# NATIONAL ADVISORY COMMITTEE FOR LABORATORY ANIMAL RESEARCH
## GUIDELINES FOR INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

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CHAPTER 1 : IACUC - THE COMMITTEE

1.1 Main IACUC Functions:

1.1.1 The IACUC assumes overall responsibility for the oversight and evaluation of all aspects of the Institution's animal care and use programme and advises the CEO of the Institution on the steps required to maintain animal research facilities and programmes that conform to the Guiding Principles and other relevant laws or guidelines.

1.2 Specific Functions

1.2.1 These are:

(a) Review of Proposals involving the use of animals in research and training
(b) Approval/rejection/modification of all Proposals and related study or activities involving the use of animals.
(c) Site inspection of the Housing and Research Facilit(ies) of the Institution
(d) Review of the animal care and use programme of the Institution.
(e) Review/investigate complaints about animal care and use
(f) Monitor compliance of approved research and training projects involving the use of animals.

1.3 Definitions

1.3.1 The term “programme” refers to relevant policies and protocols established in the Institution pertaining to the care and use of animals in research and training as well as the Institutional philosophy underpinning the protocols.

1.3.2 Unless the contrary is stated, the meaning and definition of other terms in the IACUC Guidelines shall be the same as those found in the Guiding Principles.

1.4 The Authority of the IACUC

1.4.1 The IACUC derives its authority from the Institution through the CEO. The CEO appoints the members of the committee.

1.4.2 The IACUC is mandated to perform semi-annual programme evaluations as a means of overseeing the animal care and use programme. This puts the IACUC in an advisory role to the CEO. In its semi-annual reports the IACUC advises the CEO of the Institution's compliance, establishes plans and schedules for correcting deficiencies necessary to either maintain or achieve compliance, and makes recommendation regarding any aspects of the Institution's animal programme, facilities, or personnel training. This approach of “enforced self regulation” requires that the IACUC have the full support of the CEO responsible for the programme.

1.4.3 The IACUC has the authority to review and approve research Proposals independent of the CEO. The CEO cannot overrule an IACUC decision to withhold approval of a research Proposal. However, if an IACUC approves a research Proposal, the Institution is not required or obligated to conduct the research activity. An Institution may subject research Proposals or protocols to additional Institutional review (e.g. department head, biosafety committee, etc.).
1.5 Authority to Appoint IACUC Members

1.5.1 The CEO has the authority to create an IACUC for the Institution and appoint IACUC members.

1.5.2 All reports of the IACUC will be submitted to the CEO.

1.5.3 The main function of the CEO is to provide the resources needed by the IACUC to run its operations and to enforce the recommendations of the IACUC.

1.6 Membership Composition & Qualification

1.6.1 In order not to influence IACUC decisions a maximum of only three members is allowed from the same department or unit within the Institution.

1.6.2 For the committee to have well balanced views and decisions, members must come from diverse backgrounds. An IACUC must therefore comprise at least 5 persons, including a separate person appointed from each of the following 4 categories:

(a) A veterinarian with training or experience in laboratory animal science and medicine and who has experience in the species of animals used. Where veterinarians do not have this experience, they must familiarise themselves with the biology and clinical characteristics of the species of animals used.

(b) A person with substantial recent and appropriate experience in the use of animals for scientific purposes. This will usually entail the possession of a higher degree(s). (scientists/animal scientists)

(c) A person not affiliated in any way with the Institution and not a member of the immediate family of a person who is affiliated with the Institution; who represents the general community interests in proper use and care of animals for any scientific purposes and is not a user of animal for scientific purposes. Payment of reimbursement to cover reasonable transport costs is permissible without jeopardising a member’s non-affiliated status.

(d) A person whose primary concerns or interests are in a nonscientific area (e.g. ethicist, lawyer, clergy).

1.6.3 To come up with 5 or more members, there can be more than one person from any one of the 4 categories set out above.

1.6.4 No person who is the CEO or is part of the CEO (in the case where the CEO is not a single person) is to be appointed a member of an IACUC because IACUC reports to CEO.

1.6.5 The Attending Veterinarian engaged for the Institution shall be appointed a member of the IACUC.

1.7 Main Officers in the IACUC:

1.7.1 Chairman - The Chairman who will oversee the IACUC meetings, proceedings and activities, will be appointed by the CEO of the Institution. In order to provide the intended checks and balances in the system of self-regulation, it is advisable
that veterinarians not serve as Chairman of the IACUC. While it is important that there be a collegial and effective working relationship between the other IACUC members and the veterinarian, it is important to avoid the potential for real or perceived conflicts of interest.

1.7.2 Veterinarian – will cover the veterinary aspects of all animal research Proposals and activities. If more than one veterinarian is appointed to the IACUC, the Attending Veterinarian shall be the official veterinarian of the IACUC.

1.7.3 Secretary – will ensure all records of the meetings and decisions of the committee are properly maintained. The committee has an option not to elect a secretary if they have an IACUC Staff.

1.8 Conflict of Interest

1.8.1 If a prospective Investigator submitting a research Proposal believes that an IACUC member has a potential conflict of interest, the Investigator may request that the member be excluded from the decision-making pertaining to the approval of the Proposal.

1.8.2 When a member of the IACUC has a potential conflict of interest, the member should notify the IACUC Chairman and may not participate in the IACUC review or approval except to provide information. Members who have a conflict of interest may not be counted toward any quorum requirements and may not vote. An example of conflict of interest is where a member is involved in a potentially competing research programme.

1.9 Quorum Requirements

1.9.1 Certain IACUC actions require a quorum. These are full committee reviews of a research Project and suspension/withdrawal of approval for a Project.

1.9.2 “Quorum” is defined as at least 50% of the members of the IACUC. Therefore:

(a) a protocol or Project requiring a full committee review is approved only if a quorum is present at a convened meeting, and if more than 50% of the quorum votes in favour.

(b) To suspend an activity or withdraw approval for a Project, the IACUC must review the matter at a convened meeting of the quorum of the IACUC and the suspension/withdrawal of approval must be approved by more than 50% of the quorum present.

(c) For the avoidance of doubt:

(i) members who are disqualified due to a conflict of interest may not be counted toward any quorum requirements and may not vote

(ii) abstentions from voting do not alter the quorum or change the number of votes required. For example: If an IACUC has 10 members, at least 5 undisqualified members must be present at a convened meeting to constitute a quorum and approval of a protocol would require a minimum of 3 votes whether or not there were abstentions.
1.10 Facility Review Functions of the IACUC:

1.10.1 Review, at least once every 6 months, the Research Facility’s programme for the humane care and use of animals, using the Guiding Principles as a basis for evaluation. Areas in which surgical manipulations are performed must always be included.

1.10.2 Inspect, at least once every six months, all of the Institution’s Housing Facilities (including satellite facilities) using the Guiding Principles as a basis for evaluation. Satellite holding facilities are facilities outside a core facility or centrally designated area in which animals are housed for more than 24 hours.

1.10.3 Prepare reports of the IACUC evaluation and submit the reports to the CEO. The reports must contain a description of the nature and extent of adherence to the Guiding Principles and identify specifically any departures from provisions of the Guiding Principles and state reasons for departure.

1.10.4 The IACUC may determine the best means of conducting an evaluation of its programme and facilities. The IACUC may invite ad hoc consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report.

1.10.5 Reports must distinguish significant deficiencies and must contain a reasonable and specific plan and schedule for correcting each deficiency. A significant deficiency is one that is or may be a threat to the health and safety of the animals.

1.10.6 Review concerns involving the care and use of animals at the Institution.

1.10.7 Make recommendation to the CEO regarding any aspect of the animal programme, facilities or personnel training.

1.10.8 Review and approve, require modifications or withhold approval of animal care and use activities. A complete review is required at least once a year.

1.10.9 Be authorised to suspend activities involving animals in accordance with the Guiding Principles. The CEO in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with full explanation for record purposes.

1.10.10 Reports must be made available to the AVA for inspection and copying upon request, and the IACUC must maintain a register of approved Projects.

1.11 IACUC Operation and Administration

1.11.1 Institutional Responsibility for Animal Welfare

(a) Assuring laboratory animal welfare necessitates a partnership between the CEO, the IACUC, the Veterinarian and Investigators. Ultimately, accountability for assuring human care and use of animal resides with the Institution, but this may only be achieved when all of the players, i.e. the
investigators and their research staff, the veterinary staff, animal caretakers and technicians, and the IACUC, contribute to a shared goal.

(b) Each Institution should provide a framework with appropriate resources for an animal care and use programme that is managed in accordance with the Guiding Principles. Organisations that function effectively have simple, clear and direct lines of responsibility and corresponding authority.

(c) The IACUC needs to work closely with the animal users, the animal care staff, and the responsible veterinarians to ensure a high quality animal care and use programme. The CEO must support the IACUC by providing appropriate resources.

1.11.2 Responsibilities of the CEO

(a) The CEO must have the authority to allocate organisational resources needed to maintain a smoothly functioning animal care and use programme based on the recommendations and advice from:

(i) The IACUC
(ii) The veterinarian
(iii) The animal facility professional and administrative staff

(b) The CEO should also clearly define and assign responsibilities and reporting channels for other essential programme elements such as:

(i) Personnel training
(ii) Occupational health and safety
(iii) Maintenance of facilities.

(c) The IACUC, appointed by the CEO of the Institution, must be empowered to perform its duties without interference.

1.12 Additional Manpower and Renumeration

1.12.1 IACUC Staff

(a) It is advisable that an IACUC committee, especially for large Institutions, choose to have a full time IACUC Staff. The responsibility of the IACUC Staff ranges from clerical, administrative to professional, depending on the size and complexity of the programme. The IACUC Staff:

(i) must have knowledge on Occupational Safety Health as well as Animal Research and must undergo the same training that IACUC members received, in order to be highly efficient and knowledgeable in all IACUC activities

(ii) should act to also provide constant and effective communication between all researchers, scientists, Institutions, and IACUC members

(iii) must monitor and maintain all official records.
1.12.2 Ad hoc Consultants

(a) Ad hoc consultants can be sourced by the IACUC on special cases where specific professional advice is needed. The amount of remuneration should be such that his/her recommendation will not be influenced.

1.12.3 Remuneration

(a) In order to motivate the IACUC members to participate in the meetings, a minimal remuneration can be offered. The amount should be such that his/her decision will not be influenced.

1.13 Training of IACUC members

1.13.1 At least fifty percent of the IACUC members must have undergone formal training in IACUC work. Suggested modules for Training:

(a) ARENA IACUC 101 Workshop

(b) Orientation Module - Programme & Education Training for New IACUC Members

(c) Recommended Continuing Education Module

(d) Internet On-Line Training to supplement any training done and keep the members updated on all IACUC trends and developments.

1.13.2 All IACUC members must participate in the course on “Responsible Care and Use of Laboratory Animals” as described the Training Guidelines.
CHAPTER 2 OVERSIGHT OF THE ANIMAL CARE AND USE PROGRAMME

2.1 Programme & Facility Review

2.1.1 The IACUC must review the programme for humane care and use of animals at least once every six months, using the Guiding Principles as the basis for the evaluation.

2.1.2 Benefits of the Reviews:

(a) Reviews provide an ongoing mechanism for ensuring that the Institution maintains compliance with applicable animal care and use policies, guidelines, and laws.
(b) Reviews serve as an opportunity for constructive interaction and education for the animal care personnel, research staff and IACUC members.
(c) Reviews can help an Institution prepare for subsequent visit by evaluators such as AAALAC.

2.2 Conducting Programme Evaluations

2.2.1 Key aspects of an animal care and use programme that should be emphasised in the semi-annual evaluation include:

(a) IACUC membership, functions and procedures, including protocol review
(b) Facility inspection process
(c) Provisions for reviewing and investigating concerns regarding animal care and use.
(d) Record keeping practices
(e) Methods employed to meet reporting requirements
(f) Occupational health and safety programme
(g) Veterinary medical care programme
(h) Personnel qualification and training.

2.2.2 Specific procedures to accomplish programme evaluation may include presentation by appropriate individuals (veterinarian, occupational health and safety representative, etc) and review of written Institutional policies such as standard operating procedures, guidelines on use if anaesthetics and analgesics, and euthanasia procedures.

2.3 Facility Review

2.3.1 All Housing and Research Facilities must be inspected in the semi-annual review including:

(a) Satellite facilities (containment areas outside the central/core animal facility where animals are housed for more than 24 hours).
(b) Areas in which surgical Manipulations are performed.
Animal study areas (where animals are held more than 12 hours)

Holding facilities.

2.3.2 Laboratories in which routine procedures, such as immunisation, dosing, and weighing, are conducted may be evaluated by other means such as random inspection. However, the Institution, through its IACUC, is still responsible for all animal-related activities regarding 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.

2.4 Staffing and Scheduling the Facility Inspections

2.4.1 Inspections may be accomplished by assigning specific facilities to subcommittees, each of which must consist of at least two IACUC members. However, no ACUC member should be excluded should she or he wish to participate in any inspection. The inspection team should have a working knowledge of the Guiding Principles to fully evaluate the facilities that are being inspected.

2.4.2 The IACUC may determine whether the supervisory personnel of various facilities should be notified of the date and time of inspection. Advance notification allows individuals to be available to answer questions; an unexpected visit may show the facility during usual operations but also may result in having to be rescheduled if key individuals are not available.

2.4.3 While the inspection of each facility must be conducted semi-annually there is no requirement for all facilities to be inspected at the same time.

2.5 Performing Inspections

2.5.1 The inspections are to cover the following:

(a) Sanitation
(b) Food and water provisions
(c) Animal identification
(d) Waste disposal
(e) Animal health records
(f) Controlled and/or expired drugs
(g) Environmental control
(h) Occupational health and safety concerns
(l) Staff training
(j) Knowledge of applicable rules and regulations
(k) Security.
2.5.2 Adherence to the following recommendations will assist the IACUC in performing inspections:

(a) An updated list of all the facilities to be inspected should be maintained by the IACUC.

(b) All proposals submitted to IACUC should specify locations where animal procedures will be performed.

(c) It is helpful to maintain a list of all facilities including room number, function of the room, species, and deficiencies identified during the previous inspection.

(d) For satellite areas a contact person is useful.

(e) For facilities with multiple rooms a floor plan can assist the inspectors.

(f) If a subcommittee is performing the inspection, a blend of Committee members who last inspected the area with members who did not can bring both continually and a fresh perspective to the inspection process.

(g) Notes should be taken throughout the visit to assist in preparation of the final report.

(h) Apparent deficiencies should be discussed with the person in charge of the facility to ensure that the team’s perception of the situation is accurate. In some cases an apparent deviation will be due to the experiment in progress. (e.g. withholding food prior to surgery)

(i) Use of a checklist provides consistency and helps document that all categories were assessed.

2.6 Use of AAALAC Activities as Programme Evaluation

2.6.1 Provisions permitting use of ad hoc consultants may be invoked by IACUCs to make use of either of the two AAALAC assessment programmes (Programme Status Evaluation or Accreditation), or pre-assessment preparation activities, to meet the requirements for an IACUC semiannual programme evaluation and subsequent report.

2.7 Documentation

2.7.1 A written report of the semiannual programme review and facility inspection must be prepared and must be signed by the majority of the IACUC. The report must describe the Institution’s adherence to the Guiding Principles, and identify any deviations.

2.7.2 Any deficiencies identified in these reviews must be designated by the IACUC as minor or significant. A significant deficiency is defines 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.

2.7.3 The report must indicate whether or not any minority views were filed, and minority views must be included in the final document.
2.7.4 A copy of the report is sent to the CEO and must be kept for a minimum of three years. The report must be delivered in person in order to emphasise the findings and plans for action.

2.8 Animal Environment, Housing and Management

2.8.1 General

(a) Proper housing and management of animal facilities are essential to animal well-being, to the quality of research data and teaching or testing programmes in which animals are used, and to the health and safety of the personnel. A good management programme provides the environment, housing, and care that permits the animal to grow, mature, reproduce and maintain good health; provides for their well-being and minimises variations that can affect research results.

(b) Animals should be housed in a manner that facilitates the expression of species-typical behaviour and minimises stress-induced behaviours. For social species, housing systems should be designed to accommodate pair or group housing of animals.

(c) The IACUC is responsible for the review and approval of housing systems and the follow-up objective evaluations to ensure the housing system is appropriate for the health and well-being of the species and consistent with research objectives.

2.8.2 Housing

(a) Adequate animal husbandry practices and health maintenance are facilitated by well-constructed and maintained caging or housing systems. Cages should:

   (i) Allow for social interaction within or between enclosures, adequate ventilation, and observation of animals with minimal disturbance of them

   (ii) Provide a safe and secure environment that permits the normal physiologic and behavioural needs of the animals to be expressed.

   (iii) Enable ready access to food and water receptacles and be constructed of materials that balance the needs of the animal with sanitation;

   (iv) Be constructed with materials that resist corrosion and withstand chipping, cracking or rusting.

(b) Unsealed wood may be acceptable for use as perches or other climbing structures, resting areas, or in the construction of perimeter fences, runs and pens, but wooden items need to be replaced periodically because of wear, damage, and to achieve adequate sanitation.
(c) Cage size requirements/recommendations for most common laboratory animal species are provided by the Guiding Principles. Cage complexities, vertical weight of the cage, and the cage design can influence how an animal uses the cage space provided. The cage must be such that:

(ii) it provides sufficient space so that, at a minimum, the animal can turn around and express normal postural adjustments.

(iii) the animal must have sufficient clean and unobstructed space to move and rest in.

(d) Use of wire bottom cages is discouraged for rodents, especially in long-term studies or in larger and older animals, as it may cause foot injury. Use of wire bottom cages should be scientifically justified and approved by the IACUC.

2.8.3 Temperature, Ventilation, Illumination and Noise

(a) Environmental factors can have a profound effect on the health and well-being of animals as well as on the outcome of experimental manipulation. Temperature, humidity, air pressure and air exchange rate, illumination level, and noise levels all may affect well-being and research results.

(b) Light intensity, duration of exposure, wavelength of light, light history of the animal, pigmentation of the animal and other factors should be considered when establishing an illumination level in the animal room.

(c) Because sound exposure can have variable effects on animals, noise generators should be minimised in animal areas. Environments should be designed to accommodate animals that make noise, rather than resorting to methods of reducing the noise made by animals.

(d) A review of an animal care and use programme should include consideration of environmental standards adopted for the facilities with adequate justification for deviations, which are reviewed and approved by the IACUC.

(e) While the environmental control in outdoor facilities is much less stringent. Reliable methods of monitoring environmental control systems should be in place, including an after-hours monitoring and response programme.

