Guidelines on the Care and Use of Animals for Scientific Purposes

2004

NATIONAL ADVISORY COMMITTEE FOR LABORATORY ANIMAL RESEARCH

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PUBLIC HEATH SERVICE POLICY ON HUMANE CARE AND USE OF LABORATORY ANIMALS
AND
ARENA/OLAW INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE GUIDEBOOK
THE OFFICE OF LABORATORY ANIMAL WELFARE (OLAW), NATIONAL INSTITUTES OF HEALTH, USA

PREFACE

Guidelines on the Care and Use of Animals for Scientific Purposes, which has been developed by the National Advisory Committee For Laboratory Animal Research (NACLAR), is a national guide which establishes the best practices in the use and care of animals for scientific purposes. The NACLAR *Guidelines* set out the responsibilities of all the parties involved in the care and use of animals for scientific purposes, in accordance with widely accepted scientific, ethical and legal principles. It stipulates that all proposed use of animals for scientific purposes must be evaluated by an Institutional Animal Care and Use Committee (IACUC) in compliance with the *Guidelines*.

The 3Rs Principle of *Replacement, Reduction* and *Refinemen*t is central to the NACLAR *Guidelines*. Since the concept of the 3Rs was first introduced by William Russell and Rex Burch in *The Principles of Humane Experimental Technique* in 1959, the 3Rs have been internationally accepted as the basis of the care and use of animals for scientific purposes. These are: to Replace the need for animal use by alternative means, to Reduce the numbers of animals used to an unavoidable minimum, and to Refine any procedures necessarily used, so as to minimize the impact on animals, consistent with the achievement of a justifiable scientific purpose, and which is necessary because there is no other way of achieving that purpose. The incorporation of the 3Rs at the planning stages ensures that full consideration of the principle is exercised at every juncture of the process.

The NACLAR *Guidelines* has acknowledged the best practices of countries such as Australia, Canada, New Zealand, the US, and organizations such as the Council for International Organisations of Medical Sciences (CIOMS) and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986). These countries and organisations have laid down stringent *Guidelines* and procedures governing the use and care of animals in research.

The *Guidelines* is organised into three sections which should be read together as a complete document:

The first section, *"Guiding Principles for the Care and Use of Animals for Scientific Purposes"*, describes the overall guiding principles to promote the humane and responsible care and use of animals for scientific purposes in Singapore. The basis of the principles lies in the 3Rs – Replacement, Reduction and Refinement:

Replacement of animals with other methods
Reduction in the number of animals used
Refinement of Projects and the techniques used to minimise impact on animals

The scope of the principles covers all aspects of the care and use of animals for scientific purposes including their use in teaching, field trials, environmental studies, research, diagnosis, product testing, and the production of biological products. This section outlines the responsibilities of institutions, investigators and persons involved in the care and use of animals for scientific purposes. All research facilities which house and use

animals for scientific purposes will have to operate in accordance with the *Guidelines* to qualify for licensing from the Agri-Food and Veterinary Authority (AVA).

The second section, "*Guidelines for Institutional Animal Care and Use Committee*", follows on from the *Guiding Principles for the Care and Use of Animals for Scientific Purposes* and describes in detail the operational aspects pertaining to the Institutional Animal Care and Use Committee (IACUC). The IACUC is responsible for the oversight and evaluation of animal care and use programmes of an institution, and is responsible for ensuring that the care and use of animals for scientific purposes and all animal experimental procedures are in compliance with the *Guidelines*. Under the *Guidelines*, all institutions with research facilities are required to establish their own IACUC to assume this function.

The third section, "*Training Guidelines*", outlines the training scope and requirements for users of animals and animal facilities personnel. This includes the scope of the core curriculum and the relevant core competencies, such as special courses for animal procedures. The *Guidelines* require all users of animals for research to undergo appropriate training before carrying out any experiments using animals. This section is to assist IACUCs in determining the scope and depth of education training programmes that will meet both institutional needs and the requirements of NACLAR.

Additional information and references, including sections on the care and use of fish and non-human primates, are contained in the Appendices under the first section, "*Guiding Principles for the Care and Use of Animals for Scientific Purposes*".

NACLAR acknowledges the commitment and dedication of all its Committee and Subcommittee members in this undertaking. Finally, NACLAR expresses its fullest appreciation to all contributors to the *Guidelines* and all those who provided valuable feedback.

