University of Malaya – Faculty of Medicine

Institutional Animal Care and Use Policy

1.0 The Institutional Animal Care and Use Committee (IACUC)

1.1 Authority

The *Guide* requires the Chief Executive Officer (CEO) or Institutional Official (IO) of an organization to appoint the Institutional Animal Care and Use Committee (IACUC). The Vice Chancellor of University of Malaya delegates authority through the IO to appoint the membership of the IACUC every 2 years.

Once appointed, the IACUC reports to a senior administrator known as the IO. The Deputy Dean for Research is the appointed IO at University of Malaya – Faculty of Medicine (FOM). The IO is given the administrative and operational authority to commit institutional resources to ensure compliance with Malaysian Animal Welfare Act 2015, other local regulations and Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC) requirements.

The IACUC's mandate to perform semiannual program evaluations as a means of overseeing the animal care and use program puts the IACUC in an advisory role to the IO. In its semiannual reports the IACUC advises the IO of the status of the Institution's compliance, establishes plans and schedules for correcting deficiencies necessary to either maintain or achieve compliance, and makes recommendation to the IO regarding any aspect of the Institution's animal program, facilities, or personnel training.

The IACUC's authority to review and approve protocols is independent of the IO, who may not overrule an IACUC decision to withhold approval of a protocol. If the IACUC approves a protocol, however, the Institution is not required or obligated to conduct the research activity. The Institution may also subject protocols to additional institutional review (e.g., department head, Biosafety committee, etc.).

The FOM, University of Malaya has established an IACUC, which is qualified through the experience and expertise of its members to oversee the Institution's animal program, facilities, and procedures.

1.2 Committee Composition

The IACUC is composed of regular voting members and alternate voting members. The IACUC may use, as necessary, non-voting members and consultants during review discussions. Some IACUC members fulfill specific regulatory requirements (e.g., veterinarian with program responsibility, an individual nonaffiliated with the Institution); others have unique roles by virtue of their position (e.g., Chair, Veterinarian, etc.).

Veterinarian. The appointment of a veterinarian with direct or delegated program responsibility to the IACUC. The IO may appoint more than one veterinarian to the IACUC, but the veterinarian with direct or delegated program responsibility must be designated as such. The veterinarian with program responsibility, e.g., Attending Veterinarian, must have training or experience in laboratory animal science and medicine or in the care of the species being used.

Chair. The Chair is appointed for 2 years and is a faculty member of the Institution with research experience. The chair may designate a scientist member of the IACUC as a substitute on an ad-hoc basis.

Non-affiliated. The non-affiliated member(s) represent general community interests. Neither they, nor their immediate family, have an affiliation with University of Malaya. These members have equal

status (e.g., voting) to every other committee member and are provided the opportunity to participate in all aspects of IACUC functions.

Scientist. A practicing scientist experienced in research involving animals.

Non-scientist. An IACUC member whose primary concerns are in a non-scientific area.

The Institution should consider persons with expertise in the disciplines involved in institutional research and teaching programs for service on the IACUC. In addition to the required categories of membership, it is suggested that individuals with expertise in specific areas pertinent to protocol review and program oversight be considered (e.g. statisticians, occupational health experts, information resource specialists, animal health technicians, and scientific research staff).

Alternate members may be appointed to the IACUC as long as they are appointed by the IO, and there is a specific one-to-one designation of IACUC members and alternates. An IACUC member and his/her alternate may not count toward a quorum at the same time or act in an official member capacity at the same time. Alternates should receive training identical to the training provided to regular IACUC members.

1.3 Conflict of Interest

No IACUC 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."

All investigators, consultants, and/or IACUC members are required to disclose any conflicts of interest.

An investigator or IACUC member is said to have a conflict of interest whenever that person, his or her spouse, or dependent child falls under any of the following conditions:

- Is an investigator or sub-investigator on the protocol (IACUC members only, not applicable to PI's).
- Has entered into a financial arrangement with the sponsor or agent of the sponsor, whereby the outcome of the study could influence the value of the economic interest.
- Acts as an officer or a director of the sponsor or an agent of the sponsor.
- Has identified him or herself for any other reason as having a conflict of interest.

If the investigator submitting a protocol believes that an IACUC member has a potential conflict, the investigator may request that the member be excluded. The Chair will present the declared conflict and the Committee will determine whether a conflict exists. Should an IACUC member declare involvement in any way in a research protocol under review by the IACUC, or state a conflict of interest with the research protocol, then the member(s):

- May remain in the meeting room to provide information requested by the IACUC;
- Leave the meeting room for discussion and voting; and
- Are not counted towards quorum for the protocol reviewed.

1.4 Confidentiality

To protect the integrity of the Institution and its researchers, IACUC members must not:

- Disclose confidential or proprietary information (protocol or investigator specific) to any non-IACUC member or,
- 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.

Material provided to the IACUC for review shall be considered confidential information and the members must, therefore, assure the confidentiality of the data contained therein. All IACUC applications and other sensitive review materials must be either filed in a secure location or otherwise disposed of in an appropriate manner, e.g., shredding.

The IACUC views the sharing of information for educational purposes in faculty and staff meetings an important benefit of departmental representation and is considered a vital part of the member's experience. This information may include such items as IACUC concepts, policies, regulations, and educational issues, providing no specific personal, confidential, or proprietary information is divulged.

If, following a Full Committee Review, the Committee agrees that consultation or discussions with individuals outside of the Committee are necessary; a person designated by the IACUC will first obtain permission from the Principal Investigator. If the Principal Investigator does not grant such permission, this may preclude final approval by the IACUC if questions concerning the protocol cannot be resolved.

1.5 Quorum Requirements

The University of Malaya FOM defines a "quorum" as more than half of the regular IACUC voting members.