(f) Back-up heating, ventilation, air conditioning, and lighting systems are highly desirable.

2.8.4 Husbandry

(a) Animal Identification

(i) It is imperative that research animals be adequately and appropriately identified and that the records pertaining to individuals or groups of animals be maintained. A wide range of acceptable methods can be employed, including:

(aa) Cage cards
(bb) Subcutaneous transponders
(cc) Ear notches and tags
(dd) Collars
(ee) Coloured stains
(ff) Individual animal tattoos.

(ii) The use of toe-clipping to identify individual rodents is discouraged; when necessary, it should be rigorously justified for scientific necessity and done only on very young rodents.

(iii) Animal records may consist of a cage card or may involve detailed individual animal information, depending principally on the species and research requirements. Cage cards should include:

(aa) Source of the animal
(bb) Strain or stock
(cc) Names and locations of responsible investigators
(dd) Pertinent dates
(ee) Protocol number.

(b) Feeding

(i) All animals should receive food that is:

(aa) Palatable
(bb) Free from contamination
(cc) Sufficient and nutritive value to maintain their good health

(ii) Specific diets should be selected based on the needs of each species, with special consideration of the requirements for Vitamin C by guinea pigs and some species of non-human primates. Animals should be fed at least once a day except under conditions of hibernation, veterinary treatment, procedural fasts, or other justified circumstances.

(iii) It is known that standard commercial dry bulk foods, when stored properly, retain their nutritional value for six months (generally three months for those containing Vitamin C, unless a stabilised form is used).

(iv) To help ensure that fresh, uncontaminated food is provided:

(aa) Bags should be stored off the floor
(bb) The milling date should be known (the date or code is usually stamped on each bag)

(cc) The oldest stock should be used first.

(v) Small quantities of food may be kept in animal rooms if stored in tightly covered, leak and vermin proof containers. These should however not be moved from room to room.

(vi) Food should be provided in receptacles that are accessible to all animals in a cage or pen and placed so as to minimise contamination.

(vii) More than one receptacle may be necessary for some socially housed animals.

(viii) Food receptacles should be easily cleaned and sanitised, and those functions should be performed on a schedule that meets the Guiding Principles requirements.

(ix) With limited exceptions (neonatal animals, or animals with limited mobility) food should not be placed on the bottom of the cage. Although some species may prefer this presentation, it results in waste and contamination of food.

(c) Watering

(i) Potable drinking water should be available continuously or provided as often as necessary for the health and well being of the animal, considering the animal’s species, age, condition, and any research requirements.

(ii) Water maybe provided in receptacles (bowls, bottles, and automatic watering systems.). Whatever method is used, care should be taken to ensure that the water does not become contaminated and is actually available.

(iii) Water maybe treated or purified to eliminate contaminants; however, some water treatments may cause physiologic changes, alter microflora, or affect experimental results.

(iv) Sipper tubes and automatic watering devices should be checked daily for potency and cleanliness. Animals occasionally need to be trained to use automatic-watering devise. Water bottles generally should be replaced and sanitised rather than filled.

(d) Bedding

(i) Bedding may be used in the housing of a variety of commonly used laboratory animals.

(ii) Bedding materials should be absorbent and free of any substances that might harm the animals or alter research data. Cedar and untreated softwood products can affect the animal’s metabolism (ex. Liver enzymes), which may in turn affect immunological or other physiologic parameters, and can increase the incidence of cancer.

(iii) Bedding should be stored off the floor.
(iv) Animals may be placed directly on bedding material, a common practice with many rodent species, or bedding may be placed under a slat-bottom cage.

(v) Bedding should be used in sufficient amounts and changed as often as necessary to keep the animals clean and dry and the animal room relatively odour free.

(vi) Care should be taken to keep bedding from contacting water tubes as this may lead to leakage of water into the cage.

(vii) The frequency of bedding change depends on several factors, including the number of animals, species, type of caging and type of bedding.

2.8.5 Facility Maintenance

(a) Cleaning and Sanitation

(i) Cleanliness and sanitation are essential to the operation of the animal facility.

(ii) The Guiding Principles set forth-recommended frequencies and methods for cleaning and sanitation of facilities, equipment and accessories. In general, the frequency and methods should ensure that animals are maintained and in a clean, dry environment, free from exposure to harmful contamination and excessive animal odours.

(iii) Cleaning agents that mask animal odours should not be used as a substitute for good sanitation practices.

(iv) Cleaning equipment such as mops and buckets should not be moved from room to room due to the potential for cross-contamination.

(v) The most efficient and effective method of cleaning and sanitising cages and accessories (feeders, water bottles, sipper tubes) is the use of mechanical washing machine. Alternatively, portable high-pressure spray washing and disinfection may be used. Least efficient and effective is hand washing and disinfection of such equipment.

(vi) In general, enclosures and accessories (cage tops) should be sanitised at least every two weeks. Solid bottom cages water bottles and sipper tubes should usually be sanitised weekly. The supply lines of automatic watering systems should be flushed and disinfected on a regular basis.

(b) Waste Disposal

(i) A research animal facility generates a significant amount of waste that must be removed and disposed of on a regular, frequent basis. Waste containers should be readily accessible with tight fitting lids.

(ii) Disposal of non-biohazardous material, including incineration and removal to land-fill, must conform to the "Occupational Safety and Health Guidelines for Laboratories and Production Facilities in the Biomedical Sciences Industry" put forward by the Ministry of Manpower and any relevant laws.
(iii) Hazardous waste, including carcasses of animals exposed to radioactive or bio-hazardous agents, must be adequately sterilised and/or contained prior to removal and disposal. After adequate striation, pathogen-contaminated animal carcasses could be removed and disposed in a same way as the non-hazardous animal carcasses. In particular, animal carcasses contaminated with toxic chemicals and radioactive materials should be disposed following the guidelines of disposal of toxic chemicals and radioactive materials of the Ministry of the Environment and any relevant laws.

(iv) The disposal of waste and carcasses arising from research using microbiological agents on animal models must comply with paragraphs 2.9 and 3.5.5.

(v) If waste must be stored while awaiting disposal, the storage area should be outside the animal holding and clean equipment areas. Animal carcasses and tissues should be disposed of within 24 hours.

(c) Pest Control

(i) The research animal facility is an active place, with frequent movement of personnel, animals, equipment, containers, and food and bedding, creating ideal conditions for the introduction of pests, including arthropods, birds, and wild rodents.

(ii) Pest control programmes are however implicated by the potential for harm to animals and personnel, as well as interface with research data by many commonly used pesticides. A regularly scheduled, documented pest control and monitoring programme should be implemented, which effectively combines elimination of all entry and harborage sites with good waste disposal and personnel training. If traps are used, methods should be humane.

2.9 The Use of Microbiological Agents in Research on Animal Models

2.9.1 The use of animals in research poses unique risks to research personnel and to the community. Animals generate aerosol, may scratch and bite and can be sources of important zoonotic diseases which may be introduced into the laboratory in latent forms. The risks are significantly increases when animals are used as subjects in research using microbiological agents.

2.9.2 In addition to the other safety requirements outlined in these IACUC Guidelines, Institutions carrying out research using microbiological agents on animal models must have facilities and practices that satisfy Vertebrate Animal Biosafety Level Criteria (ABSL) appropriate for the research. These criteria are set out Section IV of *Biosafety in Microbiological and Biomedical Laboratories* published by the U.S Department of Health and Human Services.

2.10 Emergency, Weekend and Holiday Care

2.10.1 Laboratory animals must be observed by qualified personnel every day, including weekends and holidays to ensure their health and well-being, as well as to promote sound research practices.
2.10.2 Skilled assistance, including veterinary care, must be readily available at all times. Names and telephone or pager numbers of those assigned these responsibilities should be prominently displayed in the facility.

2.10.3 A disaster plan should be part of the overall facility safety plan which takes into account both personnel and animals.

2.11 Behavioural Management for Laboratory Animals

2.11.1 There are varying requirements for attention to the behavioural management of laboratory animals, depending on the species of animal and the reference document.

2.11.2 The Guiding Principles provides recommendations for:

(a) Increasing the complexity of the structural environment
(b) Addressing the social environment of animals
(c) Promoting the expression of species-typical activity in a cohesive behavioural management programme for all vertebrate species.

2.11.3 In particular, a plan for environmental enhancement adequate to promote psychological well-being of non-human primates must address:

(a) The social needs of non-human primates
(b) Environmental enrichment of the primary enclosure through provision of cage complexities, manipulation, varied food items, foraging or task oriented feeding methods, and safe personnel interaction.
(c) Special needs of certain classes of primates (e.g. young animals, animals in psychological distress, some individually housed primates, and some great apes.)

2.11.4 Exemptions from some or all of the environment enhancement plan for scientific reasons must be documented in the protocol, approved by the IACUC, and reviewed not less than annually. The veterinarian may exempt individual primates from the plan.

2.11.5 Oversight

(a) The IACUC should provide oversight of the behavioural management programme in a manner similar to its oversight of other husbandry components of the animal care and use programme, and evaluate programme outcomes during semi-annual reviews.
(b) To adequately discharge this responsibility, the IACUC should have access to training or other orientation materials that will assist IACUC members in evaluating the adequacy of the programme.
(c) Formal, written plans for nonhuman primate environmental enrichment, established to provide a framework to the behavioural management
programme, should be approved by the IACUC and reviewed periodically. The committee should identify who is responsible for keeping the plan current and implementing plan (e.g. an enrichment committee, Attending Veterinarians, etc.) The NRC publication, “The Psychological Well-Being of Nonhuman Primates” (1998), adopted by the Association for Assessment and Accreditation of Laboratory Animal Care International as a Reference Resource for accredited Institutions, advises a team approach to development and oversight of the behavioural management programme to include investigators, veterinarians, and the IACUC.

2.12 Role of the Veterinarian

2.12.1 Adequate veterinary medical care is an essential component of an animal care and use programme. Institutions with smaller programmes may opt for a part-time consulting veterinarian but the veterinarian’s overall responsibilities remain in all cases.

2.12.2 It is the Institution’s responsibility to support ongoing improvements in the animal care and use programme through the development and implementation of procedures and policies (e.g. IACUC guidelines) that enhance the health of animals. Clear provisions should be made to give the veterinarian appropriate authority to execute a programme of adequate veterinary care, including access to all animals.

2.12.3 The Institution should appoint an Attending Veterinarian who will have overall responsibility for the veterinary aspects of the Care and Use of Laboratory Animals programme. This veterinarian need not however be employed full-time at the Institution.

2.12.4 Qualifications

(a) Veterinarians involved in animal research must have relevant experience and training in the care of laboratory animal under conditions of Biomedical Research. It is recognised that not all qualified veterinarian have experience in the above.

(b) Previous work experience as a veterinarian in a Biomedical Research Institution with animal facility is a useful pre-requisite. Veterinarians without such previous experience must satisfy the IACUC that they are adequately prepared for the job by showing evidence of having attended appropriate courses relevant to the job (such as those run by AAALAC or ARENA).

2.12.5 Responsibilities

(a) The chief responsibility of the veterinarian is to provide for health and welfare of animals. The details of a veterinary programme will depend on the species of animals employed and the particulars of the laboratory animal use, but in all cases the programme and care provided must comply with standard veterinary practice.

(b) The introduction of new animals is important aspect of veterinary care programme with such consideration as stabilisation periods, isolation and quarantine.
(c) Random source or wild caught animals are not bred by the supplier, but are obtained from a variety of sources including pounds, shelters, farms that may not conform to the same standards of animal husbandry and health as the research facility. Before their use, clinical evaluation and conditioning of these animals are required to ensure that they are not carrying diseases that can be transmitted to other animals, including humans, or do not introduce uncontrolled variables into research.

(d) Although selection of high quality laboratory animals has reduced the prevalence of infectious diseases in research animal colonies, preventive medicine programmes, conducted under the guidance of the veterinarian, continue to be important for maintenance of healthy animals. These programmes include:

(i) Immunisation against infectious pathogens
(ii) Surveillance of colonies for specific infectious microbial agents
(iii) Disease prophylaxis utilising pharmaceutical agents
(iv) Isolation and quarantine of incoming animals
(v) Separate housing of animals according to species, source or different background microbial floras.

(e) While preventive medicine programmes are successful in reducing the incidence of disease, illness and injury may still occur on laboratory animal colonies. The veterinarian is responsible for monitoring animal health, providing adequate diagnostic support through clinical assessments, laboratory diagnosis and necropsy when required, and treating animals when illness or injury necessitates veterinary medical care.

(f) Using a documented process, the veterinarian may delegate responsibility for care to trained technical staff but must always be available to provide rapid diagnosis and treatment.

(g) The veterinarian must attend not only to the physical health of the animals, but also the psychological well-being of non-human primates.

(h) Specific areas requiring the veterinarian’s attention and guidance are:

(i) The selection and utilisation of suitable anaesthetic and analgesic agents and methods of euthanasia
(ii) Appropriate selection of species for research projects
(iii) Proper performance of surgical procedures and adequate preoperative, surgical and postoperative care.

(i) The veterinarian should discuss with Investigators the design and implementation of study Proposals and may provide written guidelines dealing with these issues. Collegial exchanges between the investigator and the veterinarian before the submission of a proposal to the IACUC may address many of the committee’s concerns and expedite the review process.
(j) The veterinarian or his/her staff may participate directly as a co-investigator in activities involving animals by providing clinical, surgical or other scientific or technical expertise to the study. Veterinarians sometimes also serve as Principal Investigators with responsibility for their own research and training programmes. In such situations, the IACUC has the same obligation to review and approve the proposed activities as it would for any other investigator. When the veterinarian is personally involved in a research project, he/she must excuse himself/herself from the IACUC review and vote on the project.

(k) Institutions utilising animals in research and teaching must provide training and instruction to personnel on humane methods of animal maintenance and experimentation. The veterinarian and the IACUC are responsible for providing such training.

(l) Institutional Occupational Health and Safety programmes must be in place to ensure that personnel who have laboratory animal contact are included in a risk assessment process and action plan addresses workplace safety through appropriate educational, industrial hygiene and medical interventions. The veterinarian, in cooperation with appropriate health and safety officials of the Institution, is often responsible for the implementation and execution of aspects of the programme concerned with animal health and safety issues.

2.12.6 The Veterinarian and the IACUC

(a) The veterinarian occupies an essential position on the IACUC with specific defined functions. Institution employing several veterinarians may appoint more than one to the IACUC, but all Institutions regardless of size must have at least one veterinarian with direct or delegated programme authority and responsibility as a member of the IACUC.

(b) A strong veterinary presence on the IACUC has proven beneficial in many Institutions. However, Institutions should also be aware that the domination of IACUC activities by veterinarian(s) may foster or be symptomatic of the disengagement of other members, thereby resulting in a less cohesive and effective IACUC.

(c) The veterinarian should keep abreast of current literature on comparative medicine and laboratory animal science. The knowledge gained often leads to suggestions or alternative techniques, models or species that may enhance animal well-being, augment the study design and help ensure the completion of the proposed study.

2.13 Occupational Health and Safety

2.13.1 The health and safety of individuals working in animal care and use programmes is an area of Institutional concern requiring commitment from the senior officials of the Institution. This is to prevent occupational injury and illness by avoiding, controlling or eliminating hazards in the workplace.

2.13.2 The emphasis of such a programme is the prevention of illness and injury, but it also includes provisions for early diagnosis and treatment when necessary.

2.13.3 Role of the IACUC’s Responsibility for Occupational Health and Safety
(a) Role of the IACUC in the Occupational Health and Safety Programme
Procedures should be developed for conducting a health and safety review of
research activities that present hazards to personnel. These procedures
should be incorporated into the IACUC protocol review process.

(b) Procedures to identify and address non-experimental hazard should also be
implemented.

(c) Communication and other procedural links between the IACUC and the
environmental health and safety professional or office should be established,
maintained and documented.

(d) The IACUC also 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).

2.13.4 Elements of an Occupational Health and Safety Programme

(a) An effective programme design requires input from health and safety
specialists and will include the following elements:

(i) administrative procedures,
(ii) facility design and operation,
(iii) risk assessment,
(iv) exposure control,
(v) education and training,
(vi) occupational health-care services,
(vii) personal protective equipment,
(viii) equipment performance,
(ix) information management,
(x) emergency procedures, and
(xi) programme evaluation.

(b) The details of each element will be dictated by the extent and nature of
employees’ exposure and the type of animal use programme.

2.13.5 Personnel Participation in the Occupational Health and Safety Programme

(a) A wide range of personnel (e.g., animal care staff, investigators, technical
staff, students, volunteers, engineers, housekeepers, security officers, 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 OHSP.

(b) The extent and level of participation of personnel in the OHSP should be based on risk assessment, including:

(i) hazards posed by the animals and materials used;
(ii) exposure intensity, duration, and frequency;
(iii) susceptibility of personnel; and
(iv) history of occupational illness and injury in the workplace.

(c) Health and safety specialists should be involved in the assessment of risks associated with hazardous activities.

2.13.6 Education and Training

(a) There are ethical and legal requirements to inform individuals of health risks that affect them and appropriate precautions. The objectives of an Institution’s OHSP can be achieved only if employees are appropriately trained to 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.

(b) Training should include information about:

(i) zoonoses,
(ii) chemical safety,
(iii) microbiologic and physical hazards (e.g. allergens, radiation),
(iv) hazards associated with experimental procedures,
(v) handling of waste materials, and
(vi) personal hygiene.

(c) Proficiency in work assignments through education and training will also contribute to a safer work environment. Training should be a continuous process, and records of OHSP training of personnel should be maintained.

2.13.7 Preventive Medicine and Provision of Medical Care

(a) The principal means of preventing occupationally acquired illness or injury is by controlling or eliminating hazards.

(b) The efficacy of the prevention programme will depend on the Institution’s resource allocation to hazard control and the cooperation or compliance of personnel who are potentially at risk.
The quality of the preventive medicine programme can also be increased if its development and implementation involves input from trained health professionals.

In addition to established mechanisms for reporting and treating accidents and injuries, the Institution should have access to medical expertise in zoonotic diseases and other health risks associated with laboratory animal care.

Good communication with medical staff will also facilitate better management of the health of animal care personnel and minimise repeat injuries and infections.

2.13.8 Specific Medical Concerns for Individuals Working in the Animal Research Environment

The complexity of the animal research environment creates numerous classes of hazards.

Physical hazards include:

(i) animal bites, scratches and kicks;
(ii) sharps;
(iii) flammable materials;
(iv) high pressure containers and equipment;
(v) low or single colour lighting in animal rooms resulting in poor visibility;
(vi) electric hazards, particularly in areas of water usage;
(vii) ultraviolet and ionising radiation;
(viii) lasers used in surgical areas;
(ix) inadequate housekeeping practices;
(x) ergonomic demands;
(xi) machinery; and
(xii) noise.