Prof Bernard Tan
Chairman
National Advisory Committee for Laboratory Animal Research

NATIONAL ADVISORY COMMITTEE FOR LABORATORY ANIMAL RESEARCH

Chairman:	Prof Bernard Tan Professor, Department of Physics National University of Singapore
Chair, Guiding Principles Subcommittee:	Prof Ngiam Tong Tau Chief Executive Officer Agri-Food & Veterinary Authority of Singapore
Chair, IACUC Subcommittee:	Dr Pierce Chow Director, Department of Experimental Surgery Singapore General Hospital
Chair, Training Subcommittee:	Dr Leslie Retnam Acting Director, Laboratory Animals Centre National University of Singapore
Members:	A/Prof Yap Eu Hian* Director (1980 - 2003), Laboratory Animals Centre National University of Singapore
	Prof Ten Chin Liew Head, Department of Philosophy National University of Singapore
	Dr Sathivel Ponniah Deputy Director, Biological Resource Centre Agency for Science, Technology and Research
	Mr Eric Chin State Counsel, Civil Division Attorney-General's Chambers
	Ms Belinda Tang NACLAR Secretariat

**** Emeritus member, NACLAR***

GUIDING PRINCIPLES SUBCOMMITTEE

Prof Ngiam Tong Tau (Chair), Agri-Food & Veterinary Authority of Singapore
Dr Tan Lee Kim, Agri-Food & Veterinary Authority of Singapore
Dr Choo Li Nah, Agri-Food & Veterinary Authority of Singapore
A/Prof Yap Eu Hian, National University of Singapore
Prof Ten Chin Liew, National University of Singapore
Dr Pierce Chow, Singapore General Hospital
Mr Eric Chin, Attorney-General's Chambers

IACUC GUIDELINES SUBCOMMITTEE

Dr Pierce Chow (Chair), Singapore General Hospital
Dr Paul G. Pineda, Singapore General Hospital
Ms Audrey-Anne Oei, National Cancer Centre
Dr Shabbir Moochala, Defence Medical Research Institute
Mr Loke Weng Keong, Defence Science Organisation
Dr Leslie Retnam, National University of Singapore
Dr Leong Hon Keong, Agri-Food & Veterinary Authority of Singapore
Dr Sathivel Ponniah, Deputy Director, Biological Resource Centre,
Agency for Science, Technology and Research
Mr Hu Changyong, Optimerpharma
Dr Hwang San Bao, Optimerpharma

TRAINING GUIDELINES SUBCOMMITTEE

Dr Leslie Retnam (Chair), National University of Singapore
Dr Sathivel Ponniah, Deputy Director, Biological Resource Centre,
Agency for Science, Technology and Research
Dr Jason Chang, Singapore General Hospital
Mr Robert Ng, Singapore General Hospital

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NATIONAL ADVISORY COMMITTEE FOR LABORATORY ANIMAL RESEARCH
THE GUIDING PRINCIPLES FOR THE CARE AND USE OF ANIMALS FOR SCIENTIFIC PURPOSES

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CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 The National Advisory Committee For Laboratory Animal Research (NACLAR) was set up in 2003 to recommend guidelines for the care and use of animals for Scientific Purposes in Singapore. The guidelines consist of 3 parts :

(a) the Guiding Principles for the Care and Use of Animals for Scientific Purposes
(b) the Institutional Animal Care and Use Committee Guidelines
(c) the Training Guidelines

and shall be read together to form the NACLAR Guidelines.

1.1.2 The NACLAR Guidelines have been drawn up after a review of the principles and practices adopted in other countries such as Australia[1], Canada[2], New Zealand[3] and the United States[4, 5].

1.1.3 Other useful reference materials have been set out at Appendix I.

1.2 Purpose of the Guiding Principles

1.2.1 The purpose of the Guiding Principles is to :

(a) set out the framework for the NACLAR Guidelines
(b) promote the humane and responsible care and use of animals for Scientific Purposes in accordance with the principles of Replacement, Reduction and Refinement pertaining to the care and use of animals for Scientific Purposes.

1.3 Scope of the Guiding Principles

1.3.1 The Guiding Principles cover all live fish, amphibians, reptiles, birds and non-human mammals.

1.3.2 The Guiding Principles cover all aspects of the care and use of animals for Scientific Purposes including their use in teaching, field trials, environmental studies, research, diagnosis, product testing, and the production of biological products .