A protocol is approved only if a quorum is present, and if more than 50% of the quorum votes in favor of protocol approval. For reasons other than conflict of interest, abstentions from voting do not alter the quorum or change the number of votes required. For example: If the IACUC has 19 voting members, at least 10 members must be present at a convened meeting to constitute a quorum and approval of a protocol would require a minimum of six votes whether or not there were abstentions.

2.0 Functions of the IACUC

The IACUC will:

i. Review at least once every six months the Institution's program for humane care and use of animals, using the *Guide* as a basis for evaluation.
ii. Inspect at least once every six months all of the Institution's facilities, including satellite facilities, using the *Guide* as a basis for evaluation.
iii. Prepare reports of the IACUC evaluations and submit reports to the IO.
iv. Review concerns involving the care and use of animals at the Institution.
v. Make written recommendations to the IO regarding any aspect of the Institution's animal program, facilities, or personnel training.
vi. Review and approve, require modifications in (to secure approval), or withhold approval of activities related to the care and use of animals.
vii. Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities.
viii. Notify investigators and the Institution 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.
ix. Conduct continuing review of each previously approved, ongoing activity at appropriate intervals as and when determined by the IACUC, including a complete review at least once every three years.
x. Be authorized to suspend an activity involving animals

2.1 Making Recommendations to the IO

The IACUC will make written recommendations to the IO annually regarding any aspect of the Institution's animal program, facilities, or personnel training. The procedures for making recommendations to the IO are as follows:

- Recommendations regarding any aspect of the Institution's animal program, facilities, or personnel training are formulated at convened meetings of the IACUC.
- Recommendations are prepared in writing by the IACUC Chair and Attending Veterinarian and/or any IACUC member. A copy of these recommendations are reviewed and approved at a convened meeting of the IACUC. Any minority views are noted and included in the final report.
- The IACUC Chair or his/her designee submits recommendations, including minority views that are approved by the IACUC to the IO.

3.0 IACUC Animal Use Protocols

3.1 Protocol Review

The IACUC is responsible for overseeing and evaluating all aspects of animal care and use, and is charged with reviewing proposals that involve animals to ensure that they comply with the Malaysian Animal Welfare Act 2015, other local regulations and standards set in the *Guide*.

3.2 General Scope of Review

The following kinds of activities (any one or combinations) involving animals are subject to review by the IACUC prior to initiation:

- Activities performed on the premises of FOM, University of Malaya
- Activities performed with or involving the use of facilities or equipment belonging to the University of Malaya FOM
- Activities satisfying a requirement imposed by the University of Malaya FOM for a degree program or completion of a course of study.

3.3 Exemptions

The following are exempt from IACUC review:

- Use of tissues, organs or other parts of dead animals if received as such (e.g from abattoir / other research facilities); and
- Non-invasive observation of wild animals (including stray animals) in their natural habitat. Field studies that involve killing, trapping, banding, darting, implantation of telemetry devices, or any other invasive manipulation (e.g. blood sampling) require IACUC approval.

3.4 Protocol Review Criteria

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 accordance with the Malaysian Animal Welfare Act 2015, relevant local regulations and the *Guide*.

If the IACUC does not have the scientific and technical expertise to evaluate all aspects of a proposal it may bring in outside expert consultants to provide information. Such consultants must not have a conflict of interest with the research activity and may not vote on any matters pertaining to the protocol. In all cases, the onus should be on the investigator to justify and explain his or her proposed experiments to the satisfaction of the IACUC.

3.5 Protocol Review Procedures

Full Committee Review (FCR)

Full committee review of protocols requires a convened meeting of a quorum of the IACUC members. Proposals reviewed by the full committee must receive the approval vote of a majority of the quorum present in order receive approval.

At least one week prior to a meeting, the IACUC secretary distributes copies of the protocols being presented or any other items of discussion to each IACUC member, including alternate and non-voting

member(s). Protocols are assigned a primary reviewer, who at the meeting orally presents the protocol to the rest of the committee for review and discussion. In addition, each protocol is assigned to a veterinarian to conduct an in-depth review of the protocol, specifically animal care and use. The Committee then votes on protocol approval. A simple majority vote of the members present is required for approval.

The Committee has the authority to approve, require modifications in (to secure approval), withhold, or table (defer until future meeting) any proposed activity. Committee members are given the opportunity to require that any requested modification(s) be brought before the next committee meeting. Under no circumstances will animal work be permitted to resume or begin until final approval is granted.

Primary reviewers can also take the initiative to contact the investigator prior to the meeting for clarifications, additional information, or in anticipation of questions the IACUC may raise. Investigator may also be requested to attend the IACUC meeting to give an overview of the protocol prior to any committee deliberations.

Notification of Review Outcome

The IACUC will notify investigators 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. The IACUC procedures to notify investigators and the Institution of its decisions regarding protocol review are as follows:

- Upon completion of the review process, each Principal Investigator receives a written notification of review decisions (approved, modifications required in (to secure approval), approval withheld, or tabled) and whether any special monitoring provisions will be required. Records of communication are maintained within the IACUC protocol files.

Appeal of an IACUC Decision

Investigators shall have the right to appeal a decision of the IACUC within two (2) weeks of notification by the IACUC Chairperson. A Principal Investigator may appeal decisions made by the IACUC by following the below steps:

i. The appealer states in writing to the IACUC Chair specific points of disagreement with the Committee's action, reasons for disagreement, and the desired outcome of the appeal.
ii. The IACUC Chair appoints at least one IACUC member ("the hearer") to present the appeals to IACUC members at a convened meeting of a quorum of the IACUC.
iii. A quorum of the IACUC membership hears the appeal from the hearer and/or from the person appealing and determines an outcome. The appealer will in any case be invited to attend and provided comments to the IACUC regarding the appeal.
iv. All decisions of the IACUC regarding an appeal request will be conveyed to the appealer in writing and copied to the IO.
v. If the person(s) appealing is not satisfied with the IACUC's decision, he or she may appeal to the IO and thereby initiate further IACUC consideration, if the IO so requests. **Officials of the Institution, however, cannot approve an animal activity that has not been approved by the IACUC.**

3.6 Review of Modifications to Approved Protocols

Significant Changes

Significant changes to an IACUC-approved protocol must be reviewed and approved by the IACUC before they occur. The Institution interprets significant changes to mean those that have the potential to impact substantially and directly on the health and well-being of the experimental animals. Examples of significant changes include, but are not limited to, changes:

- in the objectives of a study;
- from non-survival to survival surgery;
- resulting in greater discomfort or a greater degree of invasiveness;
- in the species or in approximate number of animals used (if more than 10% of the approved protocol);
- in Principal Investigator;
- or the use or withholding of analgesics; and
- in the duration, frequency, or number of procedures performed on an animal.