Chemical hazards result from their flammable, corrosive, reactive, explosive or toxic properties. Burns and irritation of the skin are the most common chemical injuries related to animal care and use.

Allergic reactions to animals, occasionally resulting in the development of Occupation-related asthma are among the most common conditions that adversely affect the health of personnel in the animal research environment. Estimates of the prevalence of allergies in animal care workers range from 10% to 44%. Preplacement screening evaluations, attention to facility design, work practices, and the use of personal protective equipment can reduce the
potential development of laboratory animal allergy and possibly alter its severity.

(e) Infectious diseases also pose a significant risk depending on the species and health status of animals involved and the level of exposure to them by animal care personnel.

(f) Infectious diseases to which animal care personnel may be exposed include:

(i) viral infections such as contagious ecthyma,
(ii) the hepatitides, and
(iii) Cercopithecine herpes virus 1 (Herpes B)
(iv) rickettsial diseases such as Q fever and cat scratch fever
(v) bacterial diseases, such as tuberculosis, salmonellosis, and shigellosis
(vi) protozoal diseases, such as toxoplasmosis, giardiasis, and cryptosporidiosis
(vii) fungal diseases, such as dermatomycosis.

(g) In addition to infections acquired from live animals, animal tissues and excreta can serve as sources of zoonoses. Careful monitoring and quarantine of any animals with potential viral or bacterial infections or parasitic infestations are crucial components of any animal care and use programme.

(h) It is important to immunise animal care personnel against tetanus. Routine tuberculosis testing is essential and measles vaccination may also be appropriate for workers exposed to nonhuman primates.

2.13.9 Common Occupational Health and Safety Programme-wide Pitfalls

(a) Instead of being based on hazard identification and risk assessment, the programme identifies personnel risk based on animal contact time or frequency.

(b) There is inadequate training on occupational health and safety topics (e.g. zoonoses, allergies).

(c) Not all personnel at risk (e.g. students, visiting scientists) are offered inclusion in the programme.

(d) Hazard identification covers experimental hazards, but does not address hazards intrinsic to animal care and use.

(e) There will be a possible inadequate linkage between the IACUC and the Institutional safety committee(s).
2.14 Personnel Training and Education

2.14.1 All staff working with laboratory animals must be qualified to do so in order to ensure the humane treatment of animals.

2.14.2 Training is a classic performance standard where the emphasis is on the outcome (i.e. all personnel qualified to do their jobs). The requirement for such competence is mandatory.

2.14.3 Specifically it shall be the responsibility of the Institution 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 fulfil the research facility’s responsibilities.

2.14.4 Training in the recognition and alleviation of animal pain, distress, and abnormalities addresses refinement. Similarly, training in the conduct of animal procedures prepares staff to work without causing unnecessary harm to the animal. Technical proficiency also invokes reduction by avoiding wasted animal lives through failed procedures.

2.14.5 Personnel training should be seen as one of the pillars supporting the animal research programme. Training of staff is essential for safeguarding the quality of the animals as a tool of research or testing. A lack of training may result in inadequate husbandry and poor peri-procedural care, which can undermine the physiological status of the animal thereby potentially impairing the integrity of research results.

2.14.6 Who Should Receive Training?

(a) All staff 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.

(b) For training purposes, staff can be grouped as:
   (i) researchers,
   (ii) animal care technicians, and
   (iii) others (e.g. maintenance or support staff).

(c) In some Institutions, 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.

(d) Training should also be made available to temporary staff, such as students and visiting scientists. These groups may be difficult to intercept for training unless there is a way to identify them.

2.14.7 Development of a Training Programme

(a) A training programme should meet the needs of each type of staff, as described above, who work with or around laboratory animals. There are
many training resources and methodologies that can be used in the development of a training programme: courses, seminars, one-on-one training, conferences, computer-based media and videotapes.

(b) When appropriate for the job responsibilities, technicians should be encouraged to pursue certification by professional associations, such as technician certification by the American Association for Laboratory Animal Science and the Academy of Surgical Research. All staff should have exposure through training to regulatory requirements for animal welfare and occupational health and safety considerations.

(c) Staff who work directly with animals should have training that supports the humane care and use of animals in the course of day-to-day procedures.

(d) There should be requirements that training and instruction of personnel must include guidance in at least the following areas:

(i) Humane methods of animal maintenance and experimentation, including:

(aa) The basic needs of each species of animal;

(bb) Proper handling and care for the various species of animals used by the facility;

(cc) Proper pre-procedural and post-procedural care of animals; and

(dd) Aseptic surgical methods and procedures;

(ii) The concept, availability, and use of research or testing methods that limit the use of animals or minimise animal distress;

(iii) Proper use of anesthetics, analgesics, and tranquilisers for any species of animals used by the facility;

(iv) Methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility.

(v) Utilisation of services (e.g., National University of Singapore Medical Library) available to provide information:

(aa) On appropriate methods of animal care and use;

(bb) On alternatives to the use of live animals in research;

(cc) That could prevent unintended and unnecessary duplication of research involving animals.

(dd) Regarding the intent and requirements of the appropriate Act(s). Training programmes should also include information on occupational health and safety.
2.14.8 Personnel Training Records and Documentation

(a) Although there is no specific requirement to document individual training activities, training records demonstrate that staff have met the training requirements related to their responsibilities in the research animal programme, and regulatory or other oversight authorities often request to inspect personnel training records as evidence of an effective programme.

(b) Training records have value in tracking the range of topics offered, the frequency of training sessions, and the participation of Institutional staff. Such records may include training received in informal settings, e.g. one-on-one instruction for teaching animal use methodologies.

(c) Training records may be archived with the IACUC, a training coordinator, research departments or individual laboratories. Whatever the location, training records should be accessible to inspection by any oversight authority, including the IACUC. If training records of research staff are stored in laboratories, a good practice would be to include a brief review of training records.

2.14.9 Training Personnel

(a) Many Institutions with a large research programme have a training coordinator to oversee the training programme for all personnel with animal care and use training needs.

(b) The training coordinator should be involved in IACUC meetings when Institutional training issues are discussed.

(c) Training coordinators should not be the only ones with training responsibilities. The facility staff, (e.g. veterinarians, veterinary technicians, facility managers and animal care technicians), also should be involved in training activities to the greatest extent possible. Their training activities, either with individuals or groups, should be acknowledged as a valuable contribution to the animal research programme. In this way, individual expertise is fully utilised and every contact with facility staff offers a training opportunity.

(d) In addition, other staff or outside consultants with specialised expertise can be incorporated into the training programme. For example, occupational health professionals may be invited to take part in training on safety related issues. Training in specialised animal methodologies may be best performed by researchers who are accomplished in these techniques. Training programme staff, if available, should participate in or oversee the training by outside experts to ensure that the training content is appropriate.

2.14.10 Institutional Support of Training

(a) A high level of staff participation in a training programme is essential for achieving the performance standard of staff qualifications necessary for quality research and expected by regulatory authorities. Institutions with mandatory training programmes often have the most uniform results.
(b) Where training is not mandatory, there is much that an Institution can do to encourage participation in the training programme. When senior management and IACUC members take part in formal training programmes, (e.g., on compliance issues), staff recognise an imperative to attend these sessions. The involvement of outside speakers with recognised expertise is often successful to draw larger groups to a training session. Letters urging staff participation in training programmes are effective when sent by senior administrators and the IACUC to department chairpersons and principal investigators.

(c) Methods that increase awareness and availability of information within the Institution are valuable to support a training programme. A combination of a training manual, newsletters, mailings, posted flyers, brochures and a Web site inform staff about the requirements for training, the Institution’s animal welfare standards, and the services available in the training programme.

2.15 Emergency Preparedness

2.15.1 Security and Crisis Management

(a) The IACUC has responsibility for the security of the animals and personnel who care for and use these animals with other units within the Institution, such as the units responsible for security, public information, and governmental relations.

(b) The IACUC can serve a key role in advising the Institutional officer and the Institution of potential risks and vulnerabilities, and in developing a plan for responding to potential or real threats.

(c) In all cases the IACUC must consider allegations of noncompliance or animal welfare issues as concerns that must be addressed in accordance with relevant authorities.

(d) There are four key elements to an Institution’s preparedness:

(i) an animal care and use programme of impeccable integrity;

(ii) a security programme based on risk assessment;

(iii) an integrated communication plan with descriptions of research projects in lay terminology, spokespersons and a telephone tree; and

(iv) an internal and external community outreach programme that includes legislators and funding agencies.

2.15.2 Crisis Management Team

(a) The establishment of a crisis management team before a crisis occurs is important in order to respond in a timely manner. This team may be comprised of individuals representing the following areas: security, public information, laboratory animal resources, the IACUC, management/research administration (including the IO), legal affairs, and governmental relations.
(b) It is helpful for this team to meet periodically to keep abreast of current issues at the national and local level, and to be apprised of current research activities.

2.15.3 Risk Assessment – Security

(a) The first step in developing a security programme is to conduct a risk assessment of the Institution’s facilities, and evaluation of the existing security system. Organisation of a security and communication plan then follow.

(b) Some key points include:

(i) Determine facility vulnerability.

(aa) Look at the research facilities with a “public eye.”

(bb) Be aware that use of certain animal species can increase vulnerability (e.g., nonhuman primates, cats and dogs).

(cc) Be aware that some kinds of research may be perceived to be controversial (e.g., surgical and neuroscience protocols, including drug-addiction studies).

(ii) Evaluate the security system.

(aa) Review policies regarding access and electronic surveillance systems.

(bb) Check location of keys and access to animal rooms; entrances and exit sites such as stairwells and roof access.

(cc) Determine who has access to buildings during nights and weekends.

(dd) Ensure computer security, network access etc. with computer administrators.

(iii) Check storage of research data.

(aa) Ensure security of IACUC records and research data, including copies maintained offsite.

(bb) Review research protocols for confidential information.

(cc) Review protocols for graphic and/or sensitive terminology.

(iv) Organise a security plan.

(aa) Consult with local police to establish procedures.

(bb) Establish clear lines of authority and roles in a crisis situation.

(cc) Maintain a list of research projects and scientists.
(dd) Identify ongoing investigations by regulatory agencies.

(ee) Limit access of delivery persons within animal care facilities.

(ff) Keep duplicate physical layout plans available off site.

(gg) Share information with security personnel about activism at other research organisations.

(hh) Develop a document that will provide pertinent information to the police in the event of an incident such as type of incident, location, animals or property destroyed or stolen, people involved, time, method of entry, and need to check for hazardous materials.

(v) Organise a communication plan in the event of an incident during the day, after hours, weekends and holidays.

2.15.4 Communications and Risk Reduction

(a) Institutions using animals need to communicate effectively and on an ongoing basis with the internal and external community and the media. It is important to build these relationships over time and to keep individuals in all of these areas informed about the significance of the work in which animals are used, and the Institution’s commitment to scientific standards through quality animal care and use.

(b) Being proactive by conveying significant advances in research using animals ethically and humanely can reduce the potential for negative public reactions in a crisis situation. The IACUC Chairman and members can interact with Institutional public information officers, researchers, veterinarians, technicians and the research administration to identify spokespersons to address animal research issues. These spokespersons should be provided adequate training.

(c) Fact sheets should be readily available about the Institution’s policies and commitment to humane and appropriate animal care and use, the quality of its animal care and use programme (including accreditation), and brief summaries of the value and importance of any specific animal use under scrutiny. Written materials need to be written in language understandable to nonscientists. Institutions must be prepared to respond to allegations honestly (i.e., if real noncompliance with relevant policies or regulations is substantiated then the Institution must take appropriate action and should be forthcoming about the situation).

(d) In the event of a crisis the facility that is prepared can respond quickly through its spokespersons with accurate and factual information. It is also important for the Institution to notify relevant authorities of such an event so they can confirm the status of the Institution’s support, as well as AAALAC, which maintains a crisis communication plan to assist accredited Institutions.

(e) Maintaining a high quality animal care and use programme, good relationships within the Institution and the community, and an effective education programme can help to prevent and alleviate many crisis situations and significantly reduce the need for long term damage control.
2.16 Disaster Planning

2.16.1 As a fundamental component of the operational plans for most animal facilities, the Disaster Plan is a detailed, site-specific compilation of critical resources that are helpful in a variety of crisis events.

2.16.2 The Guiding Principles recommends that all animal facilities have a Disaster Plan as part of their overall programme and that the veterinarian or animal facility manager be part of the official Institutional response team. While the Guiding Principles does not outline the elements of a Disaster Plan, it does suggest that facilities maintain sufficient emergency power necessary to maintain critical services (e.g., heating, ventilation and air conditioning (HVAC)system) and support functions (e.g. freezers, ventilated racks, isolators). Unique components of the facility may require special considerations.

2.16.3 The proper Institutional authority should approve the final plan so that appropriate resources can be committed during an emergency event. Typically, the IACUC does not have primary responsibility for emergency preparedness, but because emergency events could have significant impact on animals and the animal facility, the committee may choose to assess their site’s preparedness during regular semiannual programme reviews.

2.16.4 Emergency Management

(a) In addition to the development of a Disaster Plan, an animal facility should consider approaching disaster preparedness from the more encompassing perspective of emergency management.

(b) An effective emergency management programme must be considered, which can consist of four parts:

(i) Mitigation (activities related to preventing future emergencies or minimising the effects of emergencies that occur);

(ii) Preparedness (incorporation of the planning and preparations required to handle an emergency, including the Disaster Plan);

(iii) Response (the Disaster Plan put into action when an emergency occurs);

(iv) Recovery (the actions needed to return to normal after an emergency occurs.)

2.16.5 Segments of a Disaster Plan

(a) The Disaster Plan because it is the component of an emergency management programme that the IACUC should review as a part of its semiannual programme review.

(b) The content and scope of the Disaster Plan will be shaped and determined by the individual programme and facility. The following approach is one way to create a Disaster Plan and can be useful to the IACUC in evaluating the facility’s plan.
A suggested organisation method includes:

(i) developing a planning team,
(ii) defining emergencies,
(iii) identifying critical functions and systems,
(iv) defining resources and contacts,
(v) developing policies and procedures
(vi) training staff and testing emergency equipment.

2.16.6 Defining Emergencies

(a) In emergency management various scoring methodologies help to categorise and rank emergencies.

(b) Emergencies (hazards) can generally be divided into three different categories:

(i) Natural emergencies are the most commonly occurring “disasters” and include weather, seismic or ocean related events. Examples include tornadoes, hurricanes, floods, earthquakes, flood tides, etc.

(ii) Technical emergencies are mechanical or human failures and include HVAC failures, computer system failures, chemical spills and structural failures.

(iii) Civil emergencies are deliberate human events such as terrorist attacks, sabotage and labour strikes.

(c) When developing a Disaster Plan, it may be helpful to list each type of emergency and include the primary and secondary effects. Secondary effects can greatly complicate a problem and can affect some critical functions even more than the primary. To help in planning, the list should include the probability of an event occurring. The Disaster Plan should be sufficiently general to be responsive to unplanned types of crises.

2.16.7 Identifying Critical Functions and Systems

(a) Fundamentally, the Disaster Plan should address ways to maintain or cope with the loss of critical functions and systems in the animal facility. To do this, it is important to rigorously identify all critical animal facility specific functions and systems.

(b) The critical functions and systems fall into two general categories: mechanical systems and personnel functions. It is helpful to compare the list of primary and secondary effects of the different emergencies and review their impact on the critical functions and systems. Different scenarios can become the basis for action plans and preparedness activities.
2.16.8 Defining Resources and Contacts

(a) The Disaster Plan can also include lists of available resources and contacts to be used during emergency events. The lists can include various emergency equipment, spare parts, equipment capacities, levels of redundancy built into the mechanical equipment systems and ways to put the equipment into use. Additionally, this section might include critical vendors that can supply services during an emergency, such as a supplier to perform periodic refuelling of emergency generator fuel tanks, as well as up to date emergency personnel notification lists, including criteria for contacting specific individuals.

(b) More advanced plans stage the level of an emergency and clearly prescribe the type of response for each level. Other pertinent items such as floor layouts, mechanical equipment plans, the names and numbers of national, regional and local emergency response organisations and local weather information resources, can be included.

2.16.9 Developing Policies and Procedures

(a) The core elements of a Disaster Plan are the policies, guidelines and procedures that are put into action during an emergency. The plan should address very specific emergencies and/or give general outlines for action steps in response to an emergency. Many plans will also focus on coping with the loss of a critical function or system. This approach is best when it includes evaluation of the reliability of the back-up systems affected during a complex emergency situation.

(b) Available resources should be clearly identified and information on how to access the resources included. Clear lines of authority and responsibility should be established and documented.

2.16.10 Training Staff and Testing Emergency Equipment

(a) Personnel are usually familiar with “fire drills ” through participation in regular emergency evacuation testing of buildings. Effective disaster planning borrows that concept and conducts the same types of rehearsals for other high-risk emergency situations. Exercising realistic scenarios not only provides practical training but also “tests ” the emergency plans for deficiencies or vulnerabilities.

(b) Similarly, emergency equipment should be tested and maintained in working order.

(c) Finally, the Disaster Plan should be made readily available to all staff members. Some facilities have the plan available on internal Web sites.

2.16.11 Conclusion

(a) Animal facility management should recognise that emergencies and unexpected problems are inevitable. Adopting the mindset that emergencies are a fact of life and will occur is the first step towards their prevention.

(b) Preparedness is critical for emergency avoidance and can reduce, if not eliminate, negative affects. A good Disaster Plan will ensure a quick and
effective response and faster recovery. However, the process of emergency management planning is not totally intuitive and a specific effort needs to be made to examine the issues and devise plans.

(c) Furthermore, because there are no “formulas” and very few formal requirements for backup or emergency systems, one facility’s plan will not be 100% effective at another facility.

(d) The overall process should be dynamic and should be reviewed on a regular basis by the facility. The IACUC may also choose to include it periodically as a part of their semiannual programme reviews.

(e) The modification or upgrading of functional systems is an ideal time to upgrade the emergency handling potential of the system. Unfortunately, emergency/hazard identification is clearest in retrospect, but the special efforts of prospective disaster planning pay the greatest dividends.
CHAPTER 3 REVIEW OF PROPOSALS

3.1 Fundamental Issues

3.1.1 The IACUC is responsible for overseeing and evaluating all aspects of animal care and use, and is charged with reviewing Proposals that involve animals.

3.1.2 In its review of Proposals, the Committee's primary goal should be to facilitate compliance with applicable guidelines, laws, regulations and policies consistent with the performance of appropriate and productive scientific endeavours.