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[1] *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* by the National Health and Medical Research Council, Australia.
[2] *Guide to the Care and Use of Experimental Animals, Volume 1 (2nd Edition) 1993, Canadian Council on Animal Care (CCAC), Canada*
[3] *Good Practice Guide for the Use of Animals in Research, Testing and Teaching* by the National Animal Ethics Advisory Committee, New Zealand.
[4] *Guide for the Care and Use of Laboratory Animal* by National Research Council, USA
[5] *Public Health Service Policy on Humane Care and Use of Laboratory Animals*, Office of Laboratory Animal Welfare (OLAW), National Institute of Health, USA

1.3.3 The Guiding Principles outline the responsibilities of Institutions, Investigators, Staff and others involved in the care and use of animals for Scientific Purposes.

1.4 Framework to meet Purpose of Guiding Principles

1.4.1 The Institutions, CEO, Investigators, Staff and other persons involved in the care and use of animals for Scientific Purposes must comply with all current and relevant laws.

1.4.2 Institutions are to self-regulate and take responsibility for meeting the Guiding Principles through the establishment of Institutional Animal Care and Use Committees (IACUC) that in turn act to ensure and verify that the use and care of animals for Scientific Purposes are in accordance with the Guiding Principles.

1.4.3 Investigators are to undertake Projects in accordance with the Guiding Principles and the approvals or directions given by the IACUCs.

1.5 Definitions of terms and abbreviations

Analgesia: The temporary abolition or diminution of pain perception.

Anaesthesia: A state of controllable, reversible insensibility in which sensor perception and motor responses are both markedly depressed.

Animal: All live fish, amphibians, reptiles, birds and non-human mammals.

Approved Project: A Project for a Scientific Purpose involving the use of animals which has been approved by an IACUC.

Attending Veterinarian: A veterinarian engaged under formal arrangements by an Institution on a full-time or part-time basis to advise on the appropriate care and use of animals and provide adequate veterinary care.

AVA: The Agri-Food and Veterinary Authority

Cachexia: Severe generalised weakness, malnutrition and emaciation**.**

Death as an end-point: When the death of an animal is the deliberate measure used for evaluating biological or chemical processes, responses or effects.

Distress: An acute or chronic response of an animal caused by stimuli that produce biological stress, which manifests as observable, abnormal physiological or behavioural responses.

Endangered species: A species included in the Appendices of the *Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).*

Euthanasia: The act of inducing humane death in an animal.

CEO: The Chief Executive Officer (or person of like standing by whatever name called) of an Institution who is in the position to grant resources to the Institution's IACUC and to enforce the recommendations of the IACUC.

Housing Facilities: Buildings, yards, paddocks, grounds in which animals are kept.

IACUC: Institutional Animal Care and Use Committee constituted by Institutions.

Institution: Any institution, company, organisation, association, body or person that uses or intends to use animals for Scientific Purposes and is licensed to do so.

Investigator: A person who proposes or has approval to conduct a Project involving use of animals.

Manipulation: Any interference with the normal physiological, behavioural or anatomical integrity of the animal by deliberately depriving it of its usual care or subjecting it to a procedure which is unusual or abnormal; when compared with that to which animals of that type would be subjected to under normal management or practice and which involves exposing it to any parasite, micro-organism, drug, chemical, biological product, radiation, electrical stimulation, or environmental condition or any enforced activity, restraint, nutrition, or surgical intervention.

Pain: An awareness of acute or chronic discomfort, occurring in varying degrees of severity, and resulting from injury, disease, or emotional distress, as evidenced by biological or behavioural changes or both.

Project: An experiment or series of related experiments that form a discrete piece of work or research for a Scientific Purpose. An experiment may consist of one or more separate procedures.

Proposal: A written outline of a Project put forward for consideration by an IACUC.

Research Facility: The site, building or room in which a Project is undertaken with use of animals.

Scientific Purposes: The acquisition, development or demonstration of knowledge or techniques in any scientific discipline, including for the purposes of teaching, field trials, environmental studies, research, diagnosis, product testing, and the production of biological products. When special breeding requirements are integral to a research or teaching project such as in the creation of a new strain of genetically modified animal, then procedures applicable to breeding must be regarded as part of the project and should be included in proposal submitted to IACUC for approval.

Staff: All persons involved in the housing, feeding and general care of the animals or who otherwise assist Investigators.