Proposed significant changes require IACUC review (and approval) prior to initiation.

Non-Significant Changes

The Institution interprets non-significant changes to mean those that do not have the potential to impact substantially and directly on the health and well-being of the experimental animals. Examples of non-significant changes include, but are not limited to, changes:

- in the funding source;
- in personnel (other than the Principal Investigator); and
- in the use of a new animal housing location.
- in the method of euthanasia [unless not American Veterinary Medical Association (AVMA) approved method];
- in anesthetic agent(s) (with review and approval by veterinarian)

Proposed non-significant changes require administrative review (and approval) prior to initiation.

3.7 Minimization of Pain and Distress

In design of the research, training or educational activities, it is the responsibility of the Principal Investigator to consider and include procedures that minimize animal pain or distress.

The IACUC is mandated to critically evaluate research protocols to ensure that pain and distress are minimized in laboratory animals and assure that appropriate steps will be taken to enhance animal well-being. The IACUC is required to determine that the Principal Investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animal and has provided a written narrative description of the methods and sources used to determine that alternatives were not available. The *Guide* states that the IACUC should ensure the protocol addresses:

- Appropriate sedation, analgesia, and anesthesia;
- Criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and
- Details of post-procedural care

The protocol must provide adequate information for the IACUC to assess the potential animal pain and/or distress resulting from the study and the effectiveness of the pain- and distress-relieving agents proposed for use. Criteria for re-dosing the animal should also be established. The Attending Veterinarian must be consulted for any procedure that has the potential to cause more than momentary pain or distress.

Examples of procedures which the *Guide* suggests may have the potential to cause pain or distress, include:

- physical restraint,
- survival surgeries,
- food or water restriction,

- death as an endpoint,
- noxious stimuli,
- skin or corneal irritancy testing,
- tumor burdens,
- intra-cardiac or orbital sinus blood sampling, and
- abnormal environmental conditions.

Assessing Pain and Distress

Numerous references indicate that both laboratory animals and humans receive and process noxious stimuli using similar mechanisms. An animal's response to pain is often adaptive to reduce movement to minimize re-injury and aid recuperation. This response, however, may lead to physiological and behavioral changes which impact negatively on both the animal's well-being and the research results.

Fundamental to the relief of pain is the ability to recognize its clinical signs in various species of animals. Due to the inability of animals to verbalize, it is essential that animal care staff and researchers receive adequate training on how to recognize clinical signs of pain and distress.

Alleviation of Pain and Distress

Accepted best practices for dealing with the possibility of unrelieved pain and distress should be considered and incorporated into protocols unless there is a sound scientific rationale for deviation from those practices. The investigator must also provide an assurance that unrelieved pain will continue for only the minimum period of time necessary to attain the study objectives.

Protocol methodology should be considered that decreases the potential for pain or distress. In addition to thorough searches of the literature, this can be done through the careful use of pilot studies to determine earlier endpoints or less invasive alternatives.

Pharmacologic treatment of pain or distress should be given as consistent with the type of pain/distress and the needs of the research question. The veterinarian must be consulted for all such protocols and should provide guidance to investigators and the IACUC.

It is the responsibility of the investigator to show s/he has considered all the options for minimizing pain and distress that do not compromise the scientific validity of the experiment. The IACUC's deliberations regarding the management of potential pain and distress in a protocol will be documented. Personnel should be trained in pain and distress management. The IACUC should ensure that there is a mechanism in place for prompt reporting of sick animals to the veterinary staff.

4.0 Monitoring of Approved Protocols

4.1 Post-Approval Monitoring (PAM)

Periodically, the IACUC will identify certain protocols or procedures that the IACUC determines that the laboratory could benefit from close veterinary oversight. The requirement of specific monitoring can be a provision of protocol approval and is communicated to the Principal Investigator. Once a protocol action (e.g., new protocol, revision, etc.) is approved with a provison for PAM, a specific notice to that effect will be sent to the Principal Investigator. The notice will be sent separately rather than being combined with any other correspondence (such as approval notices or review queries). The veterinary staff is notified of the need for monitoring and provided with the pertinent details. The veterinary staff coordinates this monitoring and periodically, and as necessary, provides updates to the IACUC.

In addition, the veterinary staff may conduct random, but frequent, visits to high-use areas, including satellite facilities.

5.0 Training in the Humane Care and Use of Laboratory Animals

5.1 Training

All staff working with laboratory animals must be appropriately qualified to do so in order to ensure the humane treatment of animals. Training is a classic performance standard where the emphasis is on the outcome (i.e., all personnel are qualified to do their jobs). It shall be the responsibility of the research facility to ensure that all scientists, research technicians, animal technicians, and other personnel involved in animal care, treatment, and use are qualified to perform their duties. This responsibility shall be fulfilled in part through the provision of training and instruction to those personnel. Training and instruction shall be made available, and the qualifications of personnel reviewed, with sufficient frequency to fulfill the research facility's responsibilities.

All personnel should receive training if they interact directly with or work in the vicinity of animals. Training made available for each type of staff should be specific to the animal species involved and to the kind of procedures to be performed or animal-related interactions.
For training purposes, staff can be grouped as:

- Researchers (including Principal Investigators),
- Animal care technicians, and
- Others (e.g., maintenance or support staff).