3.1.3 Protocol Review Criteria

(a) There are many aspects of research that an IACUC should review, such as food and water deprivation, use of noxious stimuli, and physical restraint. The Guiding Principles provides useful guidance on these and other practices.

(b) Protocol Review Criteria addresses many of the subjects described below in greater detail. If the IACUC does not have the scientific and technical expertise to evaluate all aspects of a protocol, it may bring in outside expert consultants to provide information. Such consultants may not vote. 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.

3.1.4 Proposal Review Procedures

(a) Institutions may develop their own meeting procedures as long as the procedures do not contradict or are not inconsistent with the requirements of The Guiding Principles.

(b) Some committees find it helpful to assign a member a given Proposal for in-depth review and liaison with the Investigator prior to committee review. Still other committees assign this task to professional IACUC staff. The Investigator may choose to consult with these individuals and request a preliminary review before formally submitting a Proposal.

(c) The IACUC may conduct either full review or designated member review of protocols and proposals.

3.1.5 Full Committee review

(a) Full committee review of Proposals requires a convened meeting of a quorum of the IACUC members to review initial protocols as well as to review proposed significant changes in previously approved protocols.

(b) Proposals reviewed by the full committee must receive the approval vote of more than 50% of the quorum present in order receive approval.

(c) Some committees designate a specific member or members to serve as primary or primary and secondary reviewers. These individuals, usually chosen for their expertise or familiarity with a given topic, are responsible for
an in-depth review of a proposal and sometimes take responsibility for describing the Proposal to the full committee and answering questions about the Proposal during review by the Committee.

(d) Primary and secondary 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. The use of primary reviewers differs from designated member review (see below), which invests authority to approve a proposal in one or more members.

(e) Review of proposals by the full committee method invokes a deliberative process, and the Guiding Principles requires that minutes of IACUC meetings reflect committee deliberations. Minutes should include records of attendance, a summary of the issues discussed and the resolution of issues, and the results of IACUC votes on proposals.

(f) The participation of the investigator can facilitate the review in a number of ways. Obviously questions can be addressed as they are raised rather than after the meeting, allowing the review process to proceed rather than be interrupted for this exchange of information. Another benefit is the opportunity for the investigator to give a broad overview of how the proposal under review fits into the larger research picture, thus providing additional information regarding the justification and scientific merit. Invariably, both the investigator and the IACUC benefit from such an exchange.

(g) The greatest deterrents to participation by investigators in the IACUC meeting are that it may make the meeting last longer, and problems arise if this is an adversarial rather than collegial exchange of information. In any event, the Investigator should leave before the final committee deliberations and if he or she is a committee member may not contribute to a quorum or vote.

3.1.6 Designated member review

(a) To utilise designated member review, each IACUC member must be provided with at least a list of the proposed research Proposals or proposed significant changes to previously approved Proposals prior to the review.

(b) Most committees provide members with an abstract of Proposals; but in all cases, written descriptions of the research Proposals must be made available to IACUC members upon request.

(c) All members must have the opportunity to request full committee review of any Proposal.

(d) If no member requests full committee review, the Chairman designates one or more qualified members to review the Proposal (or proposed amendment). These designated members have authority to approve, require modifications in (to secure approval), or request full committee review.

(e) IACUCs with a large volume of Proposals to be reviewed find the designated member review option may allow for efficient management of the IACUC workload as well as timely turnaround of requests from investigators for Proposal review. Some committees prefer to reserve the designated member review option for certain classes of protocols or amendments.
Some IACUCs have devised categories of research activities that must be reviewed by the full committee, e.g., nonhuman primate studies, survival surgeries.

3.1.7 Categories of IACUC Actions

(a) As a result of their review of a Proposal, an IACUC may take one of several different actions depending upon the findings of the committee such as granting approval, stating modifications required to secure approval, or withholding approval.

(b) An IACUC may also defer or table a review if necessary. The IACUC needs to notify Investigators and the Institution in writing of its decision to approve or withhold approval, or of modifications required to secure approval.

(c) If approval is withheld the IACUC must provide the reasons for its decision and give the Investigator an opportunity to respond.

3.1.8 Approval

(a) When the IACUC has determined that all review criteria, based on the Guiding Principles have been adequately addressed by the Investigator, the IACUC may approve the Proposal, thus providing the Investigator permission to perform the experiments or procedures as described.

(b) An IACUC-approved proposal may be subject to further appropriate review and approval by Institutional officials due to financial, policy, facility, or other Institutional or administrative considerations. However, those officials may not approve an activity if it has not been approved by the IACUC.

3.1.9 Modifications required to secure approval

(a) An IACUC may require modifications to the proposal before granting approval. If the IACUC determines that a proposal can be approved contingent upon receipt of a very specific modification (e.g., receipt of assurance that the procedure will be conducted in a fume hood), or clarification of a specific point, the IACUC may handle these modifications or clarifications as administrative details that an individual, such as the Chairman, could verify.

(b) If a study is unusually complex or involves untried or controversial procedures, the IACUC may wish to impose restrictions, (e.g., approval for the use of a limited number of animals as a pilot study with a written report of interim results, or close monitoring by veterinary or other qualified personnel.)

(c) If such modifications represent significant departures the IACUC can ask the Investigator to revise the Proposal to reflect the modifications imposed by the IACUC.

(d) If the Proposal is missing substantive information necessary for the IACUC to make a judgement or the IACUC requires extensive or multiple modifications, then the IACUC can require that the Proposal to be revised and resubmitted.
(e) If the IACUC wishes to shift to the designated reviewer mode for the approval of the modified Proposal, that shift should be explicitly noted in the minutes and the requirements for designated review must be met.

(f) IACUCs sometimes use terms such as “conditional approval,” “provisional approval” or “approved pending clarification.” Anything less than full IACUC approval via one of the accepted methods described above is not adequate for initiation of animal activities.

3.1.10 Withhold approval

(a) When the IACUC determines that a Proposal has not adequately addressed all of the requirements of the Guiding Principles as applicable, the committee may withhold approval. As indicated above, a higher Institutional authority may not overrule an IACUC decision to withhold approval of a Proposal.

3.1.11 Defer or table review

(a) If the Proposal requires clarification in order for the IACUC to make a judgement, committee members with certain expertise are not present, the IACUC wishes to seek external consultation, or any of a number of other reasons prevent the IACUC from conducting its review, then the IACUC may wish to defer or table review.

(b) Good communication between the IACUC and the Investigator can ensure that this action is needed infrequently. However, should it be necessary, the Investigator should be informed so that he or she can respond or plan accordingly.

3.1.12 Review of Changes to Approved Protocols

(a) Significant changes to an IACUC-approved protocol must be reviewed and approved by the IACUC before they occur. It is prudent for an IACUC to develop a policy on the kinds of changes that are considered significant in order to avoid ambiguity.

(b) The Guiding Principles has determined the following kinds of significant changes that may serve as examples to guide the IACUC in its determinations:

(i) change in objectives of a study;
(ii) Proposals to switch from non-survival to survival surgery;
(iii) change in degree of invasiveness of a procedure or discomfort to an animal;
(iv) change in species or in the approximate number of animals used;
(v) change in personnel involved in animal procedures;
(vi) change in anaesthetic agent(s) or in the use or withholding of analgesics;
(vii) change in methods of euthanasia; or
(viii) change in duration, frequency or number of procedures performed on an animal.
(c) Review of significant changes may be conducted using either the full committee review or the designated member review method described above.

3.1.13 Frequency of Review of Approved Protocols

(a) Complete IACUC review of protocols must be conducted at least once every three years.

3.2 Protocol Review Criteria

3.2.1 Alternatives – Replacement, Reduction and Refinement

(a) There is significant interest in the application of alternatives to animals used in research, education and testing.

(b) Research Institutions should ensure that Investigators have appropriately considered alternatives to procedures that can cause more than slight or momentary pain or distress in animals, consistent with sound research design.

(c) The minimum number of animals should be used and non-animal methods should be considered.

3.2.2 The “3 Rs”

(a) Alternatives are framed within the context of the “3 Rs” articulated originally by Russell and Burch in 1959; they include:

(i) Replacement, or utilising non-animal models;
(ii) Reduction of numbers of animals used; and
(iii) Refinement, or elimination or reduction of unnecessary pain and distress in animals

(b) Replacement alternatives utilise:

(i) living systems,
(ii) non-living systems, or
(iii) computer simulations.
(c) Living systems include in vitro methods that utilise organ, tissue or cell culture techniques. Invertebrate animals, such as the fruit fly, have long been used in research and represent another type of living alternative to vertebrate animals. Finally, microorganisms and plants represent living alternatives for some types of research and testing. If no invertebrate model is appropriate, use of species lower on the phylogenetic scale may be considered a replacement alternative.

(d) Nonliving systems include physical or mechanical systems and chemical techniques. Mechanical models may be used in the training of specific techniques (cardiopulmonary resuscitation, for example) and have replaced living animals in some cases. Chemical techniques are the most widely used nonliving systems and include such useful systems as the enzyme linked immunosorbent assay (ELISA). Techniques that identify the presence of chemical reactions and enzymes, or simply analyse chemical structure, can all be useful in the prediction of toxicity without the use of animals.

(e) Computer simulations may replace some animal use and can be particularly useful when a question is well defined and there is existing data.

(f) Although opportunities for replacement are numerous in product safety testing and education, they appear more limited in research. If it is demonstrated that there is no in vitro alternative to the use of animals, it is important for the IACUC members to focus on the other alternative approaches, reduction and refinement.

(g) Reduction of numbers of animals may be accomplished by a variety of methods as described below:

<table>
<thead>
<tr>
<th>Method</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rational selection of group size</td>
<td>Pilot studies to estimate variability and evaluate procedures and effects</td>
</tr>
<tr>
<td>Careful experimental design</td>
<td>Appropriate choice of control groups</td>
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<tr>
<td></td>
<td>Standardising procedures to minimise variability</td>
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<tr>
<td></td>
<td>Maximising use of animals</td>
</tr>
<tr>
<td></td>
<td>Performing several terminal procedures per animal</td>
</tr>
<tr>
<td>Correct choice of model</td>
<td>Animals euthanised by one investigator used for tissue needed by another</td>
</tr>
<tr>
<td>Minimising loss of animals</td>
<td>Use of healthy, genetically similar animals decreases variability</td>
</tr>
<tr>
<td></td>
<td>Good post-operative care</td>
</tr>
<tr>
<td></td>
<td>Avoid unintended breeding</td>
</tr>
</tbody>
</table>
Plan ahead so the appropriate number of animals needed for studies are ordered or bred

Statistical analysis

Appropriate use of statistical software can generate maximum information from minimum number of animals

(h) Refinement of technique to reduce or eliminate unnecessary pain and distress in study animals is the most commonly practised of the 3 Rs, although it is not always recognised as one of the applications.

(l) Investigators are required to consider alternatives to painful procedures, and to avoid or minimise discomfort, distress and pain, consistent with sound scientific practice and the goals of the research. This requires an understanding of the potential of pain or distress in the animals.

(j) When there is no consensus among IACUC members as to whether a certain procedure actually causes pain or distress in the affected animals, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

(k) To assist in this deliberation, the IACUC may need to utilise one or more of the following:

(i) pilot studies,
(ii) evaluations of clinical signs,
(iii) clinical pathology,
(iv) gross and histological necropsy studies,
(v) review of comparable literature, and
(vi) consultation with experts.

(l) If there remains any doubt about the presence of pain or distress, the IACUC should err on the side of protecting the animals against the potential of unnecessary pain or distress.

(m) Some refinement opportunities include:

(i) pain-relieving drugs
(ii) non-pharmacologic techniques,
(iii) new diagnostic and therapeutic techniques,
(iv) environmental enrichment programmes, and
(v) establishment of more humane endpoints.
Pain-relieving drugs: While it is preferable to design a protocol that prevents pain and distress, when this is not possible the AV (or designee) be consulted to develop an appropriate plan for the use of anaesthetics, analgesics, or other measures, such as anti-inflammatory agents, antibiotics, or sedatives.

New diagnostic and therapeutic techniques: In addition to the use of pain relieving drugs, new diagnostic and therapeutic techniques may have the capability to dramatically reduce the invasiveness of data collection and thereby refine animal research. These include:

(i) use of sophisticated imaging equipment to replace invasive procedures, and
(ii) blood and tissue sampling techniques that allow for easier collection and the processing of smaller sample sizes.

Environment: The IACUC should consider that environmental factor, such as noises, odours, infrequent or inexperienced handling, or boredom from lack of environmental stimulation can cause unnecessary distress.

Humane endpoints: The establishment of the earliest possible humane endpoint consistent with the research design may provide an additional opportunity to significantly reduce pain and distress, thereby refining the experiment. For any study that defines death of the experimental animal as the endpoint, the IACUC should ask if there is an earlier point in the study when the necessary data have been collected and the animal could be euthanised. The Canadian Council on Animal Care Guidelines on Choosing an Appropriate Endpoint in Experiments Using Animals for Research, Teaching and Testing (1998) is an excellent resource for IACUCs.

3.2.3 Euthanasia

The choice of a method of euthanasia depends on species, age, availability of restraint, skill of the individuals performing euthanasia and other considerations. In a research setting, the method of euthanasia must be consistent with the research goals.

The Guiding Principles require that the IACUC review and approve methods of euthanasia based on the following:

(i) minimum pain, distress, anxiety or apprehension;
(ii) minimum delay until unconsciousness
(iii) reliability and irreversibility;
(iv) safety of personnel; emotional effect on personnel;
(v) compatibility with requirement and purpose, including subsequent use of tissue;
(vi) compatibility with species, age and health status; and
(vii) drug availability and human abuse potential.
(c) Acceptable Methods

(i) Barbiturates (most species)
(ii) Carbon dioxide (CO2)-bottled gas only (most species)
(iii) Inhalant anaesthetics (most species)
(iv) Microwave irradiation (mice and rats)
(v) Tricaine methane sulfate (TMS, MS222) (fish, amphibians)
(vi) Benzocaine hydrochloride (fish, amphibians)
(vii) Captive penetrating bolt (horse, ruminant, swine)
(viii) Ether and carbon monoxide are acceptable for many species, but relatively
dangerous to personnel.

(d) Conditionally Acceptable (Requires IACUC Approval of Scientific Justification)

(i) Cervical dislocation (birds, small rodents and rabbits)
(ii) Decapitation (birds, rodents, some other species)
(iii) Pithing (some ectotherms)
(iv) Various pharmacological and physical methods

(e) Unacceptable

(i) Chlora hydrate, chloroform and cyanide
(ii) Decompression
(iii) Neuromuscular blockers
(iv) Various pharmacological and physical methods
(v) Dry ice-generated CO₂

(f) Methods described as conditionally acceptable are considered acceptable when used in deeply anaesthetised animals. Some euthanasia methods (e.g., KCl or formalin by intracardiac injection, or exsanguination) are acceptable only under deep general anaesthesia.

3.2.4 Humane Endpoints

(a) Animals used in research and testing may experience pain from induced diseases, procedures, and toxicity. Procedures that cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anaesthesia.
(b) However, research and testing studies sometimes involve pain that cannot be relieved with such agents because they would interfere with the scientific objectives of the study. Accordingly, the Guiding Principles requires that IACUCs determine that discomfort to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research, and that unrelieved pain and distress will only continue for the duration necessary to accomplish the scientific objectives.

(c) Animals that would otherwise suffer severe or chronic pain and distress that cannot be relieved should be painlessly killed at the end of the procedure, or if appropriate, during the procedure.

3.2.5 Developing Humane Endpoints

(a) Criteria used to end experimental studies earlier in order to avoid or terminate unrelieved pain and/or distress are referred to as humane endpoints. An important feature of humane endpoints is that they should ensure that study objectives will still be met even though the study is ended at an earlier point. Ideally, humane endpoints are sought that can be used to end studies before the onset of pain and distress.

(b) It is important to understand that stress may lead to distress when major shifts in biologic function, to which the animal cannot adapt, threaten the animal’s well-being.

(c) Humane endpoints will be used to determine when animals can be removed from the study, treated, or euthanised. There should be clear directions concerning who can make the decision to euthanise or treat animals, including procedures to follow if a situation arises on weekends, holidays, or in the absence of the responsible Investigator.

(d) The development and use of humane endpoints can reduce the severity and duration of unrelieved pain and distress. Establishing and implementing humane endpoints is best achieved by a collaborative effort on the part of investigators, veterinarians, and animal care staff.

3.2.6 Moribund Condition as a Humane Endpoint

(a) Moribund has been defined as “in the state of dying,” or “at the point of death.” A moribund condition may be an appropriate humane experimental death.” Pre-emptive euthanasia of moribund animals can prevent further pain and distress.

(b) Various clinical signs are indicative of a moribund condition in laboratory animals. These typically include one or more of the following:

(i) impaired ambulation which prevents animals from reaching food or water,

(ii) excessive weight loss and emaciation,

(iii) lack of physical or mental alertness,

(iv) difficult laboured breathing, and
(v) inability to remain upright.

(c) Animals should be observed frequently enough to detect signs of impending death so they can be euthanised in a timely manner. When increased morbidity or mortality is expected, a minimum of twice daily observation is recommended. Animals not likely to survive until the next scheduled observation should normally be euthanised.

(d) In situations where animals are often found dead, closer and more frequent observation for moribund animals should be considered to reduce spontaneous deaths.

(e) Euthanasia of animals that are moribund or experiencing severe pain and distress should always be done in a manner that produces the least possible amount of additional pain and distress.

3.2.7 Other Humane Endpoints in Research

(a) Animals used to study tumour biology, to develop new cancer therapies, and to evaluate the carcinogenic potential of substances may experience pain and distress. Frequent and appropriate monitoring of animals during tumour development is necessary to allow for appropriate intervention before significant deterioration or death.

(b) Effective monitoring systems and endpoints should include limits on tumour size and severity of tumour-associated disease.

(c) Altered physiologic, biochemical, and other biomarkers may be potentially more objective and reproducible endpoints than clinical signs for such studies.

(d) Genetically engineered animal models are sometimes accompanied by unintended and unpredicted alterations that adversely affect animal well being. Investigators need to establish a plan for addressing unanticipated adverse outcomes for genetically altered animals. There should be a plan for systematic characterisation of phenotypes to facilitate assessment of their possible utility and timely decisions on disposition or retention. IACUCs should provide oversight of such studies to ensure that animal welfare problems are handled in an effective and prompt manner.