Tranquillisers: Drugs which are used to reduce anxiety or produce sedation.

Wildlife: All species of animals from free living populations whether indigenous or otherwise. but does not include domestic dogs and cats, horses, cattle, sheep, goats, pigs, poultry and ducks.

CHAPTER 2: GENERAL PRINCIPLES FOR THE CARE AND USE OF ANIMALS FOR SCIENTIFIC PURPOSES

2.1 Matters to be considered

2.1.1 Projects involving animals must be designed and undertaken only after due consideration of their value to human or animal health and the advancement of knowledge on humans or animals weighed against the potential effects on the welfare of the animals.

2.1.2 Investigators and Staff must treat animals as sentient and must regard their proper care and use and the avoidance or minimisation of discomfort, distress, or pain as imperatives.

2.1.3 The approach known as the 3 Rs is to be considered at all times :

(a) Replacement of animals with other methods
(b) Reduction in the number of animals used
(c) Refinement of Projects and the techniques used to minimise impact on animals.

2.2 Replacement of animal experimentation with alternative methods

2.2.1 Alternative methods, such as mathematical models, computer simulation and *in vitro* biological systems, which replace or complement the use of animals must be considered before embarking on any Project involving use of animals and the alternative methods used wherever appropriate.

2.3 Reduction in the number of animals used

2.3.1 The number of animals used must be the minimum number required to obtain scientifically valid results.

2.3.2 The principle of reducing the number of animals used should not be implemented at the expense of greater suffering of individual animals.

2.3.3 Scientific activities involving the use of animals must not be repeated or duplicated unnecessarily.

2.4 Refinement of Projects and techniques used to minimise impact on animals

2.4.1 The following are to be considered in the selection of animals:

(a) Animals chosen must be of an appropriate species and quality for the scientific activities concerned taking into account their biological characteristics, including behaviour, genetic constitution and nutritional, microbiological and general health status.

(b) Wildlife should be taken from natural habitats only if animals bred in captivity are not available or are unsuitable for the specific Project or experiment concerned.

2.4.2 The following are to be done to minimise impact on animals:

(a) Projects must be designed to avoid pain or distress to animals. If this is not possible, pain or distress must be minimised.

(b) Unless the contrary is established, it must be assumed that procedures that will cause pain or distress in human beings will cause pain or distress in animals.

(c) Procedures with animals that may cause more than momentary or minimal pain or distress should be performed with appropriate sedation, analgesia, or anaesthesia in accordance with accepted veterinary practice.

(d) Surgical or other painful procedures should not be performed on unanaesthetised animals paralysed by chemical agents, unless the animals have undergone appropriate surgical procedure which eliminates sensory awareness. If such agents are used, continuous or frequent intermittent monitoring of paralysed animals is essential to ensure that the depth of anaesthesia is adequate to prevent pain or distress.

(e) At the end of, or, when appropriate, during the procedures, animals that would otherwise suffer severe or chronic pain or distress, that cannot be relieved promptly, must be killed humanely.

(f) An animal which develops signs of pain or distress of a kind and degree not predicted in the proposal for the Project, must have the pain or distress alleviated promptly. Alleviation of such pain or distress must take precedence over finishing the Project. If severe pain or distress cannot be alleviated promptly, the animal must be killed humanely.

(g) If it is not possible to use anaesthetics or analgesics in any Project (or part of a Project), the end-point of the Project must be as early as possible to avoid or minimise pain or distress to the animals.

(h) Death as an end-point must be avoided if at all possible. If Death as end-point must be used, the Investigator must ensure that the animal's distress or pain is minimised and use appropriate sedation, analgesia, or anaesthesia to relieve the animal's distress or pain.

(i) Projects involving the use of animals must be as brief as possible.

(j) The transportation, housing, feeding, handling of animals should meet species-specific needs; including behavioural and biological needs.

CHAPTER 3: ANIMAL HOUSING AND MANAGEMENT

The references for these matters are given in Appendixes I and II

3.1 General

3.1.1 Housing Facilities where animals are kept should be appropriately staffed, designed, constructed, equipped and maintained to achieve a high standard of animal care and should fulfil scientific requirements.

3.1.2 In general, housing and management practices should be designed to provide a high standard of animal care, and should follow acceptable standards of animal welfare for the particular species concerned. In determining the standard of animal care, the criterion should be animal well-being rather than the mere ability to survive under adverse conditions such as environmental extremes or high population densities.