In some instances, staff may not be clearly divisible into these groups if job responsibilities are more diversified than this classification suggests. For example, facility staff such as animal health technicians may have job functions that include both animal care and research procedures.

Training should also be made available to temporary staff, such as students and visiting scientists. Principal Investigator's are responsible for identifying these people and assuring that appropriate training is accomplished.

5.2 Training Requirements for Institution's Laboratory Animal Users

The IACUC requires all personnel that conduct any research and/or teaching that involves handling, manipulating, or performing procedures on live vertebrate animals, whether in the laboratory to be appropriately trained. Personnel listed on a protocol must be current with their training, however new researchers may conduct animal work under supervision by trained personnel, until they complete their animal training.

5.3 Education and Training for IACUC Members

New Member Orientation

New IACUC member orientation consists of the following: a description of the IACUC and responsibilities; criteria for membership; authority of the IACUC; protocol review process; monitoring of approved protocols, periodic review; protocol modifications; records; semiannual reviews; roles and responsibilities; and regulations. Documentation of training is maintained through the use of IACUC member files.

The objectives of providing this information are the following:

- To introduce members to the role of the IACUC and its evolution;
- To provide the basic information necessary for IACUC members to discharge their responsibilities; and
- To provide a forum for response to, and discussion of, members' concerns and questions.

Continuing Education

Continuing education for IACUC members usually occurs at each IACUC meeting. The objectives of providing ongoing training for IACUC members is to increase their knowledge, understanding, and awareness of current laws and regulations, new directives, best practice guidelines and institutional

policies. It also provides a regular forum for the IACUC to discuss concerns or questions brought forth by the faculty, staff or members of the community. Information provided for these sessions will include questions and concerns brought to the attention of the IACUC, official directives, relevant publications, conference announcements, seminar proceedings, animal facility staff and/or veterinarian's observations/recommendations, issues involving facility inspections and program evaluations, and compliance issues.

6.0 Occupational Safety and Health (OSH) Program

The health and safety of individuals working in animal care and use programs is an area of institutional concern requiring commitment from the senior officials of the institution. The goal of the OSH is to prevent occupational injury and illness by avoiding, controlling or eliminating hazards in the workplace. The emphasis of such a program is the prevention of illness and injury, but it also includes provisions for early diagnosis and treatment when necessary.

6.1 The IACUC's Responsibility for OSH

The Institution is responsible for ensuring a safe working environment for personnel involved in the animal care and use program. An effective OSH Program works with many separate institutional components including animal care and use, research, environmental health and safety, occupational health, and administration and management. A natural point of convergence for these functionally distinct institutional elements at many institutions is the IACUC. Assurance of a safe working environment is one of the topics the IACUC should consider in each animal use proposal (in the form of a risk assessment) and as part of the semiannual program evaluation. It is generally necessary to involve health and safety specialists in the design and implementation of the IACUC review guidelines.

6.2 Role of the IACUC in the OSH Program

Procedures should be developed for conducting a health and safety review of research activities that present hazards. These procedures should be incorporated into the IACUC protocol review process. Procedures to identify and address non-experimental hazards (e.g., during semiannual facility inspections and program reviews) should also be implemented. Communication and other procedural links between the IACUC and the environmental health and safety professional or office should be established, maintained and documented. The IACUC has a role in ensuring that personnel comply with health and safety requirements (e.g., ensuring personnel have received appropriate training, evaluating compliance with standard operating procedures or institutional policy during semiannual facility inspections, etc.).

6.3 Elements of the OSH Program

An effective program design requires input from health and safety specialists and will include the following elements:

- Administrative procedures,
- Facility design and operation,
- Risk assessment,
- Exposure control,
- Education and training,
- Occupational healthcare services,
- Personal protective equipment,
- Equipment performance,
- Information management,
- Emergency procedures, and
- Program evaluation

The details of each element will be dictated by the extent and nature of employees' exposure and the type of animal use program.

6.4 Participation in the OSH Program

A wide range of personnel (e.g., animal care staff, investigators, technical staff, students, engineers, and maintenance personnel who care for or use animals, their tissues or fluids, or who may be exposed to them as a consequence of their job) should be provided the opportunity to participate in the OSH.

The extent and level of participation of personnel in the OSH should be based on risk assessment, including:

- hazards posed by the animals and materials used;
- exposure intensity, duration, and frequency;
- susceptibility of personnel; and
- history of occupational illness and injury in the workplace

Persons exposed to animals in a laboratory or animal facility environment or to fresh (unfixed) animal tissues must complete a risk assessment. The completion of a baseline health assessment questionnaire is encouraged to provide additional details that can assist in offering targeted health risk counseling to program participants. The questionnaire(s) are submitted to OSH approved clinic for review. The clinic will evaluate the risks and review the person's health information and vaccination status provided on the health risk questionnaire, and the baseline health assessment questionnaire.

If the clinic determines that there is a particular reason for a follow-up screening appointment, one will be arranged. An example of this would be in the case of reported animal allergy symptoms or other potentially work-related health problems associated with animals.

6.5 OSH Program Education and Training

There are ethical and legal requirements to inform individuals of workplace health risks that could potentially affect them and appropriate precautions to mitigate those risks. The objectives of the Institution's OSH can be achieved only if employees are appropriately trained and understand the hazards associated with their work area and job duties, and how those risks are mitigated through institutional policies, engineering controls, work practices, and personal protective equipment.

Training should include information about:

- Zoonoses,
- Chemical safety,
- Microbiologic and physical hazards (e.g., allergens and radiation),
- Hazards associated with experimental procedures,
- Handling of waste materials, and
- Personal hygiene

7.0 Semiannual Program Review and Facility Inspections

7.1 Semiannual Reviews

The IACUC must review the program for humane care and use of animals at least once every six months, using the *Guide* as the basis for evaluation and must inspect all institutional animal facilities at least once every six months.

