflow is critical for containment or protection. Wherever possible, water lines, drainpipes, reheat coils and valves, electric service connections, and other utilities should be accessible via interstitial space or through access panels or chases in corridors outside the animal rooms. Fire alarms, fire extinguishers, and telephones should be recessed, installed high enough, or shielded by protective guards to prevent damage from the movement of large equipment.

7.3.2 Animal Doors

Doors should be large enough (approximately 42 × 84 in.) to allow the easy passage of racks and equipment and they should fit tightly in their frames. Both doors and frames should be appropriately sealed to prevent vermin entry or harborage. Doors should be constructed of and, where appropriate, coated with materials that resist corrosion. Self-closing doors equipped with recessed or shielded handles, sweeps, and kick plates and other protective hardware are usually preferable. Hospital or terminated stops are useful to aid in cleaning. For safety, doors should open into animal rooms; if it is necessary that they open toward a corridor, there should be a recessed vestibule.

Where room-level security is necessary or it is desirable to limit access (as with the use of hazardous agents), room doors should be equipped with locks or electronic security devices. For personnel safety, doors should be designed to open from the inside without a key.

Doors with viewing windows may be needed for safety and other reasons, but the ability to cover these windows may be considered if exposure to light or hallway activities would be undesirable (e.g., to avoid disturbing the animals' circadian rhythm). Red-tinted windows, which do not transmit specific wavelengths of visible light between corridors and animal rooms, have proved useful for mouse and rat holding rooms as both species have a limited ability to detect light in the red portions of the spectrum.

7.3.3 Exterior Windows and Floors

The presence of windows in an animal facility, particularly in animal rooms, creates a potential security risk and should generally be avoided. Windows also create problems with temperature control of the area and prevent strict control of the photoperiod, which is often required in animal related protocols (and is a critical consideration in rodent breeding colonies). However, in specific situations, windows can provide environmental enrichment for some species, such as nonhuman primates.

Floors should be moisture resistant, nonabsorbent, impact resistant, and relatively smooth, although textured surfaces may be required in some high-moisture areas and for some species (e.g., farm animals). Floors should be easy to repair and resistant to both the action of urine and other biologic materials and the adverse effects of hot water and cleaning agents. They should be capable of supporting racks, equipment, and stored items without becoming gouged, cracked, or pitted. Depending on their use, floors should be monolithic or have a minimal number of joints. Some materials that have proved satisfactory are epoxy resins, hard-surface sealed concrete, methyl methacrylate, polyurethane, and special hardened rubber-base aggregates. The latter are useful in areas where noise reduction is important. Correct installation is essential to ensure the long-term stability of the surface. If sills are installed at the entrance to a room, they should be designed to allow for convenient passage of equipment.

7.3.4 Drainage

Where floor drains are used, the floors should be sloped and drain traps kept filled with liquid. To minimize prolonged increases in humidity, drainage should allow rapid removal of water and drying of surfaces. Drainpipes should be at least 4 in. (10.2 cm) in diameter, although in some areas, such as dog kennels and agricultural animal facilities, larger drainpipes (>6 in.) are recommended. A rim- and/or trap-flushing drain or an in-line comminutor may be useful for the

disposal of solid waste. When drains are not in use for long periods, they should be capped and sealed to prevent backflow of sewer gases, vermin, and other contaminants; lockable drain covers may be advisable for this purpose in some circumstances.
Floor drains are not essential in all animal rooms, particularly those housing rodents. Floors in such rooms can be sanitized satisfactorily by wet vacuuming or mopping with appropriate cleaning compounds or disinfectants. But the installation of floor drains that are capped when not in use may provide flexibility for future housing of non-rodent species.

7.3.5 Walls and Ceilings

Walls and ceilings should be smooth, moisture resistant, nonabsorbent, and resistant to damage from impact. They should be free of cracks, unsealed utility penetrations, and imperfect junctions with doors, ceilings, floors, walls, and corners. Surface materials should be capable of withstanding cleaning with detergents and disinfectants and the impact of water under high pressure. The use of curbs, guardrails or bumpers, and corner guards should be considered to protect walls and corners from damage, and such items should be solid or sealed to prevent access and harborage of vermin.
Ceilings formed by the concrete slab above are satisfactory if they are smooth and sealed or painted. Suspended ceilings are generally undesirable in animal holding rooms unless they are sealed from the space above with gaskets and clips. When used, they should be fabricated of impervious materials, have a washable surface, and be free of imperfect junctions. Exposed plumbing, ductwork, and light fixtures are undesirable unless the surfaces can be readily cleaned.