3.1.3 The standard of animal care shall be maintained over weekends and holidays.

3.1.4 Emergency care procedures shall be available at all times.

3.2 Outdoor Housing Facilities

3.2.1 These should be compatible with the needs of the species, provide adequate shelter and water, protect the animals from predation, and comply with established farm, zoological garden or general outdoor housing practices.

3.3 Indoor Housing Facilities

3.3.1 Housing Facilities should be compatible with the needs of the species to be housed.

3.3.2 Housing Facilities should be designed and operated to facilitate control of environmental factors, exclude vermin, and limit contamination associated with the housing of animals, delivery of food, water, bedding, and the entry of people and other animals.

3.3.3 Housing Facilities should be maintained in good repair. Walls and floors should be constructed of durable materials with surfaces that can be cleaned and disinfected readily.

3.3.4 Housing Facilities should be kept clean and tidy, and operated to achieve maximum possible hygiene.

3.3.5 There should be a pest control programme to monitor and control vermin.

3.3.6 There should be adequate and appropriate storage areas for food, bedding and equipment.

3.3.7 The choice of detergents, disinfectants and pesticides should be made in consultation with Investigators in order not to contaminate the animal's environment Deodorants designed to mask animal odours should not be used in Housing Facilities as they may

expose animals to volatile compounds which can alter metabolic processes. In addition, deodorants must not be used as a substitute for good cage and equipment cleaning practices and good ventilation.

3.3.8 Cleaning practices should be monitored on a regular basis to ensure effective hygiene and sanitation. This can include visual inspection, monitoring water temperatures and microbiological testing of surfaces after cleaning.

3.3.9 There should be proper water supply and drainage, as appropriate.

3.3.10 There should be adequate contingency plans to cover such emergencies as flooding and fire, or the breakdown of lighting, heating, cooling or ventilation.

3.3.11 In the interest of disease prevention and general animal welfare, access to the Housing Facilities by unauthorised persons should be restricted.

3.4 Environmental factors

3.4.1 Animals should be provided with environmental conditions which suit their behavioural and biological needs unless contrary conditions are approved by the IACUC for the purposes of a Project.

3.4.2 Air exchange, temperature, humidity, noise, light intensity and light cycles should be maintained within limits compatible with the health and well-being of the animals.

3.4.3 Effective ventilation is essential for the comfort of animals and the control of temperature, humidity, and odours. Ventilation systems should distribute air uniformly and achieve adequate air exchange, both within cages and within a room.

3.4.4 Noxious and potentially harmful waste gases, particularly ammonia, should be kept to a level compatible with the health and comfort of the animals. The adequacy of the ventilation system, design, construction and placement of cages and containers, cage population densities, number of cages in a room, effectiveness of housekeeping and frequency of bedding changes will all influence the level of noxious gases.

3.4.5 Environmental factors potentially affect the welfare of the animals and may affect the results of experiments. The IACUCs and the Investigators should be informed in advance of planned changes to the environmental conditions by the Staff who manage the Housing Facilities.

3.5 Pens, cages and containers and the immediate environment of the animals

3.5.1 Pens, cages and containers should be designed, constructed and maintained to ensure the comfort and well-being of the animals, taking into account the following factors:

(a) species-specific behavioural requirements, including free movement and activity, sleep requirements, privacy, and contact with others of the same species;

(b) species-specific environmental requirements such as lighting, temperature, air quality, appropriate day/night cycles and protection from excessive noise and vibrations;

(c) provision of single housing for animals when it is appropriate for the species or if it is necessary for the purpose of the experiment, e.g. during recovery from surgery or collection of samples;

(d) the need to provide ready access to food and water;

(e) the need to clean the pen, cage or container;

(f) protection from spread of pests and disease;

(g) requirements of the experiments; and

(h) the need to observe the animals readily.

3.5.2 Pens, cages and containers should also :

(a) be constructed of durable, impervious materials;

(b) be kept clean;

(c) be maintained in good repair;

(d) be escape-proof;

(e) protect the animals from climatic extremes;

(f) not cause injury to the animals;

(g) be large enough to ensure the animals' well-being - animals should be able to stretch out when recumbent and to stand upright and stretch;

(h) be compatible with the behavioural needs of the species.

3.5.3 Wire floor cages should not be used for rodents unless essential to the Project and then only for brief periods. Animals should have a solid resting area when housed in wire floor cages.