7.2 Program Review

The animal care and use program review includes an evaluation of institutional policies and responsibilities (lines of authority and reporting channels), IACUC membership and functions, and

IACUC recordkeeping and reporting procedures. It also includes a review of the adequacy and appropriateness of the veterinary medical care program, the training program for personnel, and the OSH program.

The IACUC will review at least once every six months the Institution's program for humane care and use of animals, using the *Guide* as a basis for evaluation. Findings from the Program Review, including a Deficiency Correction Schedule are compiled and prepared for IACUC review and discussion at a regular, convened IACUC meeting following the Program Review.

7.3 Facility Inspections

The facility inspections are a physical inspection of all buildings, rooms, areas, enclosures and vehicles (including satellite facilities in which animals are housed for more than 24 hours) that are used for animal confinement, transport, maintenance, breeding, or experiments.

Laboratories in which routine procedures, such as immunization, dosing, and weighing, are conducted may be evaluated by other means such as random inspections. The Institution, however, through the IACUC, is responsible for all animal-related activities regardless of where animals are maintained or the duration of the housing. The IACUC must have reasonable access to these areas for the purpose of verifying that activities involving animals are being conducted in accordance with the proposal approved by the IACUC.

The IACUC inspects, at least once every six months, all of the FOM's animal facilities, including satellite facilities, using the *Guide* as a basis for evaluation. Findings from the Facility Inspections, including a Deficiency Correction Schedule are compiled and prepared for IACUC review and discussion at an IACUC meeting following the inspections.

Staffing and Scheduling the Facility Inspections

The IACUC must conduct inspections of facilities at least once every six months. This may be accomplished by assigning specific facilities to subcommittees, which must consist of at least two IACUC members. No IACUC member should be excluded should she or he wish to participate in an inspection. The inspection team should have a working knowledge of the *Guide* in order to fully evaluate the facilities that are being inspected. Use of a checklist provides consistency and helps document that all categories were assessed.

7.4 Deficiency Correction Schedule

All deficiencies identified during the Facility Inspection and/or Program Review are designated by the IACUC as minor or significant. A significant deficiency is defined as a situation that is or may be a threat to animal health or safety. For both categories of deficiencies, a reasonable and specific plan and schedule with dates for correction must be included in the final report. All individuals to be involved in the corrections should be consulted to ensure that the plan is realistic.

7.5 Documentation

A written report of the semiannual program review and facility inspection is prepared. The report to be signed by a majority of the IACUC members at a convened meeting. The report describes the Institution's adherence to the *Guide*, and identifies specifically any deviations from this document.

The report will indicate whether or not any minority views were filed, and minority views will be included in the final document. A copy of the report is sent to the IO and is kept on file for a minimum of three years.

8.0 Animal Welfare Concerns And Non-Compliance Situations

8.1 Evaluation of Animal Care and Use Concerns

To help ensure that laboratory animals receive humane care, use or treatment in accordance with the highest ethical standards, laws, regulations and policies governing animal research, the IACUC must review and, if warranted, address any animal-related concerns raised by the public or institutional employees. Procedures must be established to ensure that concerns are communicated to the IACUC. The Committee must review each concern in a timely and systematic manner and, when necessary, take prompt, appropriate corrective actions.

8.2 Methods for Reporting

To facilitate communication, there are a number of options available to communicate concerns about animal care and use at the University of Malaya, FOM, or to report instances of suspected non-compliance with laws, rules, regulations and policies. The names and phone numbers of contact persons including the Attending Veterinarian, should be posted in or near the entrance to animal facilities, readily available to institutional employees.

Although written concerns are more convenient to handle, complainants may not be willing to submit them in this manner. In such cases, the individuals who receive concerns should document them fully to ensure that the issues are clear and to prevent misunderstandings.

Requests for anonymity should be honored to the extent possible. This includes protecting the confidentiality of those who report concerns as well as anyone against whom allegations are directed, while allegations are under investigation. The policy of the Institution is to prohibit unlawful retaliation against employees as a consequence of good faith actions in the reporting of, or the participation in an investigation pertaining to, allegations of wrongdoing.

8.3 Procedures for the Investigation of Animal Care and Use Concerns

Initial Evaluation and Actions

Concerns may include situations or activities ranging from those in which animals are reported to be in immediate, actual or perceived jeopardy to those in which violations of the guide are alleged to be occurring but animals are not in apparent danger. They may focus on allegations of past policy and procedure violations or protocol non-compliance.

The course of action taken by the IACUC should be driven by the potential significance of the alleged situation. For example, conditions that reportedly jeopardize the health or well-being of animals should be evaluated immediately. To cope promptly with such situations, the Attending Veterinarian is authorized to halt procedures which they believe do not comply with institutional policies until the IACUC can be convened and consider the matter formally. Emergency meetings may be necessary in these cases to ensure prompt consideration of concerns.

The Complaint Assessment Subcommittee

Upon receipt of a concern, the IACUC Chair should convene a meeting of the Complaint Assessment Subcommittee (CAS) comprised of IACUC members designated by the Chair. The CAS can either meet in person, or via email discussion. After initial review of the complaint, the CAS will determine whether it requires further investigation and immediate action, further investigation but no immediate action, or no action. Once this decision has been made, the CAS should determine which individuals or other institutional or non-institutional offices may require notification at this time.

If immediate action appears warranted because animal or human welfare may be compromised, the IACUC should notify the IO and proceed accordingly. Veterinary medical intervention, suspension of a

research activity, and/or notification of appropriate safety, occupational health, or other officials, are examples of actions that may be taken immediately to protect animal or human welfare.

Investigation

Should the IACUC determine that further investigation is required, the CAS should conduct the investigation and report back to the IACUC. It is important to avoid actual or perceived conflicts of interest in this process.