(e) Animals with induced infections may experience significant pain and/or distress during progression of the disease. Early physiologic and biochemical changes during infection have been found to be useful humane endpoints rather than death or moribund condition. Specific decreases in body temperature have been found to be effective early predictors of eventual death for some infections in rodents. Vaccine potency testing typically involves challenging immunised animals with infectious agents. While such testing has commonly used lethality as the endpoint indicative of insufficient protection, some regulatory authorities now allow euthanasia of moribund animals.
3.2.8 Toxicity Testing

(a) Animals in toxicology studies obviously in pain or showing signs of severe and enduring distress should be euthanised, rather than allowing them to survive to the end of the scheduled study. Humane endpoints should be established and used for toxicology studies in order to further minimise pain and distress.

3.2.9 Death as an Endpoint

(a) Since it provides an objective and unequivocal data point, death has historically been used as an endpoint in cancer, infectious disease and other animal studies, especially for regulatory purposes (e.g., drug safety/efficacy studies).

(b) Increased public interest and regulation have led to a re-evaluation of this practice. Much of the concern arose from the use of traditional LD 50 tests for chemicals and drugs to determine acute toxicity. However, regulatory testing requirements for acute toxicity now allow for animals that are moribund or exhibiting clinical signs of severe pain and distress to be euthanised rather than to die spontaneously.

(c) Euthanasia also provides tissues more appropriate for subsequent study and alleviate potential suffering by the animal. Hence, euthanasia is often preferable to death for both scientific and ethical reasons.

(d) The use of death as an endpoint is discouraged and must always be justified in writing in Proposals and its use must be approved by the IACUC prior to beginning a Project. Endpoints other than death must be considered and should be used whenever the research objective can be attained with non-lethal endpoints.

(e) Examples of Humane Endpoints for Studies with Potential Lethality are described below:

### Examples of Humane Endpoints for Studies with Potential Lethality

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Characteristics</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour growth or effects</td>
<td>Tumour exceeds 10% of normal body weight; necrosis, infection, ulceration, interference with ambulation or eating/drinking</td>
<td>Subcutaneous or intraperitoneal tumours and hybridomas</td>
</tr>
<tr>
<td>Prolonged inappetence/Cachexia</td>
<td>Rapid loss of weight (&gt;20% of normal body weight) and/or condition</td>
<td>Metastatic disease, chronic infectious disease</td>
</tr>
<tr>
<td>Inability to ambulate</td>
<td>Prolonged recumbency</td>
<td>Many</td>
</tr>
</tbody>
</table>

3.2.10 Minimisation of Pain and Distress

(a) It is the responsibility of the IACUC to critically evaluate all research protocols for the potential to cause pain or distress and assess the steps that are to be taken to
enhance animal well-being. As required by the Guiding Principles, the IACUC is mandated to review protocols to ensure that pain and distress are minimised in laboratory animals.

(b) The Guiding Principles states that the IACUC should ensure the protocol addresses:

(i) appropriate sedation, analgesia, and anaesthesia;
(ii) criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and
(iii) details of postprocedural care.

(c) Examples of procedures which the Guiding Principles suggests may have the potential to cause pain or distress, include:

(i) physical restraint,
(ii) survival surgeries,
(iii) food or water restriction,
(iv) death as an endpoint,
(v) noxious stimuli,
(vi) skin or corneal irritancy testing,
(vii) tumour burdens,
(viii) intracardiac or orbital sinus blood sampling, and
(ix) abnormal environmental conditions.

3.2.11 Assessing Pain and Distress

(a) Numerous references indicate that both laboratory animals and humans receive and process noxious stimuli using similar mechanisms and with similar thresholds of awareness. The pain tolerance, or maximum stimulus intensity voluntarily accepted, varies between species and between individuals of the same species, including humans.

(b) Pain typically results from stimuli that damage tissue or have the potential to damage tissue. An animal’s response to pain is often adaptive to reduce movement to minimise re-injury and aid recuperation. However, this response may lead to physiological and behavioural changes which impact negatively on both the animal’s well-being and the research results.

(c) Fundamental to the relief of pain is the ability to recognise its clinical signs in various species of animals. Due to the inability of animals to verbalise, it is essential that animal care staff and researchers receive adequate training on how to recognise clinical signs of pain and distress.
While there are no generally accepted criteria for distress, there are a number of metabolic, physiologic and behavioural parameters that are altered in distressed animals. These include changes in reproductive performance, elevation in glucocorticoid levels and elevation in catecholamine levels. It is necessary to use objective assessments, which means choosing appropriate parameters and quantifying observations.

Numerous models for scoring pain and distress have been published and involve assigning a numeric score to observations with the aid of descriptors. It is often useful to start with a general set of observations for assessing pain and distress such as change in body weight, physical appearance/posture or changes in unprovoked and provoked behaviour.

The assessment system should then be modified on a case-by-case basis using specific changes that may be anticipated in a particular study.

3.2.12 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 which 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.

The responses of different species to different anaesthetics, analgesics or tranquillisers vary and are not fully defined. Often the effects of a given drug have only been examined in a single species and definitive information, for example, on cardiovascular and respiratory function or on the ability to relieve the perception of noxious stimuli, is missing. As a result, dosages have been developed on the basis of the amount required to produce cessation of movement when the animal is confronted by what is assumed to be a painful manipulation, in conjunction with an adequate recovery. Because of the imprecise nature of the studies, dosage ranges are often quite wide, requiring a very conservative approach to their use. The use of drug mixtures further complicates the choice of an adequate dose. Numerous reference texts exist and IACUCs may request that the veterinarian prepare current charts of recommended doses as an Institutional resource for Investigators.

Non-pharmacologic treatments should also be employed. This may include special housing considerations, dietary and other environmental enrichments, adjustments and careful supportive care.
3.2.13 Summary

(a) It is the responsibility of the Investigator to show she or he has considered all the options for minimising pain and distress that do not compromise the scientific validity of the experiment.

(b) The committee’s deliberations regarding the management of potential pain and distress in a protocol should be documented.

(c) Personnel should be trained in pain and distress management.

(d) The IACUC should ensure that there is a mechanism in place for prompt reporting of sick animals to the veterinary staff.

(e) Definitions of Terminology Related to Pain and Distress

Analgesia  A complete loss of sensitivity to pain.

Anaesthesia  A total loss of sensation in a part of or in the entire body.

Distress  An aversive state in which an animal is unable to adapt completely to stressors and the resulting stress and shows maladaptive behaviour.

Pain  An unpleasant sensory or emotional experience associated with actual or potential tissue damage.

Sedation  A state characterised by decreased awareness of surroundings, relaxation, and sleepiness. Analgesia is not present.

Tranquillisation  A state of mental calming, decreased response to environmental stimuli, and muscle relaxation. No sleep, analgesia or anaesthesia is present, even at increased dosage.


(f) Signs of Acute Pain

**Signs**  **Explanations**

Guarding  Attempting to protect, move away, or bite

Vocalisation  Crying out when palpated or forced to use affected area

Mutilation  Licking, biting, scratching, shaking, or rubbing

Restlessness  Pacing, lying down and getting up, or shifting weight

Sweating  In species that sweat (horses)

Recumbency  Unusual length of time

Depression  Reluctance to move or difficulty in rising

Abnormal appearance  Head down, tucked abdomen, hunched, facial distortion, or pallor
### Signs, Degree and Length of Surgically Produced Pain*

<table>
<thead>
<tr>
<th>Surgical Site</th>
<th>Sign of pain</th>
<th>Degree of pain</th>
<th>Length of pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head, eye, ear, mouth;</td>
<td>Attempts to rub or scratch, self-mutilation, shaking, reluctance to eat drink, or swallow, reluctance to move</td>
<td>Moderate to high</td>
<td>Intermittent</td>
</tr>
<tr>
<td>Rectal areas</td>
<td>Rubbing, licking, biting, abnormal bowels movement or excretory behaviour</td>
<td>Moderate High</td>
<td>Intermittent to continual</td>
</tr>
<tr>
<td>Bones</td>
<td>Reluctance to move, lameness, abnormal posture, guarding, licking, self-mutilation</td>
<td>Moderate to high: upper part of axial skeleton (humerus, femur) especially painful</td>
<td>Intermittent</td>
</tr>
<tr>
<td>Abdomen</td>
<td>Abnormal posture (hunched), anorexia; guarding</td>
<td>Not obvious to moderate</td>
<td>Short</td>
</tr>
<tr>
<td>Thorax</td>
<td>Reluctance to move, respiratory changes (rapid, shallow) depression</td>
<td>Sternal approach, high; lateral approach, slight to moderate</td>
<td>Continual</td>
</tr>
<tr>
<td>Spine, cervical</td>
<td>Abnormal posture of head and neck, reluctance to move, abnormal gait—&quot;walking on eggs&quot;</td>
<td>Moderate to severe</td>
<td>Continual</td>
</tr>
<tr>
<td>Spine, thoracic or lumbar</td>
<td>Few signs, often moving immediately</td>
<td>Slight</td>
<td>Short</td>
</tr>
</tbody>
</table>

*Based on observations of dogs.

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### 3.3 Personnel Qualifications

3.3.1 In evaluating proposed research Projects, the IACUC should assess whether personnel conducting procedures are appropriately qualified and trained in those procedures.

3.3.2 Developing Guidelines

(a) To facilitate evaluation of personnel qualifications and training during protocol review, each IACUC should develop a list of items to be assessed as well as a list of classifications of personnel required to participate in such training. This could be a list of qualifications and training items specific to protocols according to procedures and or manipulations proposed or the list could be broad enough to cover all aspects of the Institution’s training requirements.
(b) A procedure specific checklist might include:

(i) proficiency in handling specific specie(s),
(ii) proficiency in pain-relieving methods,
(iii) proficiency in surgical manipulations,
(iv) proficiency in aseptic techniques,
(v) proficiency in pain management,
(vi) proficiency in euthanasia,
(vii) proficiency in pre- and post-operative care,
(viii) approval by safety office.

(c) A checklist of Institutional requirements that need to be satisfied as a component of protocol review might include the following in addition to those above:

(i) completion of occupational health and safety risk assessment,
(ii) demonstrated knowledge of relevant rules and regulations,
(iii) enrolment in safety programme,
(iv) attendance at compliance training session, and
(v) viewing of safety training video.

(d) Classifications of employees whose qualifications and training may require assessment include:

(i) investigators,
(ii) research technicians,
(iii) animal husbandry personnel, and
(iv) veterinarian and veterinary technicians.

(e) An important decision to be made by the IACUC is the level of training required of an Investigator not actually involved in the day-to-day manipulation and care of the animals. If the Investigator is responsible for the research activity and the animals involved, should she or he demonstrate proficiency in the areas indicated above? Is the investigator responsible for training personnel in the lab? If yes, should she or he demonstrate proficiency in those areas? An IACUC policy on this issue will prevent conflict later.
3.3.3 Evaluating Qualifications and Training

(a) To prevent problems related to assessment of qualifications and training during protocol review, it is helpful if the IACUC determines any training needs during the protocol development and veterinary consultation. Discussion of new techniques, procedures, or manipulations at this time can provide the impetus for a training opportunity for both the veterinary staff and the research staff with demonstrated proficiency completed prior to protocol review. This training experience should be so noted in the protocol or otherwise documented.

(b) Maintaining a database of all participants in the facility’s training programme who use laboratory animals will facilitate assessment of qualifications and training. With such a database, preliminary evaluation of an individual’s expertise can be an administrative task performed by the IACUC or staff assigned to assist with managing the animal care programme. If a deficiency is noted, a follow-up memo can be sent to the investigator stating that protocol review is pending until training requirements have been completed.

(c) IACUCs should note that high morbidity or mortality rates or requests for more animals than originally planned may indicate a training opportunity and should be followed up in the context of the relevant protocol, either immediately or during the semiannual review.

(d) Evaluating the qualifications and training of new personnel or those proposing to use new techniques, procedures, or manipulations will necessitate another approach by the IACUC.

3.3.4 New Personnel

(a) One way to manage the training of new personnel is to initiate an IACUC policy that no protocol will be reviewed until training requirements have been satisfied.

(b) Such training would need to incorporate all Institutional requirements as well as those specific to the work expectations of the individual, and might include those listed above.

3.3.5 New Techniques, Procedures or Manipulations

(a) When an Investigator proposes new techniques, procedures, or manipulations, the IACUC must assure itself that the personnel are qualified to perform the work. If no training module on a particular technique, procedure, or manipulation exists, it is possible that the most closely aligned existing module can be used.

(b) If the personnel have not demonstrated proficiency through one of the training modules, the IACUC can consider the following options:

(i) The IACUC may mandate that the individual(s) complete pertinent training before the protocol can be reviewed. This assumes the IACUC has a policy that stipulates adequate qualifications and training as a condition of protocol review.
(ii) If no relevant training module exists, a possible course of action would be to stipulate that the veterinarian supervise the new technique, procedure, or manipulation pending certification of training or demonstration of proficiency. If there are no in-house personnel with the necessary expertise, the IACUC can seek a consultant for advice and training. This should not be viewed as a confrontational event, but rather one with educational value for both the veterinarian and the research staff. Documentation of this training experience should be made in the IACUC files or database.

3.3.6 In summary, evaluation of personnel qualifications and training is an essential component of the review of animal use protocols to ensure the humane care and use of laboratory animals. The challenge to IACUCs is to perform this evaluation in an efficient, consistent and uniform manner.

3.4 Veterinary Review and Consultation

3.4.1 Each IACUC is required by The Guiding Principles to have as one of its members a veterinarian with direct or delegated programme authority and responsibility for animal activities at the Institution.

3.4.2 The veterinarian must be trained or experienced in laboratory animal science and medicine for the species used at the Institution.

3.4.3 Reviewing Animal Use Protocols
(a) The veterinarian can integrate his or her experience and training with that of the Investigator and advise the Investigator on selection of species, their sex, age and/or size.

(b) The veterinarian can assess the ability of the animal facility and its staff to support the proposed species and associated procedures.

(c) When the selection criteria have been established, the veterinarian can assist the IACUC in reviewing the proposed procedures and techniques appropriate to the goals of the Project.

3.4.4 Reviewing Protocols for Potential Pain and Distress
(a) The Guiding Principles require that Investigators proposing procedures that may cause more than momentary or slight pain or distress to the animals will consult with the Attending Veterinarian or his or her designee.

(b) Similarly, the veterinarian has implicit responsibilities outlined in the Guiding Principles to assess the potential for pain and distress that might be associated with the proposed animal activities, and to recommend the use of pain alleviating drugs, whenever possible, to counteract those conditions.
3.4.5 Reviewing Protocols Involving Surgery

(a) The veterinarian can ensure that appropriate provision is made for preoperative and post-operative care of the animals in accordance with established veterinary medical and nursing practices.

(b) As noted in the Guiding Principles, all survival surgery should be performed using aseptic procedures, including the use of surgical gloves, masks, sterile instruments, and aseptic techniques.

(c) The veterinarian may provide the IACUC with assessment of the following:

(i) preparation of the animal for the surgical intervention, to include the use of pre-anaesthetic drugs where indicated, and appropriate anaesthetic agents;

(ii) that the individual(s) performing the surgery has adequate experience or training for the specific procedures outlined in the study.

(iii) that aseptic techniques are appropriate for the procedure; and

(iv) that adequate post-operative care, to include post-operative analgesics where indicated, is provided.

3.4.6 Reviewing Protocols To Ensure Humane Euthanasia of Animals

(a) The veterinarian on the IACUC can use the publication “2000 Report of the AVMA Panel on Euthanasia” (JAVMA Vol. 218, No. 5, pages 669-696) or subsequent editions as the principal reference to assess the Investigator’s proposed method of euthanasia.

3.4.7 After Protocol Review and Approval

(a) Following IACUC approval of protocols, the veterinarian is in a position, through periodic visits to the animal facility and animal activity areas, to observe and evaluate animal well-being and decide whether the animal activities are being conducted in accordance with the conditions described or referenced in the protocol.

(b) The veterinarian, by virtue of training and experience, is able to serve in advocacy, oversight, and intervention roles that are distinct and unique among the IACUC members and research staff.

3.4.8 Some Examples of the Veterinarian’s Responsibilities During Protocol Development and Review*

(a) Choice and use of appropriate analgesics/anaesthetics

(b) Verification of appropriate drug dosages, route of administration and choice of agent

(c) Assistance in selection of appropriate animal model
(d) Identification of refinement initiatives to ensure that manipulations have a minimal impact on animal welfare

(e) Oversight of aseptic surgery and peri-operative care

(f) Oversight of animal health and husbandry pertinent to the protocol and the entire colony

(g) Identification of possible iatrogenic complications of model and procedures selected

(h) Ensuring there are appropriate remediation efforts for iatrogenic complications

(i) Serving as an occupational health and safety (including zoonoses) resource

(j) Serving as a regulatory compliance resource

(k) Assistance in identifying appropriate endpoints and in ensuring humane euthanasia.

*This checklist is not all-inclusive; rather it provides examples of the veterinarian’s responsibilities, which may vary with each Proposal.

3.5 Other Protocol Review Considerations

3.5.1 Agricultural Research

(a) Farm animals are used in a variety of research contexts, including:

(i) vaccine trials,

(ii) studies of basic biological processes,

(iii) studies of pharmacokinetics and organ transplantation, and

(iv) studies of nutritional, breeding and management methods to increase the supply and quality of food and fibre.

(b) Unlike typical laboratory animals, farm animals used for research and teaching may be housed in many different kinds of environments, ranging from traditional laboratory environments to enclosed or extensive farm settings. Because of these factors, as well as the regulatory complexity surrounding farm animal oversight, determining standards for the evaluation of research, teaching, and testing using farm animals is more complicated than for other laboratory animals.

(c) Review of Protocols and Facilities

(i) Institutions employ a number of different approaches to reviewing activities involving animals used for agricultural research and teaching. Some have a single committee that reviews all protocols, while others have a subcommittee or even a separate committee that reviews agricultural animal research protocols. There are benefits and limitations associated with each of these approaches.
(ii) What is most important is that the Institution ensures uniform and high-quality oversight of all research, teaching, and testing activities involving animals, regardless of the species or the type of research being conducted.

(iii) For thorough oversight of agricultural animal care and use, it is particularly important that there be agricultural expertise on the IACUC. It is suggested that the IACUC include, among other members:

(aa) a scientist from the Institution with experience in agricultural research or teaching involving agricultural animals;

(bb) an animal, dairy or poultry scientist who has training and experience in the management of agricultural animals; and

(cc) a veterinarian who has training and experience in agricultural animal medicine and who is licensed or eligible to be licensed to practice veterinary medicine.