3.5.4 The population density of animals within cages, pens or containers and the placement of these in rooms should be such that acceptable social and environmental conditions for the species can be maintained.

3.5.5 Where it is necessary to individually house social animals, the conditions should be managed so as to minimise the impact of social isolation. Such isolation should be kept to a minimum.

3.5.6 Bedding and litter should be provided as appropriate to the species and should be comfortable, absorbent, dust-free, non-palatable, non-toxic, able to be sterilised (if needed).

3.5.7 Pregnant animals must be provided with nesting materials where appropriate to the species.

3.5.8 Changes in housing conditions may affect the welfare of the animals and the results of experiments. The IACUC and the Investigators should be informed in advance of planned changes to the housing conditions by the Staff who manage the Housing Facilities.

3.6 Enrichment and environmental complexity

3.6.1 Most animals used in Projects are housed in environments dissimilar to their natural habitats. Wherever possible, such animals should be provided with stimuli that promote the expression of normal behaviour appropriate to the species.

3.6.2 Almost all species of animals used in Projects have well defined social structures and prefer to live in groups, although care must be taken to ensure that animals are socially compatible. Individual housing is stressful for such animals, and social isolation should be avoided whenever possible and limited to meet specific Project objectives. The effects of physical isolation should be minimised where possible by :

(a) the use of non-contact communication, whether visual, auditory or olfactory;

(b) the judicious use of mirrors which can be helpful;

(c) increasing the complexity of an environment with apparatus such as climbing equipment, objects and gnawing sticks as may be appropriate to the species concerned

3.7 Food and water

3.7.1 Animals should receive appropriate, uncontaminated and nutritionally adequate food according to accepted requirements for the species. The food should be in sufficient quantity and of appropriate composition to maintain normal growth of immature animals, normal weight of adult animals or provide for the requirements of pregnancy or lactation.

3.7.2 When animals are fed in groups, there should be sufficient trough space or feeding points to cater to the number and size of animals that eat together at one time so as to avoid undesirable competition for food, especially if feed is restricted.

3.7.3 Uneaten perishable food should be removed promptly unless contrary to the eating habits or needs of the species.

3.7.4 Any alteration to dietary regimes should be gradual.

3.7.5 Food should be stored such as to minimise deterioration of nutritional value and palatability and to prevent contamination by vermin.

3.7.6 Drinking water should be constantly and reliably available, and be clean, fresh and uncontaminated. Water sources should be designed to prevent faecal contamination.

3.7.7 Feed and water equipment should be constructed of materials that can be easily and effectively cleaned.

3.7.8 Variations to these requirements as part of a project (e.g. nutrition type trials) must receive IACUC approval.

3.8 Routine husbandry procedures

3.8.1 Husbandry procedures such as clipping coats and nails must be performed by competent personnel and in accordance with acceptable practices to ensure that welfare of the animals is not compromised.

3.9 Identification of animals

3.9.1 Animals should be identified by a method such as tattoo, neck-band, individual tag, electronic numbering device, physical mark, or by a label or marking attached to the cage, container, pen, yard or enclosure in which the animals are kept.

3.9.2 The method of identification should be reliable and done such as to cause the least stress or injury possible.

3.10 Disposal of animal carcasses and waste

3.10.1 Appropriate provision must be made for prompt and sanitary disposal of animal carcasses and waste material in accordance with current laws and any other guidelines or requirements of the National Biosafety Committee, the Ministry of Health and the National Environmental Agency.

3.11 Admission of new animals

3.11.1 Institutions should have quarantine facilities for new animals to be housed separately from existing animals in the Housing Facilities and Research Facilities.

3.11.2 New animals should be immediately inspected by a veterinarian or a person designated by a veterinarian and then placed in quarantine. The new animals should be evaluated in terms of:

(a) health. To assess the health status of rodents and for some other animals, the attending veterinarian could obtain a certificate from the supplier stating which pathogens had been tested for the last 6 months, and the results of the test.

(b) suitable condition for proposed Projects.

3.11.3 The quarantine period should be sufficient to allow the animals to acclimatise to the Housing Facility and the Staff; provided that for imported new animals, the duration of quarantine and site of quarantine will be as determined by the AVA.