The IACUC should charge the designated person or group with its requirements for information gathering and impose a completion date. The assigned completion date will depend on the IACUC's determination of whether immediate remedial action may be required. The nature of the information required will vary depending on the circumstances, but often involves:

- Interviewing complainants (if known), any persons against whom allegations were directed, and pertinent program officials;
- Observing the animals and their environment; and
- Reviewing any pertinent records, (e.g., animal health records, protocol, and other documents).

The CAS should provide a report to the IACUC, which summarizes:

- The concern(s),
- The results of interview(s),
- The condition of animals and their environment, and
- The results of records and other document reviews.

The report should also contain:

- Any supporting documentation such as correspondence, reports, and animal records,
- Conclusions regarding the substance of the concerns vis-à-vis requirements of the *Guide*, and institutional policies and procedures, and
- Recommended actions, if appropriate

Outcomes and Final Actions

Upon receipt and evaluation of the report, the IACUC may request further information or find that:

- There was no evidence to support the concern or complaint,
- The concern or complaint was not sustained, but related aspects of the animal care and use program requires further review or
- The concern or complaint was valid

9.0 Non-Compliance with IACUC Protocol, Policies, Procedures, or Decisions

Protocol non-compliance occurs when procedures or policies approved by the IACUC are not being followed. Examples include performing unauthorized surgery, unauthorized persons participating in a research project, or injecting drugs that the IACUC has not approved. When faced with protocol noncompliance, the IACUC's first step, if possible, should be to find a way to bring the protocol into compliance.

If allegations of animal mistreatment or protocol non-compliance are verified, the IACUC can apply sanctions. If, in the opinion of the IACUC, sanctions are not appropriate, they need not be applied. A clearly minor and unintentional misinterpretation of an IACUC policy that has created no problem for an animal is an example of where a verified allegation of protocol non-compliance might lead to an explanation, not a sanction.

9.1 Consequences of Non-Compliance

Subsequent actions of the IACUC may include:

- Implementing measures to prevent recurrence;
- Notifying the IO and the Attending Veterinarian of its actions;
- Notifying funding or regulatory agencies, as required; and/or
- Notifying the complainant, any persons against whom allegations were directed, and pertinent program officials (appropriate supervisory and management staff, the public affairs office, institutional attorneys, etc.).

Corrective Actions and Institutional Sanctions

Examples of corrective actions and institutional sanctions that have been devised include:

- counseling;
- issuing letters of reprimand;
- mandating specific training aimed at preventing future incidents;
- monitoring by the IACUC or IACUC-appointed individuals of research, testing, or training that involving animals;
- temporary revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals, pending compliance with specific, IACUC-mandated conditions;
- permanent revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals; and
- recommending to the IO that institutional (e.g., reassignment, termination of employment) sanctions be imposed.

Suspension of Animal Activities

The IACUC is empowered to suspend a project if it finds violations of Malaysian Animal Welfare Act 2015 and other local regulations, FOM IACUC policy, the *Guide*, or Animal Welfare Regulations. Suspension may occur only after review of the matter at a convened meeting of a quorum of the IACUC, and a vote for suspension by a majority of the quorum present. Furthermore, the IACUC must consult with the IO regarding the reasons for the suspension.

It may be necessary for the IACUC to subsequently inform AAALAC and other regulatory bodies or funding organizations of the suspension.

10.0 Recordkeeping

10.1 Maintaining IACUC Records

The Institution is responsible for maintaining:

- Minutes of IACUC meetings;
- Records of IACUC activities and deliberations;
- Minority IACUC views;
- Documentation of protocols reviewed by the IACUC, and proposed significant changes to protocols;
- IACUC semiannual program evaluations and facility inspections, including deficiencies identified and plans for correction; and
- Accrediting body determinations (AAALAC)

All records are to be kept for a minimum of seven years.

Records documenting such activities as the provision of adequate veterinary care, training, and occupational safety, are expected to conform with the recommendations of the *Guide* and with commonly accepted professional standards.

10.2 Meeting Minutes

Review of proposals by the IACUC invokes a deliberative process, and the institution is required by AAALAC to maintain "minutes of IACUC meetings, including records of attendance, activities of the Committee, and Committee deliberations" The IACUC has some latitude in the degree of detail in these minutes.

Recorded minutes from IACUC FCRs are intended to reflect the substantive discussion of protocols. Minutes are intended to contain sufficient information that a reasonable person could understand the nature of the discussion. Meeting minutes are not intended to provide a verbatim transcript of discussion nor to reiterate shared knowledge of the Committee such as recent discussions about a protocol in previous minutes. Historical evidence of compliance or non-compliance would be recorded in the minutes if it is related to the discussion. Minutes of each meeting are recorded in writing and include records of attendance, a summary of the issues discussed and the resolution of issues, and the results of IACUC votes on protocols.

11.0 AAALAC

The AAALAC is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs.

The University of Malaya voluntarily participates in AAALAC's program, in addition to complying with the local, laws that regulate animal research. Participating institutions receive an independent, unbiased expert assessment, and those that meet or exceed applicable standards are awarded accreditation.

Institutions choose to participate in the AAALAC accreditation program for a variety of reasons. Some use accreditation as a symbol of quality—it shows that an institution is serious about setting, achieving and maintaining high standards for animal research programs. AAALAC accreditation also promotes scientific validity—when research involves animals, reliable results depend on healthy animals and superior animal care.

12.0 Animal Care and Use Policies

12.1 Movement of Animals

Removal of Animals from the Animal Facility

Except during quarantine periods, animals may be moved to other laboratory buildings within the FOM. Small animal cages (rabbits and smaller) must be completely covered with a clean cloth sheet or large towel (investigator must provide covering). Additionally, rodents, which will be returning to the facility, must be transported in micro isolator cages to prevent unnecessary exposure to pathogens. Unless specific IACUC approval has been granted, animals cannot remain outside the animal facilities for 24 hours or longer.

The transportation of animals between the FOM and any off campus locations must be arranged in advance with the Attending Veterinarian's approval. This includes the pick up and delivery of animal's to/from the airport.