(iv) There are unusual aspects of agricultural research that deserve careful consideration by IACUCs. There are certain husbandry practices common on commercial farms that have the potential to cause pain or distress that would not ordinarily be permitted under the regulations governing research. It is recommended that IACUCs review these procedures, as well as husbandry conditions that do not meet accepted animal welfare standards even if they are considered normal practice.

(v) Another unusual aspect of agricultural research is that the animals may be killed and marketed for human food at the end of studies, which means that there are special considerations with respect to avoiding residues from therapeutics and other drugs.

(vi) The extent of oversight is another issue that IACUCs need to address. Animals may be housed at off-site facilities at some distance from the main unit. The IACUC needs to ensure that there is adequate oversight of all animals under approved protocols. Research may be conducted using privately owned animals on private farms, and the IACUC should consider whether or not these activities need to be covered by protocols.

(vii) Finally, the facilities in which agricultural animals are housed are often older than typical laboratory animal facilities. Because many of these facilities are semi-enclosed or open, there may be problems with rodent control and some other aspects of maintenance.

(viii) Recordkeeping in agricultural animal facilities may be less complete than that required in conventional lab animal facilities. The IACUC should be aware that there can and should be a high standard of animal care even in modest facilities. The development and implementation of standard operating procedures for these facilities can help to ensure a consistent standard of animal care.
(d) Conclusion

(i) Although not always required by law, the monitoring of food and fibre animal research and teaching activities can significantly benefit an Institution by improving the overall quality of the animal care programme. Because agricultural research often has the improvement of food or fibre production as an endpoint, standards may differ from those for research animals. This does not mean, however, that different ethical standards should be used by an IACUC in considering the use and care of farm animals used for food and fibre research. Experimental goals and animal welfare should both be considered when evaluating the use and treatment of these animals.

3.5.2 Antibody Production

(a) Antibodies are important tools for research. Depending on research needs antibodies may be produced by polyclonal or monoclonal technique. Each technique requires that specific issues be addressed in animal protocols.

(b) IACUCs should ensure adequate training of personnel in the use of proper technique when any method of immunisation is proposed. The advantages of a centralised service utilising skilled technicians to meet multiple research groups’ needs for polyclonal and monoclonal antibodies is another refinement which may enhance animal welfare in larger research programmes. There are also many commercial sources of antibodies made to order.

(c) A good resource is “Information Resources for Adjuvants and Antibody Production: Comparisons and Alternative Technologies.” AWIC Resource Series, No. 3. August 1997. Call Number: aHV4701.A94no.3. ISBN 090076791X. The document includes over 500 bibliographic citations regarding adjuvants and antibody production methods compiled from scientific journals, proceedings and newsletters. A company/institute listing of suppliers of antibodies and antibody production products is included. Emphasis is placed on citing comparative studies and research into alternative methods.

(d) Polyclonal Antibody Production

(i) Injection of an immunogen (e.g., protein, virus, bacterium) into an animal produces a humoral response, which induces the production of a population of heterogeneous antibodies, with varying specificities toward different molecular regions (epitopes) of the immunogen. Two types of lymphocytes (T cells, derived from the thymus, and B cells, derived from marrow) are responsible for the production of polyclonal antibodies. Polyclonal antibodies produced in response to infection can be effective in recognising and eliminating foreign material, but the heterogenicity of the product limits its use in research and industry.

(e) Adjuvants

(i) To increase the immune response, the immunogen may be combined with an adjuvant. Adjuvants stimulate the rapid and sustained production of high titres of antibodies with high avidity. Adjuvants may facilitate the immune response through three basic mechanisms:
(aa) Adjuvants may serve as a depot for the antigen, which should increase the duration of antigen exposure and the antibody response.

(bb) Adjuvants may stimulate immune cells.

(cc) Adjuvants may enhance macrophage phagocytosis after binding the antigen as a particulate (a carrier/vehicle function).

(ii) The use of adjuvants is required for many antigens which by themselves are weakly immunogenic. Adjuvant selection remains largely empirical. Antigens that are easily purified or available in large quantities may be good choices for starting with the least inflammatory adjuvants for immunisation. Should antibody response not be suitable, a gradual increase in the inflammatory level of the adjuvant would then be warranted.

(iii) The choice of the appropriate adjuvant is important from both the aspect of the end result (high antibody response) and the welfare of the immunised animal. Many of the adjuvants have the capacity to cause inflammation, tissue necrosis and pain in animals. A major charge to Investigators is to minimise animal use and discomfort.

(iv) Freund's incomplete adjuvant (IFA) is a water/oil emulsion containing immunogen, paraffin oil and an emulsifying agent. Addition of killed mycobacteria to the oil phase (Freund's complete adjuvant, CFA) enhances the immune response. Multiple exposures to CFA will cause severe hypersensitivity reactions. The use of CFA can be painful and alternative adjuvants should be considered. Abscesses, granulomas and tissue sloughs may occur at injection sites. However, a recent report (Halliday) suggests that when the NIH intramural guidelines are meticulously followed, assuring aseptic technique and adding the judicious use of chemical sedation, the use of CFA for immunisation is a humane procedure. Undesirable and painful side effects must be minimised or eliminated by careful preparation of inoculum, the use of appropriate routes of administration, adequate separation of injection sites, and the use of a small amount of inoculum per site.

(v) Because of the severity of the secondary immune response to mycobacterium in CFA, IFA must be used with booster antigen administrations in cases where CFA has been used in the initial injection.

(vi) For many years CFA was the only effective adjuvant, but this is no longer true. Other adjuvants are available as alternatives and may be suitable for use in an Investigator's experiments.

(f) Route of Injection

(i) The range of recommendations for routes and sites of administration of antigen-adjuvants preparations, volumes per site and number of sites per animal for different species vary in the literature and Institutional guidelines.

(ii) Particularly with the use of CFA, it is important to note that the severity of potentially painful inflammatory reactions may be minimised by injection of a small volume of inoculum per site and the use of multiple injection sites when appropriate.
(iii) Injection sites must be sufficiently separated to prohibit coalescing of the inflammatory lesions.

(iv) Using multiple sites for immunisation also provides more foci for antigen presentation and the involvement of more lymph nodes. Intradermal and subcutaneous routes are commonly used to take advantage of antigen-processing dendritic cells present within the dermis.

(v) Hair should be clipped from intradermal and subcutaneous injection sites, and the site should be aseptically prepared with betadine or nolvasan scrub followed by alcohol or other appropriate antiseptics.

(vi) The following recommendations apply primarily to antigen solutions in CFA or IFA. Volumes ranging from 0.05 ml to 0.10 ml per site have been recommended for intradermal injections in rabbits. A total of five intradermal sites has been recommended. Because intradermal sites ulcerate with FCA, sterile inocula must be used and the site must be properly disinfected to prevent secondary bacterial infection. Subcutaneous injection volumes in the rabbit vary from recommendations of 0.10 ml to 0.25 ml to 0.40 ml per site. Number of sites recommended varies from 4 to 10.

(vii) Footpad injections in rabbits are prohibited. Where scientific justification is provided, footpad injections may be permitted in rodents, but only in one hind foot, and with the animals housed on soft bedding. Suggested maximum injection volumes can range from 0.01 to 0.05 for mice and 0.10 ml for rats. The need for footpad injections must be critically evaluated by the IACUC before approval.

(viii) Sometimes direct inoculation into lymph nodes, such as the popliteal lymph node, is used. With practice these nodes often can be palpated and the injection performed percutaneously.

(ix) Intramuscular injections, usually made in the biceps femoris or quadriceps muscle mass, generally are lower volumes of 0.25 ml to 0.20 –0.40 ml. Care must be exercised to avoid adjacent nerves and blood vessels as well as fascial planes when injecting into a muscle bundle. Disagreement exists as to the appropriateness of intramuscular injection of CFA. The intramuscular route of injection is recommended in some Institutional guidelines and specifically discouraged in other guidelines. Intramuscular injection is generally not recommended in rodents because of limited muscle mass.

(x) For TiterMax®, intradermal, subcutaneous, and intramuscular routes are recommended with volumes per injection site ranging from 0.01 to 0.25 ml in small and large animals.

(xi) For Ribi®, intradermal, subcutaneous and intramuscular routes are recommended with volumes per injection site ranging from 0.05 to 0.50 in small and large animals.

(g) Monoclonal Antibody Production

(i) Monoclonal antibodies (mAbs) are homogeneous because they are produced by hybrid cells derived from a single antigen-stimulated B cell. The production
of mAbs involves two phases. In the first phase an animal (usually a mouse) is immunised with the antigen of interest. Immunisation of the antigen is often performed with an adjuvant, as discussed above. Splenocytes are harvested from the responding animal, and are fused with a myeloma cell line for in vitro propagation.

(ii) Before the immunisation protocol begins, the methodology for detecting the specific antibody of interest in the mouse sera and tissue culture supernatants is developed. Otherwise, significant time and animal resources may be wasted later in the mAb-developing phase.

(iii) Test bleeds should be performed in order to determine if the mice are responding to the immunisations. Most immunologically based assays for determining if the desired antibodies are being produced require less than 10 microliters of mouse serum. Once an appropriate response has been confirmed the mice should be boosted again and typically after three days from the boost the mice should be euthanised and spleens harvested.

(iv) The second phase is production of adequate quantities of mAb for a project or analysis. There are two major methods: in vitro and the ascites method..

(v) The ascites method has been one of the most popular means for producing large quantities of highly concentrated monoclonal antibodies since its inception in 1972. However, improved techniques and culture media have demonstrated that mAbs can be produced by in vitro techniques at a quality and concentration that are similar to that of ascites. The National Research Council’s report on Monoclonal Antibody Production specifically states “in vitro methods for the production of monoclonal antibodies should be adopted as a routine method unless there is a clear reason why they cannot be used…”. Therefore alternatives to the use of animals (in vitro techniques) for the production of mAbs must be considered in place of the ascites method.

(vi) The ascites method should only be used after in vitro failure of each cell line has been demonstrated, or other adequate justification is provided. Analysis of individual cell lines is necessary because the production performance of each hybridoma cell line grown in vitro is highly variable. Despite this variability, work performed by Petrie indicates that at least 90% of all hybridomas that are placed on in vitro production protocols will yield adequate amounts of high quality mAbs.

(vii) Several resources for the in vitro production of mAb are available. Some Institutions have core facilities that may provide an in vitro mAb production service. The NIH also sponsors a national cell culture core facility (National Cell Culture Centre, Minneapolis, MN; http://www.nccc.com).

### 3.5.3 Breeding Colonies

(a) Investigators maintain breeding colonies for a variety of reasons. A breeding colony may be required for an established animal model because:

(i) the animal model is not commercially available,
(ii) young animals have very specific age or weight requirements that cannot be fulfilled by a commercial breeding colony, or
(iii) physiological status of the mutant animal is too severely affected for it to survive shipment.

(b) Investigators developing a new spontaneous or induced mutant animal model need to maintain their own breeding colony because there is no alternative source for this mutant. While trying to establish a breeding colony for a new mutant model, the investigator is also simultaneously working to determine phenotype, to identify affected physiological system(s), and define inheritance pattern.

(c) To review standard operating procedures for breeding colonies, the IACUC will need information about colony management. Examples of necessary information include:

(i) number of breeders and number of young per cage,
(ii) breeding system including number of females per male or continuous versus interrupted mating,
(iii) weaning age,
(iv) separation of animals at weaning, and
(v) methods for identification of individual animals.

(d) Large numbers of animals may be required to maintain a breeding colony. The exact number of animals can only be approximated because it is impossible to predict in advance the exact number and sex of offspring. The estimated number of animals should clearly distinguish between:

(i) breeders,
(ii) young that cannot be used in experiments because they are of the wrong genotype or sex, and
(iii) animals that will be subject to experimental manipulations.

(e) Colony management practices should be briefly described in the investigator’s animal protocol, and justification provided for departure from standard Institutional practices.

(f) Determining which animals to include in the estimated number of animals on an animal protocol can be challenging to the investigator and the IACUC in the absence of IACUC-developed guidelines. The estimated number of animals that are kept for breeding purposes and not subject to any experimental manipulations should be part of the animal protocol.

(g) Studies involving genetic analysis are animal intensive. Genetic analysis can involve determining if a single gene has dominant or recessive inheritance, identifying different genes involved in a quantitative (polygenic) trait, or fine mapping to determine chromosomal location of a mutant gene. It is possible for the investigator to estimate the number of animals required, but difficult for the IACUC to evaluate this estimate in the absence of experience.

(h) Up to 1200 mice are required to map a single gene with recessive inheritance and full penetrance, and have adequate numbers of progeny for developmental studies, phenotyping and linkage analysis. This number assumes a breeding colony of 10 to 12 pair matings with a 6- to 8-month reproductive lifespan, around 90% productive matings, replacement of breeders, and no unusual mutant infertility or mortality.
(l) Up to 1100 mice are required for quantitative trait loci analysis using analysis of F2 progeny. The number assumes small breeding colonies of two inbred parental strains (4 to 6 pairs) and two reciprocal F1 hybrids (2 to 4 pairs), no unusual infertility, replacement of breeders at 6- to 8-month intervals, and generation of between 500 and 1000 F2 mice for genotyping.

(j) Up to 750 mice are required to construct a congenic strain using “speed” congenic genotyping methods. This number assumes a breeding colony of 10 to 12 breeding pairs, replacement of breeders, and progeny for phenotyping and genetic linkage. If the homozygous mutant does not breed and the congenic strain must be developed using intercross matings, the estimated number of mice increases to 1,200.

(k) After founder transgenic or ‘knock-out’ mice have been identified, between 80 and 100 mice may be needed to maintain and characterise a line. The number assumes up to five breeder pairs per line, breeder replacement, no unusual infertility and adequate numbers of weanlings for genotyping and phenotyping characterisation.

(l) If a study requires fertilised one-cell eggs, embryos or foetuses, the protocol should indicate the number of eggs, embryos or foetuses that are required for proposed studies.

(m) The estimated number of experimental animals may be limited to the number of female animals that are mated and euthanised or surgically manipulated to collect the required eggs, embryos or foetuses. In this situation, males might be listed as breeders if they are not subject to any experimental manipulation.

(n) If a suckling animal will be subject to any manipulation, such as thymectomy, toe clip or ear notch for identification, tail tip excision for genotyping, or behavioural tests, the estimated number of manipulated sucklings must be included in the number of animals used. If suckling animals will be euthanised at or prior to weaning because they are the wrong genotype or sex for the experiment, then they may be included as animals held or euthanised but not subject to experimental manipulations.

(o) One option is for the IACUC to request estimated animal numbers as follows:

| Estimated number of weaned and adult animals to be subject to experimental manipulations | * |
| Estimated number of suckling animals to be subject to experimental manipulations | * |

TOTAL

| *Estimated numbers should be further subdivided based on invasiveness of procedures using Institutional criteria: |

| Estimated number of breeders held but not subject to experimental manipulations |
| Estimated number of suckling animals to be euthanised at or prior to weaning, and not subject to experimental manipulation |

(p) In summary, the IACUC’s role for oversight regarding breeding colonies includes ensuring that the need for a breeding colony has been established based on scientific or animal welfare concerns, that the procedures used in the breeding colony
are evaluated and approved by the IACUC on a regular basis (e.g., as part of the semiannual programme review), that there is a mechanism for tracking animals, and that the standards of care and animal wellbeing for the animals in the breeding colony are consistent with the guidelines issued by AVA.

3.5.4 Field Studies

(a) The Guiding Principles focus primarily on the care and use of laboratory animals in research facilities. The same guiding principles, however, apply to the use of vertebrate species in field studies.

(b) Application of the requirements and guidelines often pose unique challenges to the Investigator and the IACUC because of the nature of field research. For example, field sites are often at a distance and may be remote, making it impractical for IACUC inspections. One solution is to require the Investigator to provide photos, videotapes or other information that can help the committee evaluate the use of animals.

(c) For some projects the committee can find a consultant near the field site to perform an inspection and report to the IACUC. Other difficulties relate to the nature of the research and the populations to be studied, which may be unfamiliar to the IACUC.

(d) Professional field biologists in organisations devoted to the study of fish, amphibians, reptiles, birds, and mammals have prepared guidelines for field work with these populations; these guidelines form a useful reference and can assist the investigator in planning, and the IACUC in reviewing, field research using vertebrate animals. The references at the end of this section cite such guidelines. Professional societies and like organisations can assist by referring the IACUC to appropriate individuals and authorities.

(e) The Animals and Birds Act, the Wild Animals and Birds Act and the Endangered Species (Import and Export) Act protect animal and wild animal populations. The Investigator must be able to assure the IACUC that all necessary licenses and permits have been or will be obtained before research begins.

(f) The proposed study can be assessed by the IACUC in a manner similar to laboratory studies if the protocol prepared by the PI addresses the following relevant items:

(i) species selection,

(ii) site selection, and

(iii) methodologies employed.

(g) Species Selection

(i) The Investigator should provide information on the population to be studied and a rationale for choosing that particular population. Import of animals from overseas sources require import permits from the AVA.

(ii) An IACUC that has additional questions about the selection of species or the impact on the population to be studied may require the investigator to provide additional information or the Committee may consult with biologists with relevant expertise.
(h) Site Selection
(i) The selection of the study site for the research should maximise the opportunity for data collection and minimise the disruption caused by the investigator. The selection process should also take into consideration other activities in the area, such as agricultural practices, tourism or land development, which may interfere with the research protocol.

(ii) Permission to utilise the site may be necessary and the investigator must be able to assure the IACUC that necessary permits or permission have or will be obtained.

(l) Methodologies Employed
(i) The potential short- and long-term effects of procedures on individual animals should be evaluated in all protocols. If animals are to be captured, the methods used and the numbers involved should be detailed in the protocol submitted to the IACUC. There should be a description of measures taken to prevent potential injuries and alleviate potential distress, and of the possible impact of capture on subsequent behaviour and survival of the animals.

(ii) If animals are to be monitored individually, the investigator must indicate whether they will be identified by natural markings or will be artificially marked. If the animals are to be artificially marked, there must be a description of methods to be used and potential trauma (e.g., paint markings may increase visibility to predators).

(iii) Capture and marking methods are often a matter of practicality and usually have been developed and evaluated over a period of time. There is a substantial body of literature regarding the effect of mark-and-recapture studies and other study techniques on wild animals. The IACUC or investigator may rely on consultation with experts in the relevant discipline for this information.

(iv) Field experimental procedures are commonly used to test hypotheses. In all instances, any potential pain or distress to an individual animal must be assessed and the investigator’s justification evaluated in the context of the potential value of the data to be obtained.

(v) Techniques for remotely recording behavioural or physiological data in the field are valuable and often minimally invasive. When possible, the least invasive procedures should be chosen (e.g., use of hormone assays of urine or faeces rather than blood samples).