7.3.6 Heating, Ventilation and Air Conditioning (HVAC)

HVAC systems should be designed for reliability (including redundancy where applicable), ease of maintenance, and energy conservation; able to meet requirements for animals. They should be capable of adjustments in and ideally maintain dry-bulb temperatures of ±1°C (±2°F). Relative humidity should generally be maintained within a range of 30-70% throughout the year. Ideally relative humidity should be maintained within ±10% of set point.
Most HVAC systems are designed for average high and low temperatures and humidity experienced in a geographic area within ±5% variation. In the event of an HVAC system or component failure, systems should at the minimum supply facility needs at a reduced level, address the adverse effects of loss of temperature control, and, where necessary, maintain critical pressurization gradients. It is essential that life-threatening heat accumulation or loss be prevented during mechanical failure. Temporary needs for ventilation of sheltered or outdoor facilities can usually be met with auxiliary equipment.
Air handling system intake locations should avoid entrainment of fumes from vehicles, equipment, and system exhaust. While 100% outside air is typically provided, when recirculated air is used its quality and quantity should be in accord with recommendations in Chapter 3. The type and efficiency of supply and exhaust air treatment should be matched to the quantity and types of contaminants and to the risks they pose. Supply air is usually filtered with 85–95% dust spot efficient filters. In certain instances, higher efficiency filters (e.g., HEPA) may be beneficial for recirculated supply air and air supplied to or exhausted from specialized areas such as surgical and containment facilities.

7.3.7 Power and Lighting

A time-controlled lighting system should be used to ensure a uniform diurnal lighting cycle. Override systems should be equipped with an automatic timeout or a warning light to indicate the system is in override mode, and system performance and override functions should be regularly evaluated to ensure proper cycling. Dual-level lighting may be considered when housing species that are sensitive to high light intensity, such as albino rodents; low-intensity

lighting is provided during the light phase of the diurnal cycle, and higher-intensity lighting is provided as needed (e.g., when personnel require enhanced visibility). Light bulbs or fixtures should be equipped with protective covers to ensure the safety of the animals and personnel. Moisture-resistant switches and outlets and ground-fault interrupters should be used in areas with high water use, such as cage-washing areas and aquarium-maintenance areas.

7.4 Barrier Facilities

Barrier facilities are designed and constructed to exclude the introduction of adventitious infectious agents from areas where animals of a defined health status are housed and used. They may be a portion of a larger facility or a free-standing unit. While once used primarily for rodent production facilities and to maintain immune-deficient rodents, many newer facilities incorporate barrier features for housing specific pathogen-free (SPF) mice and rats, especially valuable genetically engineered animals, and SPF animals of other species.

Barrier facilities typically incorporate airlock or special entries (e.g., air or wet showers) for staff and supplies. Staff generally wear dedicated clothing and footwear, or freshly laundered, sterile, or disposable outer garments such as gowns, head and shoe covers, gloves, and sometimes face masks prior to entry. Consumables, such as feed or bedding, that may harbor infectious agents are autoclaved or are gamma-irradiated by the supplier and surface decontaminated on entry. Drinking water may be autoclaved or subject to specialized treatment (e.g., reverse osmosis filtration) to remove infectious agents. Caging and other materials with which the animals have direct contact may be sterilized after washing before reuse. Strict operational procedures are frequently established to preclude intermingling of clean and soiled supplies and personnel groups, depending on work function. Only animals of defined health status are received into the barrier, and once they leave they are prohibited from reentering without retesting. Personnel entry is restricted and those with access are appropriately trained in procedures that minimize the introduction of contaminants.

Engineering features may include high-level filtration of supply air (e.g., HEPA or 95% efficient filters), pressurization of the barrier with respect to surrounding areas, and directional airflow from clean to potentially contaminated areas. Specialized equipment augmenting the barrier may include isolator cages, individually ventilated cages, and animal changing stations. Detailed information on barrier design, construction, and operations has been recently published.

7.5 Barrier Facilities

The goal of containment is to “reduce or eliminate exposure of laboratory workers, other persons, and the outside environment to potential hazardous agents”. This is accomplished by employing appropriate practices and equipment, vaccinating personnel if a vaccine is available, and ensuring the proper design and operation of the physical plant.

Animal facilities used to study biologic agents that are infectious to humans are categorized into different biosafety levels of escalating containment requirements as described in Biosafety in Microbiological and Biomedical Laboratories. Each animal biosafety level (ABSL) reflects a combination of practices, safety equipment, and facilities based on risk of human infection. As described in the 2009 edition of the BMBL, ABSL-1 contains agents not known to cause human infection; ABSL-2 contains agents of moderate risk that cause human disease by ingestion or percutaneous or mucosal exposure; ABSL-3 contains agents that cause serious and potentially lethal infections and have known potential for aerosol transmission; and ABSL-4 contains nonindigenous (exotic) agents that pose high individual risk of life-threatening disease and for which there is no available vaccine or treatment. Facility design, engineering criteria,

construction methods and materials, commissioning, and validation become more important with each increasing level. The BMBL should be consulted for specific design and engineering requirements. Considerable care should be taken when selecting the team of professionals responsible for the design, engineering, construction, and commissioning of a containment facility.

Guidelines have also been developed for containing agricultural pathogens, recombinant DNA molecules, arthropod vectors, and hazardous chemicals. Biologic agents and toxins pose a threat to animal and plant health or public health and safety, and facilities in which they are used must adhere to APHIS, USDA, and CDC Select Agent Regulations and/or other applicable federal, state, or local regulations. These regulations stipulate, among other requirements, that the institution registered to use select agents establish and adhere to stringent security measures. The specific facility features, equipment, and safety practices to be employed will depend, to a considerable extent, on whether a specific hazard is a particulate, volatile, or both. Facility features applicable to all hazards include isolation of the animals and their waste, provision of sealed