If animals must be transported by hand or on carts across campus, animals should be moved as unobtrusively as possible, at times of low activity, such as before 8:00 A.M. and after 5:00 P.M.

Removal of Animals from the Institution

Animals may not be removed from the Institution without clearance from the Attending Veterinarian. Persons adopting animals must sign a release form in order to obtain an animal, which must be approved by the Attending Veterinarian.

Housing of Animals in Research Laboratories

Unless specific IACUC approval has been granted, animals cannot be removed from the animal facilities for 24 hours or longer. Once IACUC approval has been granted, animals must be looked after by FOM animal care staff, to ensure compliance with applicable regulatory requirements.

Experimental Procedures in Animal Housing Areas

Painful or stressful procedures may not be conducted in animal holding rooms, as such procedures stress other animals in the room. To assist researchers, procedure rooms are available in the facility and animals may be taken to these rooms or to approved research laboratories.

Procedures can be conducted in rooms where laminar flow workbenches or biological safety cabinets are provided. Procedures may be conducted in the laminar flow hood or biological safety cabinets, as long as the hood is turned on and functioning properly.

Animals cannot be taken from clean barrier rooms and returned without going through quarantine (duration to be advised by the Attending Veterinarian), unless barrier procedure rooms are used and animals are transported in microisolator or individually ventilated cage caging.

12.2 Animal Surgery

All survival surgery performed in animals must be performed under aseptic conditions.

Survival Rodent Surgery

Survival surgery on rodents may be carried out in investigator laboratories if aseptic techniques are followed. Caps, masks, and sterile gloves must be worn and sterile instruments; supplies and drapes must be used. In addition, in accordance with approved guidelines, for non-rodents there must be an animal prep area separate from the surgery area. This is to keep hair and dirt from clipping and prepping the animal away from the area in which a sterile procedure is to be performed. Generally, the surgery area should be in a separate room, or laminar flow hood or biological safety cabinet dedicated to surgery. If these are not available, an individual area of a room may be dedicated to surgery, and must not be used for other purposes.

AAALAC requires that all surgical instruments must be sterilized, either by heat, gas, or chemical means prior to use. Use of only disinfecting agents such as alcohol, povidone iodine, etc., is not acceptable. Sterilants kill all microorganisms, with the possible exception of some parasitic life forms, while disinfectants have a much lower level of effectiveness. Acceptable methods of sterilization include steam, gas, glass bead, and chemical agents. Chemical agents include phenols, glutaraldehyde, and chlorine dioxide. Glutaraldehyde is mutagenic, phenols are corrosive and both require special disposal procedures. Chlorine dioxide has a short sterilizing useful life (one day) and is corrosive to metals. All agents require rinsing with sterile solutions prior to tissue contact. Glass bead sterilizers will sterilize only the portion of the instrument placed in the beads. The following standards have been reviewed and approved by our IACUC and Attending Veterinarian:

- It is recommended that all instruments used in survival rodent surgeries be steam sterilized prior to each surgery or group of surgeries (periodic biological indicator monitoring of sterilizer efficiency is required).
- Instruments must be kept on sterile nonporous towels during use.
- Instruments must be cleaned of blood and debris by brushing or wiping with sterile water and gauze sponges between surgeries.
- If contamination has occurred, instruments must be placed in a chemical agent or a glass bead sterilizer for the appropriate period of time for the method used to be effective (or the pack replaced by a new one).

- If a chemical agent is used, instruments must be rinsed with sterile water or saline before being used on the next animal.
- Surgical gloves and blades should be changed between each animal and/or after contamination.
- Following surgery, all instruments must be thoroughly cleaned and preferably placed in an ultrasonic cleaner and rinsed.

Major Survival Surgery and Multiple Major Survival Surgeries

Major surgery is defined as surgery which invades a body cavity or results in physiological or anatomical alteration of the surgical subject. All major surgery in rabbits and higher species on the phylogenetic scale is to be performed in the dedicated surgery room within the Animal Experimental Unit or other approved location.

The University of Malaya FOM allows the performance of more than one major surgery on an animal with the animal surviving. This is known as Multiple Major Survival Surgery. There is provision for these surgeries with adequate scientific justification by the Principal Investigator with express written approval by the IACUC.

Animal Reuse

Animals that have been used for non-invasive and non-stressful techniques, such as for behavioral observation and simple experimental procedures such as a single blood withdrawal, or a single injection of a vehicle or saline, for example, may be transferred with the approval of the IACUC and Attending Veterinarian, from one protocol to another.

In no case may a veterinarian independently approve a transfer that would involve an animal having multiple major survival surgeries across protocols (ie, one surgery in one protocol, and the second in a different protocol).

Euthanasia, Anesthesia, Analgesia

The IACUC requires the use of methods to relieve pain and distress for animals experiencing these adverse reactions. Euthanasia procedures are outlined in the AVMA Guidelines on Euthanasia, and must be adhered to unless specifically exempted and documented in the IACUC review process. Anesthesia and analgesia procedures have been established for animals at the Institution. The Attending Veterinarian can assist researchers in selection of these agents.

The veterinarian, laboratory staff, and animal care personnel monitor the use of anesthetics and analgesics. Observation of anesthetic technique, depth of anesthesia, apparent level of pain, as well as physiological parameters, are the means by which anesthesia and analgesia are monitored. If animals are observed to be in pain at any time, the investigator will be contacted and the use of analgesics discussed. If the investigator determines that analgesics cannot be used, the Veterinarian will decide whether the animal can continue on study, or must be euthanatized.

Use of Biohazardous Materials/Radioisotopes

For hazardous chemicals, such as carcinogens and/or biohazards, the Principal Investigator submits application to the relevant Institutional authorities for approval, which may be submitted concurrently with animal protocol application to IACUC for approval. IACUC's review and approval of the animal protocol is independent of other required regulatory approvals. Once all approvals are obtained, the user contacts the Animal Facility Coordinator for room assignment.