(vi) When removal of individuals is necessary to take measurements or tissue samples, the IACUC should take into account the degree of invasiveness of the procedure and potential problems associated with return of the animal to the field. For example, animals should be released in a condition that enables them to avoid predators, seek shelter, and survive inclement weather.

(vii) Individual animals may also be treated experimentally to alter their behaviour or physiology by surgery or drugs. Any invasive surgery, such as organ removal or implanting transmitters, should be done using aseptic technique.
The use and choice of anaesthesia will be affected by field conditions because some agents are difficult to transport or use in field conditions. Anaesthetics that do not clear from the system quickly may require holding the animal longer as they may compromise the animal's ability to survive when released. The potential for human consumption of contaminated game species should also be considered.

Procedures involving site manipulation should be adequately justified by the Investigator.

Conclusion

Many of these issues are difficult to address definitively, but their consideration will help the IACUC judge the potential impact and value of the study proposed, and can be expected to assist the Investigator in obtaining maximum information from the study with minimum negative impact on the animals studied or their environment.

The IACUC should ensure that the investigator complies with applicable regulations and policies and obtains any required permits; the IACUC may wish to obtain copies. Many of the issues arising from proposals to conduct field research on vertebrate animals will require the judgement of experienced professionals in the field and the IACUC should feel free to seek advice or consultation if necessary.

3.5.5 Hazardous Materials

The IACUC must pay particular attention to proposals employing potentially hazardous materials, including:

(i) radioactive substances,
(ii) infectious microorganisms,
(iii) biological toxins,
(iv) hazardous chemicals, and
(v) recombinant DNA.

These all have the potential of causing harm to animals in the facility and the personnel caring for and using them.

Radiation Safety Committees (RCS) and Institutional Biosafety Committees (IBC) should be set up to ensure that certain radioactive materials and recombinant DNA materials are handled safely. The role of these committees may be extended to consider research involving human and animal pathogens. The IACUC should be generally familiar with the responsibilities of the various safety committees and organisations at their Institution and the Institution should ensure that the functions of the committees are coordinated. Animal research proposals should be consistent with the procedures required by the IBC.
(d) In addition to the various safety committees, Institutions should have professional staff or resources available to handle chemical, biological and radiological agents. (The US National Research Council publication, Occupational Health and Safety in the Care and Use of Research Animals, is a valuable resource for IACUC members.) This publication covers a wide variety of occupational health and safety issues, including information on working with hazardous materials in research animals.

(e) Radioactive Materials

(i) RCS have oversight for the procurement, use and disposal of radioactive materials; therefore, their approval should be coordinated with IACUC review of any proposal that involves radioactivity.

(f) Biohazardous Materials

(i) Infectious diseases may be a factor in many animal studies due to natural infections as well as those specifically induced as part of research. The guidelines on Biosafety in Microbiological and Biomedical Laboratories provide a key reference for assessing risks and selecting appropriate safeguards.

(ii) The US NIH publication, Guidelines for Research Involving Recombinant DNA Molecules, promulgated by the NIH Office of Biotechnology Activities, also includes four biosafety levels and represents a key reference for work involving recombinant microorganisms. Recombinant DNA experiments involving animals also require approval from the IBC.

(g) Hazardous Chemicals

(i) In addition to animal care concerns, activities involving hazardous chemicals require procedures for:

(aa) chemical storage and disbursement,

(bb) dosage preparation and challenge procedures, and

(cc) waste management and disposal practices.

(ii) It is also necessary to determine whether the chemicals will be present in feed, faeces or urine. A rigorous review to ensure appropriate safety practices, containment equipment and facility safeguards is essential for animal experiments involving chemical inhalation.

(iii) Proposals submitted to the IACUC must include sufficient documentation to assess the adequacy of precautions to control exposure of personnel to the hazardous agents involved in animal experiments.

(iv) The identification by the IACUC of protocols involving hazardous chemicals (e.g., the use of known carcinogens to induce tumours in animal models, determinations of carcinogenicity, mutagenicity, or teratogenicity, or acute toxicity studies) is essential for Institutional compliance with health and safety standards. (The US Occupational Safety and Health Administration (OSHA) laboratory standard “Occupational Exposure to Hazardous Chemicals in the Laboratory” is of particular importance.) The IACUC should be familiar with
the requirement in this standard for a chemical hygiene plan for controlling exposures to hazardous chemicals. Written standard operating procedures may be required describing appropriate safety precautions and specific “designated areas” where hazardous chemicals will be used or stored.

(v) One health and safety issue common to most IACUCs concerns the use of the inhalation agent ether for anaesthesia and euthanasia. Ether forms explosive peroxide when stored in metal containers and must be used with special precautions because of its volatility and flammability. Ether must be used with special ventilation and kept away from flames or electrical ignition sources. Carcasses of animals euthanised with ether should be stored in explosion proof well-ventilated areas and not incinerated until the ether is volatilised. Other inhalation anaesthetics, such as halothane, methoxyflurane and nitrous oxide, although not without some degree of toxicity in an occupational setting, are less hazardous when used with proper precautions and a waste gas scavenging system. Methoxyflurane is the most toxic of these inhalation agents to humans, and safe practices should be closely scrutinised by the IACUC.

(vi) Another class of hazardous chemical routinely encountered in the laboratory environment is aldehydes. (Specific OSHA guidelines are available for handling aldehydes and other chemicals.) Material Safety Data Sheets, which provide useful information on specific hazardous chemicals, must be accessible on site for each hazardous agent present.

(h) Hazardous Waste

(i) Animal wastes contaminated with radioactive materials, recombinant organisms, infectious agents or other hazardous chemical agents must be carefully managed to avoid human exposure or damage to the environment. Special efforts should be made in experimental design to minimise the generation of wastes containing hazardous chemicals.

(ii) Those containing radioactivity in addition to hazardous chemicals are particularly difficult to deal with. Wastes containing infectious agents should be decontaminated, preferably in a steam autoclave, before disposal.

(iii) Incineration is the recommended treatment for contaminated feed and bedding.

(iv) The professional health and safety staff, who have responsibility for hazardous waste management at the Institution, should review Institutional policies when animal care proposals involving hazardous materials are received.

3.5.6 Instructional Use of Animals

(a) All instructional use of animals, regardless of funding source or species should be reviewed by the IACUC.

(b) It may be appropriate for students to participate in the conduct of experiments involving laboratory animals for the purpose of education. All instructional proposals should clearly identify the learning objectives and justify the particular value of animal
use as part of the course, whether it is demonstration of a known phenomenon, acquisition of practical skills, or exposure to research.

(c) Adequate supervision and training are especially important as the techniques learned by students may be carried into subsequent research careers. It is recommended that students receive instruction in the ethics of animal research and applicable rules and regulations prior to undertaking any experimentation.

(d) When students work in an investigator’s laboratory, the IACUC must ensure that the students receive appropriate supervision and training in animal care and use.

(e) Student projects involving protocols different from those approved for the instructor’s laboratory must be reviewed and approved on their own merits by the IACUC.

(f) Experiments sometimes entail behavioural observation with no intervention, or minor painless interventions, such as choices of food or living accommodations. Such projects teach the rigors of conducting a research project and the variability inherent to biological or biobehavioural systems. These exercises generally involve little or no distress to the animals, but still require IACUC approval.

(g) Some procedures present additional concerns. Selected examples are listed below:

(i) Behavioural studies that involve conditioning procedures in which animals are trained to perform tasks using mildly aversive stimuli, such as the noise of a buzzer, may be potentially stressful to the animals.

(ii) For other behavioural studies using non-aversive stimuli, such as running mazes, it may be necessary to maintain animals at a reduced body weight to enable food treats to be used as an effective reward. Experiments involving food and water restriction for teaching purposes must be rigorously justified and carefully monitored.

(iii) Some behavioural studies produce potentially high levels of distress, including those using aversive stimuli, such as unavoidable noxious electric shock and surgical ablations or drug-induced lesions designed to affect the animal’s behaviour or performance. The educational benefits of such procedures should be carefully reviewed and clearly justified, bearing in mind that studies involving unrelieved pain or distress are generally inappropriate when employed solely for instructional purposes.

(iv) Laboratory studies in physiology, neurophysiology, biology, and pharmacology often involve observations and experiments using animals. For all procedures, including those in which animals are euthanised to obtain tissues (e.g., in the teaching of anatomy or tissue harvest for in vitro procedures), the procedures and method of euthanasia, if any, must be reviewed by the IACUC. The number of animals used should always be the minimum necessary to accomplish the objectives of the proposed educational activity.

3.5.7 Surgery

(a) Surgical procedures are a common component of animal research activities, and IACUCs are often called upon to assess the details of these procedures. Further, the
IACUC is responsible for determining that personnel are qualified and trained in the procedures to be performed.

(b) Definitions

Major surgery: Penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions.

Minor surgery: Does not expose a body cavity and causes little or no physical impairment.

Survival surgery: The animal awakes from surgical anaesthesia.

Non-survival surgery: The animal is euthanised before recovery from anaesthesia.

(c) Reviewing Protocols for Surgical Procedures

(i) Some of the aspects of a surgical procedure that the IACUC reviews are:

(aa) details of the procedure (e.g., the actual procedure itself, pre and post-operative care, aseptic technique, sequence of multiple procedures);

(bb) appropriateness of the species for the procedure proposed;

(cc) qualifications of the personnel performing the surgical procedures;

(dd) species-specific and procedure-specific facility requirements;

(ee) patient monitoring practices in the surgical and post-surgical periods; and

(ff) personnel occupational health and safety issues.

(ii) The veterinarian should always be one of the IACUC’s primary sources of information on surgery and post-operative issues. While the numerous references are available to provide background and a basis for reviewing surgical protocols, the IACUC relies on professional judgement to review the unique situations surrounding surgery in an experimental setting. Surgical procedures performed in a research setting have review requirements that may be different from those in a routine veterinary clinical setting.

(iii) Some of the surgical procedures proposed in research are experimental and may require ongoing review by the IACUC as the procedure is developed. Model development protocols, and close collaboration with the veterinarian and other experienced individuals, can be helpful in these circumstances.

(iv) To perform a meaningful review, the IACUC must be provided with details of proposed surgical procedures. Such details give the IACUC the opportunity to assess the level of the Investigator’s knowledge and need for additional training.
(d) Multiple Major Survival Surgery (MMSS)

(i) Animals may not be used in these procedures unless:

(aa) there is a scientific justification (e.g., related components of the same study) provided by the principal investigator in writing;

(bb) the MMSS are required as a routine veterinary procedure or to protect the health and well-being of the animal, as determined by the attending veterinarian; or

(cc) under other special circumstances which have been approved

(ii) Subsequent to approval of MMSS, the IACUC should ensure that there is sufficient ongoing oversight of the project.

(e) Special Considerations

(i) Some procedures are difficult or impossible to perform in some species of animals due to the nature of the animal (e.g., anatomical variation such as lack of a gall bladder, size of the animal, or size of a particular organ; sensitivity to antibiotics; or tolerance to a particular procedure). This can be an issue when a protocol involves an established procedure in a new animal model. Such protocols require particular attention and guidance from the IACUC.

(ii) If a procedure may cause more than momentary or slight pain or distress, paralytics should not be used without concurrent anaesthesia.

(iii) Some procedures may require specialised facilities to ensure their success. For example, major survival surgery in non-rodents requires dedicated surgical facilities. The IACUC should assess the availability of necessary facilities during the protocol review process.

(f) Patient Monitoring

(i) The sophistication of patient monitoring required varies with the species and the procedure, but during protocol review, the IACUC should expect evidence of the following:

(aa) a pre-surgical assessment;

(bb) adequate monitoring of depth of anaesthesia and animal homeostasis during the surgical procedure;

(cc) support such as fluid supplementation, external heat or ventilation;

(dd) monitoring and support during anaesthetic recovery; and

(ee) post-surgical monitoring details, (e.g., what will be done and how often, who will be responsible, and the name and phone number of the individual to contact in the case of post-surgical complications).
Recordkeeping

(i) Recordkeeping is an essential component of peri-operative care. For major surgical procedures on non-rodent mammals, an intra-operative anaesthetic monitoring record should be kept and included with the surgeon’s report as part of the animal’s records. This record should be available to the personnel providing post-operative care.

(ii) Post-operative records, at a minimum, should reflect that the animal was observed until it was extubated and had recovered the ability to stand. These should be supplemented by records evaluating the animal’s recovery, administration of analgesics and antibiotics, basic vital signs, monitoring for infection, wound care, and other medical observations.

Occupational Health and Safety

(i) Surgical situations can present certain occupational health and safety risks related to:

(aa) use of inhalation anaesthetics,

(bb) use of certain species or a species under certain circumstances (e.g., pregnant sheep), or

(cc) use of certain devices (e.g., lasers).

(ii) If the circumstances warrant it, the IACUC should consult with the applicable biosafety personnel.

3.5.8 Transgenic Animals

(a) A spontaneous mutation is a naturally occurring heritable alteration in the genetic code. Spontaneous mutations have been observed in virtually all species.

(b) An induced mutation is a man-made alteration in the genetic code. Induced mutant is a generic term including transgenic and targeted mutations that are created to study over-expression or under-expression of a specific gene. The altered gene must be predictably transmitted to offspring for a spontaneous or an induced mutation to be useful in research.

(c) To date, the majority of induced mutations have been made in laboratory mice of the genus Mus or laboratory rats of genus Rattus. Although mice are used as examples in the following discussion, the general considerations are applicable to induced mutants of any species.

(d) Transgenic refers to insertion of exogenous DNA (deoxyribonucleic acid) into cells. Typically, cDNA (complimentary deoxyribonucleic acid) made from specific mRNA (messenger ribonucleic acid) is inserted into cells using microinjection, electroporation or certain nonpathogenic viruses. (Electroporation is the brief application of an electric field to a cell to increase permeability of the cell membrane for purposes of introducing drugs or genes into the cell.) Each of these methods has been used to insert new DNA into the pronucleus of a fertilised mouse egg and to create transgenic mice. The manipulated fertilised eggs may or may not be cultured.
in vitro for one to three days before they are surgically implanted into the oviducts or uterus of pseudopregnant female mice. The inserted DNA incorporates in chromosomes of a percentage of embryos developing from the microinjected eggs. The DNA incorporates at different genetic locations and a different number of copies of the DNA may incorporate in different embryos. Thus, each embryo has the potential to become a unique transgenic mouse even though the same quantity and type of DNA was injected into genetically identical fertilised eggs. All manipulated, fertilised eggs do not become live born transgenic mice. Losses occur at every step from injection through gestation and delivery.

(e) Mice can carry transgenes, but unless the cDNA is incorporated into germ cells, the mouse is unable to transmit the transgene to its offspring. A mouse that passes the transgene to the descendants is called a ‘founder. Thus, many fertilised eggs have to be injected to obtain a few transgenic mice, and only a few of these transgenic mice will be ‘founders’ of this transgenic line.

(f) Targeted mutation refers to a process whereby a specific gene is made nonfunctional (‘knocked-out’) or less frequently made functional (‘knockedin’). Creation of a targeted mutation requires several steps in the laboratory. The specific gene is identified, cloned and manipulated to make it nonfunctional (‘knocked-out’). The manipulated gene is attached to another DNA sequence called a promoter and introduced into embryonic stem (ES) cells by electrical or chemical methods. These ES cells are cultured in special media that permits identification of ES cells incorporating the manipulated gene. ES cells incorporating the manipulated gene are injected into an early embryo (blastocyst). The ES cell injected blastocysts are surgically implanted into the uterus of pseudopregnant female mice. Some injected blastocysts develop into viable embryos and gene deficient ‘knock-out’ mice are born.

(g) Many blastocysts have to be injected to obtain a few new ‘knock-out’ mice, and only a few of the new ‘knock-out’ mice will incorporate the ‘knocked-out’ gene in their germ cells and become ‘founders’.

(h) If a Project uses a spontaneous or induced mutant model and the mutant animal can be purchased from a resource or commercial colony, review of this project is similar to review of any other project. If a project uses an induced mutant model and only breeders are available from the source, review of this project is similar to review of any other breeding colony. In either case, the IACUC should determine if the mutant gene will result in a severely debilitating phenotype, if anything can or will be done to ameliorate such phenotype, and what endpoints will be used to determine when a mutant animal will be euthanised. Simple husbandry measures can modify the severity of some mutant phenotypes. For example, ground feed or moist feed can extend life and improve growth of mutants with missing or malformed teeth. Food and water on the bottom of the cage may be easier for mutant rodents with neuromuscular abnormalities to access than food in a traditional feeder built into a cage lid. Extra bedding helps dwarf mice reach food and water. Extra bedding helps absorb urine produced by diabetic mice or other mice that excrete large quantities of urine. A normal cage mate, a solid bottom cage with extra bedding, or a slight increase in room temperature can benefit mutant rodents that have problems maintaining body temperature (Beamer, 1986).

(i) When an Investigator prepares a Proposal that includes development of a new mutant model, information about clinical abnormalities associated with the phenotype, special husbandry requirements, etc. will not be available. However, the Investigator should include general criteria for euthanasia if a severe debilitating
phenotype develops, and provide the IACUC with this information when the new mutant has been developed or at the next annual review.

(j) The standard of ‘normal’ for a mutant animal may or may not be the same as for a non-mutant animal. If the mutant phenotype does not impact clinical well-being of the animal, the same standard of ‘normal’ can be used for mutant and non-mutant animal. In the mouse, brown (gene symbol Tyr<bp>) and short ear (Bmp5.sel) are examples of spontaneous mutations that produce no observable, clinical impact on the well-being of the mouse. If the mutant phenotype has minimal impact on the well-being of the animal, the standard of ‘normal’ can be similar for mutant and non-mutant animal. Hypogondal (Gnhr<hp>) and ‘little’ (Ghrhr<lt>) are examples of spontaneous mutations with minimal impact on well being of the mouse. Homozygous hypogondal mice are normal in all ways except for small, nonfunctional gonads. Homozygous ‘little’ mice are smaller than non-mutant littermates. Growth hormone transgenic mice tend to have larger body size than normal, but are otherwise clinically normal with the exception of reduced fertility.

(k) In the case of mutants where phenotype involves clinical abnormalities, the standard for ‘normal’ may have to be modified to encompass the expected phenotype. For example, 4 to 5 week old homozygous dystrophic mice (Lama<dy-2J>) have difficulty abducting hindlegs and have an abnormal gait. As these mice age, muscular weakness progresses in hindlegs and eventually extends to involve all skeletal muscles. The standard for ‘normal’ for homozygous dystrophic mice must include difficulty abducting hindlegs and an abnormal gait. Adenopolyposis coli ‘knock-out’ mutant mice (Apc<Min>) are clinically normal until the intestinal polyps develop, after which time the mice become anemic and lose weight. Experimental endpoints for these latter and similar mutant models should focus on (1) ability of the mutant to access feed and water, (2) response of the mutant to stimuli, and (3) general condition of the mutant (i.e., is the mutant excessively thin, showing progressive weight loss or hunched posture?).

(l) Many Institutions have a centralised induced mutant facility that receives the genetic material from investigators and performs the manipulations to develop ‘founder’ transgenic or ‘knock-out’ mice. The ‘founder’ mice are returned to the investigator who undertakes breeding to expand the line. Review of the centralised induced mutant facility should focus on personnel qualifications, animal related practices such as aseptic surgery, and average number of mice required to produce ‘founders’ for a single DNA construct, recognising, however, that the number of mice required is a very rough estimate because of differences in responses of different strains or stocks of mice, variations in success rate for different DNA constructs, and subtle or less subtle uncontrollable environmental changes.

(m) In many non-mutant model experiments, an investigator can accurately estimate the exact number of animals required to test a hypothesis. However, when creating an induced mutant, there are major variables that make it difficult to accurately estimate the number of required animals, including:

(i) differences in percent successful microinjections of pronuclei or successful incorporations of altered gene into ES cells,

(ii) differences in percent successful surgical transfers of fertilised eggs or blastocysts, and

(iii) differences in percent successful incorporation of exogenous DNA or altered gene into germ cells of induced mutant mice.
Different strains of mice vary in their responses to each of these manipulations. Different genes (‘constructs’) vary in the ease with which they insert as a transgene or are ‘knocked-out’. These variables remain even when the same skilled people perform each manipulation.

3.6 Monitoring of Approved Protocols

3.6.1 After the IACUC has approved a protocol, it has a responsibility to ensure that procedures are carried out in the laboratory or classroom as described in the protocol. This section will briefly review ways that the IACUC can monitor the conduct of approved protocols.

3.6.2 Acquisition and Tracking
(a) Animals should be obtained only from licensed dealers or other legal sources, and it is incumbent upon an Institution to establish mechanisms to monitor and document the number of animals acquired and used in approved activities.

(b) Any animals to be imported require import permits from AVA. This is best accomplished if animal purchases may be made only through the Institution’s animal resource facility or other appropriately designated office.

(c) Once animals have been acquired, they should be included in a tracking system. Many Institutions have automated systems that will alert an appropriate individual when an investigator has reached a preset percentage (e.g., 80 to 90%) of the number of animals approved for a specific project, and can prevent ordering animals in excess of the number approved. Institutions with small programmes using limited numbers of animals may choose to maintain a manual log of IACUC approved activities and numbers of animals acquired.

(d) Tracking animal use becomes more complicated when Investigators maintain breeding colonies. Keeping track of animal usage may be accomplished by requiring that Investigators with breeding colonies maintain accurate records. Investigators can be required to report to the designated office, at regular intervals, the number of animals born, weaned, or used in studies. This report can be tallied against the numbers in the approved protocol.

3.6.3 Compliance Specialist
(a) Some IACUCs have a full or part-time compliance specialist who monitors procedures in vivaria, laboratories, and classrooms, and reports his or her observations to the IACUC. This individual should have laboratory animal training and experience, and be authorised to conduct announced or unannounced laboratory inspections on behalf of the IACUC.

(b) In addition, the compliance specialist may periodically survey individual laboratories to ensure that actual procedures used are consistent with protocols. The survey may include meeting with Investigators and staff to review concerns, answer questions, and identify procedures that may deviate from those originally approved by the IACUC. In cases of deviation, the specialist should notify the IACUC.
3.6.4 Eyes and Ears

(a) Research, veterinary, and husbandry staff should be aware of approved procedures for use on animals when they have responsibility for those animals. This may be accomplished by informing these individuals in staff meetings or by making standard operating procedures and animal use protocols readily accessible in the laboratory or vivarium.

(b) These practices help to ensure that procedures being used are, in fact, those that were approved by the IACUC. Maintaining an open environment in which staff can discuss apparent departures from approved procedures with the investigator often facilitates compliance and the rapid correction of deviations. Staff must also be free to report perceived deviations to the IACUC, which must then consider such concerns.

3.6.5 Semiannual Inspection

(a) During the semiannual facility inspections, IACUC members should note the use of animals and may verify that the observed procedures are consistent with the protocol on file.

3.6.6 Retrospective Reporting of Adverse Events

(a) The number of covered animals used in each pain/distress category should be reported annually.

(b) Institutions may choose to require an accounting of unexpected, unintentional, or adverse events as a means of identifying deficiencies in procedures, faults in study design, or need for additional personnel training.

3.6.7 Review of Publications

(a) In academic institutions and many companies, much research is eventually published. Some IACUCs choose to review some published descriptions of animal use to verify that work was done according to the approved protocol.

3.6.8 Conclusion

Although no IACUC has the staff or time to observe all animal use in an institution, the IACUC can help establish a climate of compliance. To ensure that animal use conforms to local policy and federal regulations, it is prudent for the IACUC to confirm that animals are used according to protocol.
CHAPTER 4 EVALUATION OF ANIMAL CARE AND USE CONCERNS

4.1 General

4.1.1 To help ensure that laboratory animals receive humane care and 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.

4.2 Compliance

4.2.1 To ensure compliance with the Guiding Principles, it is strongly recommended that each IACUC develop and implement policies and procedures to ensure that all animal care and use concerns are brought to its attention for consideration. Some of the elements that should be included in these procedures are described below (see IACUC Responses to Complaints).

4.2.2 Institutional policy should contain provisions to protect the confidentiality of those who report concerns as well as anyone against whom allegations are directed, while allegations are under investigation. The policy should also address mechanisms for protecting complainants from reprisals.

4.3 Origins of Concerns or Complaints

4.3.1 Some common sources include:

(a) animal care and use personnel: these individuals should receive instruction in Institutional training programmes to report perceived deficiencies in animal care or use to the IACUC.

(b) other personnel: these persons (e.g., secretarial, maintenance, security staff) are likely to direct concerns to a member of the research, animal care or veterinary staff, but they should be instructed to report concerns to the IACUC.

(c) employee “hotlines” or ombudsmen: personnel responsible for these functions should be sensitive to animal-related concerns and notify the IACUC Chair of any that may arise.

(d) the public: they are most likely to direct complaints to senior Institutional representatives who should promptly forward them to the IACUC Chair.

(e) anonymous: these complainants may or may not be Institutional employees.
(f) the media: stories appearing in newspapers, and on television or radio, etc. may contain or evoke concerns about animal care and use; such reports should be evaluated by the IACUC, and, when appropriate, the Institution should proactively address them.

4.4 Methods for Reporting Concerns

4.4.1 To facilitate communication, the names and phone numbers of contact persons, including IACUC members, the veterinarian, security office, and ombudsman/hotline, if one exists, should be posted in or near the entrance to animal facilities or listed on a Web site that is readily available to Institutional employees. This information should also be provided during training sessions as described above.

4.4.2 Although written concerns are more convenient to deal with, 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 honoured to the extent possible.

4.5 IACUC Responses to Complaints

4.5.1 While specific methods for evaluating concerns about animal care and use may vary from Institution to Institution, all methods should contain these elements:

(a) There should be a procedure for verifying stated concerns.

(b) There should be guidelines for effecting appropriate corrective measures, when necessary.

4.5.2 One of the roles of the IACUC is to review all concerns about the animal care and use programme, regardless of origin, and investigate them if warranted. The IACUC Chairman is normally responsible for ensuring that concerns are addressed, but may delegate investigation to a subcommittee. If the Chair has, or is perceived to have, a conflict of interest, the CEO should delegate the responsibility for assuring that the concern is addressed to another non-conflicted member of the IACUC.

4.5.3 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 Guiding Principles are alleged to be occurring but animals are not in apparent danger.

4.5.4 The course of action taken by the IACUC should be driven by the potential significance of the alleged situation. For example, conditions that reportedly jeopardise the health or well-being of animals should be evaluated immediately. To
cope promptly with such situations, some Institutions have policies whereby a veterinarian or other designated person is authorised to halt procedures which they believe do not comply with Institutional policies until the IACUC can be convened and consider the matter formally.

4.5.5 Situations that may involve potential criminal activity or human safety should be reported promptly to the Institution's law enforcement or occupational health and safety officials.

4.5.6 Allegations of other ongoing policy or procedural matters may not require such same-day attention, but should not be deferred merely as a matter of convenience. Emergency meetings may be necessary in these cases to ensure prompt consideration of concerns.

4.5.7 IACUC procedures for handling complaints may involve reviewing them with the veterinarian. Depending on the nature of the concern, the CEO, legal counsel, and the person who submitted or fielded the complaint may also be invited to participate. Based on the results of its initial evaluation, a course of action—which may include further investigation—will then be determined and implemented.

4.5.8 The IACUC should acknowledge receipt of concerns when the complainant is known. Details concerning the complaint, complainant, persons against whom allegations may have been directed, and the investigations in progress are usually considered confidential.

4.5.9 The Guiding Principles authorises the IACUC to suspend an activity after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present. Suspensions must also be reviewed by the CEO in consultation with the IACUC.

4.5.10 Most Institutions have developed self-regulatory policies and procedures that supplement formal suspensions by the IACUC and are intended to ensure adherence to Institutional and regulatory requirements. Depending on the severity of noncompliance or deviation from accepted practices, these range from counselling and mandatory remedial training to specific monitoring of animal use, temporary revocation of animal use privileges, or termination of employment.

4.6 Model - Suggested IACUC Procedures for the Investigation of Animal Care and Use Concerns*

4.6.1 One model for considering concerns about animal care and use is outlined on the following pages. This example may not apply to all Institutions, and may be adapted, as needed, in designing guidelines that are appropriate for individual Institutions.

4.6.2 Initial Evaluation and Actions

(a) Upon receipt of a concern the IACUC Chair should convene a meeting of the IACUC. After initial review of the complaint the IACUC should 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 IACUC should determine which individuals or other Institutional or non-Institutional offices may require notification at this time.

(b) If immediate action appears warranted because animal or human welfare may be compromised, the IACUC should notify the CEO 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.

4.6.3 Investigation

(a) Should the IACUC determine that further investigation is required, the Chairman, or another individual or subcommittee appointed by the Chairman, should conduct the investigation and report back to the IACUC. It is important to avoid actual or perceived conflicts of interest in this process.

(b) 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.

(c) The nature of the information required will vary depending on the circumstances, but often involves:
   (i) interviewing complainants (if known), any persons against whom allegations were directed, and pertinent programme officials;
   (ii) observing the animals and their environment; and
   (iii) reviewing any pertinent records, (e.g., animal health records, protocol, and other documents).

(d) The designated Investigator(s) should provide a report to the IACUC which summarises:
   (i) the concern(s),
   (ii) the results of interviews,
   (iii) the condition of animals and their environment, and
   (iv) the results of records and other document reviews.

(e) The report should also contain:
   (i) any supporting documentation such as correspondence, reports, and animal records;
(ii) conclusions regarding the substance of the concerns vis-a-vis requirements of the Guiding Principles, and Institutional policies and procedures; and

(iii) Recommended actions, if appropriate.

4.6.4 Outcomes and Final Actions

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

(i) there was no evidence to support the concern or complaint,

(ii) the concern or complaint was not sustained, but a) related aspects of the animal care and use programme require further review or b) other Institutional programmes may require review, or

(iii) the concern or complaint was valid.

(b) Subsequent actions of the IACUC may include:

(i) Implementing measures to prevent recurrence (such measures often include changes in administrative, management or IACUC policies and procedures, and may include sanctions*);

(ii) notifying the CEO and the AV of its actions;

(iii) notifying funding or regulatory agencies, as required; and

(iv) notifying the complainant, any persons against whom allegations were directed, and pertinent programme officials (appropriate supervisory and management staff, the public affairs office, Institutional attorneys, etc.).

(c) Some Institutions, as part of their programmes, have developed policies and procedures that authorise the IACUC to impose sanctions on behalf of the Institution. In other Institutions, IACUCs recommend actions to the CEO for implementation, and in still others, there exists a combination of these approaches. Some of the Institutional sanctions that have been devised include:

(i) counselling;

(ii) issuing letters of reprimand;

(iii) mandating specific training aimed at preventing future incidents;

(iv) monitoring by the IACUC or IACUC-appointed individuals of research, testing, or training involving animals;
(v) 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;

(vi) permanent revocation of privileges to provide animal care or to conduct research, testing, or training that involves animals; and

(vii) recommending to the CEO that Institutional (e.g., reassignment, termination of employment) sanctions be imposed.

(d) Concerns Unrelated to Animal Care and Use

(i) The IACUC may determine, either in its initial evaluation of a concern or as a result of investigation, that violations of non-animal-related Institutional policies and procedures, may have occurred (e.g., scientific misconduct, misuse of monies, fraud, theft, etc). In such cases, those findings should be reported to appropriate Institutional officials or committees for their consideration.
5.1 Introduction

The responsibility for these functions should be clearly delegated. Usually the IACUC office is assigned this task. The individuals responsible should understand national animal use requirements and the Institution’s programmes. Reports may be written using language that is clear and precise to ensure accurate interpretation as they may be required to meet national regulations.

5.2 Record keeping

5.2.1 Minutes

(a) Records of attendance: Although members may arrive late or leave during a meeting, generally a member is marked as either present or absent. An exception would be when the IACUC member leaves the meeting room during discussion of a protocol on which that member is a participant. If the temporary absence of a member drops the number of members present below the quorum, this should be noted in the minutes. Certain official IACUC actions require a quorum.

(b) Activities of the Committee include corrections or approval of previous minutes; presentation of programme, policy, facility and compliance reports; and decisions on policies, protocols, and amendments.

(c) Deliberations refers to the discussion and reasons leading to particular IACUC decisions. Although some IACUCs maintain a verbatim record (e.g. audio or videotapes), minutes should include as a minimum a summary of the key points discussed prior to a committee decision.

5.2.2 Protocols

(a) Animal applications and proposed significant changes should be retained for the duration of the animal activity and for an additional three years after the end of the activity or as otherwise directed by local Acts and Guidelines.

(b) Proposals submitted to the IACUC must be kept for three years even if approval was not granted or animals were not used. The records must show whether or not IACUC approval was given.

5.2.3 Other records

(a) The Guiding Principles require that semiannual IACUC reports and recommendations be retained by the Institution.

(b) The Guiding Principles also require that reports of accrediting and/or other relevant agencies (e.g. AAALAC) be kept on file.

(c) Animal health records are not usually maintained by the IACUC but are kept in the animal facility. All these records must be kept for at least three years; and must be accessible to AVA, and funding agencies for inspection or copying.
5.3 Communications

5.3.1 Semiannual Facility Inspections and Programme Evaluations

(a) The Guiding Principles require that the IACUC evaluate the Institution ’s animal programme at least once every six months, including an inspection of facilities, and submit a report to the CEO.

(b) The Guiding Principles allow the IACUC discretion in how it evaluates its facilities and programme. The report must contain a description of the nature and extent of the Institution ’s compliance with the Guiding Principles; any departures must be identified and modifications proposed, with a plan and timetable for correction. Any minority views of IACUC members must be included.

(c) Minor and significant deficiencies must be distinguished. A significant deficiency is defined as one that “is or may be a threat to the health or safety of animals.” Programme or facility deficiencies, including accidents or natural disasters, which cause injury, death, or severe distress in animals, are, by definition, ‘significant.’ Examples of minor deficiencies include chipped paint and burnt-out light bulbs. The report must also identify any facilities that are AAALAC accredited.

(d) The IACUC may utilise AAALAC programme status evaluations, accreditation, or pre-assessment preparation activities as a semiannual evaluation. To be used as the semiannual report, the report must include all the information required, and be approved by vote of the IACUC.

(e) Semiannual reports are only submitted to AVA upon request.

5.3.2 Suspension and Noncompliance

(a) The IACUC must report promptly, through the CEO, the circumstances and actions taken in the following instances:

(i) any serious or continuing non-compliance with the Guiding Principles,

(ii) any serious deviation from the provisions of the Guiding Principles, and

(iii) any suspension of any activity by the IACUC.

(b) It is recommended that the Institution prepare a formal report describing the circumstances and any actions taken after IACUC and IO review. Similarly, accredited Institutions must report promptly to AAALAC serious issues relating to the animal care and use programme, such as investigations by the AVA, or other serious incidents or concerns that negatively affect animal well-being.
5.4 Annual Report

5.4.1 The research facility shall prepare an annual report. The report shall be signed and certified by the CEO, and shall cover the previous year (the reporting period is 1 Jan to 31 Dec of the year).

5.4.2 The annual report shall include the information required by AVA, including the following:

(a) Assurance

(i) Assure that professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anaesthetics, analgesic, and tranquillising drugs, prior to, during, and following scientific activities were followed by the Housing and Research Facility.

(ii) Assure that each Investigator has considered alternatives to painful procedures.

(iii) Assure that the facility is adhering to the Guiding Principles, and that it has required that exceptions to the Guiding Principles be specified and explained by the Investigator and approved by the IACUC. A summary of all such exceptions must be attached to the annual report. In addition to identifying the IACUC-approved exceptions, this summary must include a brief explanation of the exceptions, as well as the species and number of animals affected.

(b) Background information and statistics

(i) State the composition of IACUC

(ii) State the name(s) of Attending Veterinarian(s) and whether they are full-time or part-time.

(iii) State the location of all facilities where animals were housed, used or held for Scientific Purposes and for each of these location:

(iv) State the common names and the numbers of animals used for Scientific Purposes involving no pain, distress, or use of pain-relieving drugs. Routine procedures (e.g., injections, tattooing, blood sampling) should be reported with this group.

(v) State the common names and the numbers of animals used for Scientific Purposes involving accompanying pain or distress to the animals and for which appropriate anaesthetics, analgesic, or tranquillising drugs were used;

(vi) State the common names and the numbers of animals used for scientific purposes involving accompanying pain or distress to the animals and for which the use of appropriate anaesthetics, analgesic, or tranquillising drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used
shall be attached to the annual report;

(vii) State the common names and the numbers of animals being bred, conditioned, or held for scientific purposes but not yet used for such purposes.

(c) Self-regulation

(i) Indicate the dates of reviews and inspections by IACUC

(ii) State the significant deficiencies identified in the 6-monthly reviews and inspections by the IACUC, and whether the actions taken to correct these deficiencies were as planned and scheduled in the IACUC reports. A significant deficiency is one that is or may be a threat to the health and safety of the animals and which is classified as such by the IACUC in its reports.