The AEU staff and appropriate personnel oversee rooms in the Animal Experimental Unit where animals containing hazards are housed (ABSL2 facility) and all procedures performed in these animals. Protocols and precautionary measures for each study must be provided by the Principal Investigator

and posted within each animal room. Additionally, appropriate identification of hazards must be placed on the outside door of each affected room.

Specific Pathogen Free Mandate for Laboratory Animals

The IACUC in consultation with Animal Experimental Unit and the research community, is committed to a long-term plan to prevent contamination of FOM animal colonies. As a result of this Plan, where possible rodents should be housed in microisolators or individually ventilated cage systems, or housed within a barrier facility to minimize the potential for exposure.

Physical Restraint

Prolonged physical restraint (lasting longer than 15 minutes) must be scientifically justified and requires prior approval by the IACUC. The *Guide* defines "Physical Restraint" as the use of manual or mechanical means to limit some or all of an animal's normal movement for such purposes as examination, collection of samples, and drug administration. Typically, animals are restrained for brief periods, usually minutes, in most research applications.

It is frequently necessary to physically restrain animals during examination as well as while administering substances and collecting samples. In most cases, only a short period of immobility is required. Occasionally administrations, sample collections, or treatments require a prolonged period of physical restraint.

The IACUC therefore is required to ensure that:

- the method of restraint is appropriate for the species of animal
- the period of restraint is the minimum required for experimental objectives
- the personnel performing the restraint have been appropriately trained
- when prolonged physical restraint is necessary, the physical, physiological and psychological effects on the animal are minimized

Food and Fluid Restriction

Food and/or fluid restriction are typically used in the research setting under three main categories:

i. studies that use food/fluid consumption to motivate animals to perform novel or learned tasks,
ii. studies of the motivated behaviours and physiologic mediators of hunger and thirst,
iii. homeostatic regulation of energy metabolism or food balance.

Rodents and rabbits are offered access to a continuous supply of food and water (ad-libitum) and can eat and drink as much and as often as they want.

Scientific justification should be provided for regulating or withholding feed or water from laboratory animals and the least amount of time that will achieve the scientific objective should be used. This justification should include an alternatives literature search and also provide rationale for the level and length of time the regulation proposed.

In accordance with the *Guide*, in the case of conditioned response research protocols, use of a highly preferred food or fluid as a positive reinforcement, instead of restriction, is recommended.

For any study requiring chronic (over 24 hour) regulation, the investigator should provide ad-libitum normals for the exact background strain, sex and age group used in the study. Published values for the same age, sex, background strain, and weight may be used in lieu of in-house determination.

The investigator should provide the formula used for the proposed regulation, (An example is food regulation of 70% of ad libitum until the rodent is at 80% body weight of peer controls). Rodents

should be acclimated over 3 days to new regulation paradigms unless specifically approved by the IACUC. Rats cannot go without water for more than 24 hours and mice cannot go without water for more than 12 hours, without specific approval from the IACUC. Regulation is not recommended in rodents under 14 weeks of age. Consideration should be made to allow food and water to be available concurrently, as rodents typically do not eat caloric requirements without available water. For animals undergoing scheduling, access to food and/or water should be for 15 minutes at a minimum. Regulated levels of food should not be lower than 30% of ad libitum values.

Animals on regulation /scheduling should be monitored daily and weighed at least twice weekly, but it is encouraged to do so as often as the critical aspects of the study permit. Weight should be compared to either age and strain-matched controls or the baseline body weight (if an adult). Additionally, a body condition score (BCS) system should be used to evaluate the animals twice weekly.

Food and water availability should be recorded daily during any time period that regulation/scheduling is being done. The records should contain the following information:

- General Information (i.e. protocol number, animal identification number, Principal investigator, contact person, contact phone number)
- Baseline weight (before restriction period began)
- Date (daily documentation is necessary)
- Indication that water was given (daily)
- Indication that food was given (daily)
- Weight and BCS (twice weekly)
- Health
- Initials

For food regulation, a rodent may not lose more than 20% of age-strain-sex matched controls or baseline body weight (if adult). After 20% weight loss has been achieved (the animal weight is 80% of baseline weight or matched controls), the daily food allowance must be increased to prevent additional weight loss. Regulation cannot be attempted again until the animal weighs at least 80% of its original weight.

Rodents on fluid regulation/scheduling with a weight loss of 10% of baseline weight should be considered clinically dehydrated and should be treated as outline below.

Any rodent appearing dehydrated (displaying listlessness/inactivity, increased “skin tent”, and/or sunken eyes) must have drinkable fluid provided immediately by supplying a measured volume of fluid. Enough fluid should be provided to allow the animal to freely drink without interruption. In addition, 1-2 mL of subcutaneous lactated ringers or saline (0.9% NaCl) must be administered. Lab members involved in water restriction should be able to identify dehydration and be comfortable giving subcutaneous fluids.

If a rodent appears dehydrated, listless, hunched, or in signs of pain/distress contact the Attending Veterinarian in addition to providing additional food/water.

Environmental Enrichment

All singly housed rats and mice will receive environmental enrichment. At a minimum, mice will receive nesting material and rats will be provided a nylabone or comparable chew toy.

Other rodents and non-rodent mammals will receive environmental enrichment in accordance with the Standard Operating Procedure. Enrichment may include housing with littermates, food treats, "toys" (e.g., chew blocks), and resting / hiding places.

Investigators are encouraged to develop and utilize forms of enrichment (e.g., plastic tubes or nesting huts for rodents, in addition to the standard methods described above. Alternative methods may be implemented on a trial or case-by-case basis following consultation with the Attending Veterinarian; however, routine use of additional or alternative means of enrichment should be described in the approved research protocol. Investigators are also encouraged to contact the Attending Veterinarian to discuss currently available methods of enrichment.

Exceptions to this policy will only be permitted following specific review and approval by the IACUC.