3.11.4 New animals in quarantine are not to be used for any Project but they may be bred.

3.11.5 New animals that do not adapt satisfactorily to their new environment should not be kept.

3.12 Housing standards

3.12.1 Apart from the general principles set out above, detailed standards that must be met for housing, environmental conditions and other physical facilities are set out in **Appendix II.**

3.12.2 Where standards have not been set out, judicious extrapolation from existing knowledge and consultation with veterinarians, laboratory animal specialists and other relevant individuals should be done to arrive at housing and environmental setups that will be conducive to the well-being of the animals.

3.13 Non-human Primates

3.13.1 Non-human primates are recognised as having highly-developed mental and emotional capacities, more so than most other animals. In many ways, they are similar to humans and exhibit many similar external manifestations of emotions such as facial expressions, vocalisations, postures, gestures, and reactions. They have been known to react in ways similar to humans under comparable situations. Investigators, Attending Veterinarians and Staff should familiarise themselves with the references and information in **Appendices I and III**.

CHAPTER 4: PROCUREMENT AND TRANSPORT OF ANIMALS

4.1 Animals from a local source

4.1.1 All animals obtained locally must be from a licensed or otherwise legally permitted source.

4.1.2 For animals such as dogs, cats and farm animals such as pigs, sheep, goats and cattle, the animals should be properly identified and the supplier must have appropriate papers to prove legal ownership of the animals.

4.1.3 Under the Wild Animals & Birds Act, all wild animals are protected by law except those listed in the Schedule. A permit must be obtained from the AVA to kill, take or keep any wild animal.

4.2 Animals from an overseas source

4.2.1 No animal is to be imported without a permit from the AVA as required under the *Animals & Birds Act.*

4.2.2 The source of the animal must be recognised by the exporting country as a legitimate supplier of the particular species of animal.

4.2.3 The transport, import and use of genetically modified (GM) animals shall be in accordance with the 'Singapore Biosafety Guidelines for Research on GMOs' as set out by the Genetic Modification Advisory Committee.

4.3 Particular considerations in procurement of Endangered animals

4.3.1 No Endangered animal is to be imported without proper CITES certificates and export permits from the exporting country and import permits from the AVA, as required under the *Endangered Species (Import and Export) Act*.

4.3.2 An Endangered animal which is included in CITES* Appendix I must not be used in Projects unless the Project concerned will be of direct benefit to the conservation of that species or a closely related species and will not further endanger the species.

4.4 Particular considerations in procurement of wildlife

4.4.1 Animals are to be taken from natural habitats only if animals bred in captivity are not available or are unsuitable for the specific scientific activity.

4.4.2 Capture and restraint is stressful to animals. Strategies must be employed to minimise distress during capture and disruption of the colonies from which they are taken. There must be careful choice of suitable capture techniques, skilled persons must be used, and appropriate and safe enclosures or caging must be used. Animals must be monitored for

* Convention for the International Trade of Endangered Species of Wild Fauna and Flora (CITES)

signs of distress following capture and appropriate measures taken to minimise the stress. Any animal suffering from capture-induced trauma should receive treatment without delay.

4.5 Transport of animals

4.5.1 Transportation can cause distress due to confinement, movement, noise and changes in the environment and personnel. The extent of any distress will depend on the animals' health, temperament, species, age, sex, the number travelling together and their social relationships, the period without food or water, the duration, the mode of transport, environmental conditions, (particularly extremes of temperature) and the care given during the journey.

4.5.2 The animal must be provided with adequate shelter, food and water and shall have sufficient space to lie down, stand and stretch.

4.5.3 Animals must be transported under conditions which are appropriate to the species and which meet standards generally adopted in veterinary and laboratory animal medicine so as to ensure that the welfare of the animals is not unduly compromised. Potential sources of distress should be identified and steps taken to avoid or minimise their effects on the animals.

4.5.4 Containers must be escape and tamper proof and there should be adequate nesting or bedding material where appropriate.

4.5.5 Animals should be protected from sudden movements and extremes of climate.

4.5.6 Institutions must ensure that animals are received by a responsible person and transferred to appropriate accommodation without delay.

4.5.7 The transfer of GM animals between approved institutional containment facilities shall be in accordance with the guidelines set out by the Genetic Modification Advisory Committee.

4.5.8 Transport by air must be in accordance with IATA (International Air Transport Association) regulations or other applicable regulations. Please also refer to references in **Appendix I**.

CHAPTER 5: STAFF AT HOUSING AND RESEARCH FACILITIES

5.1 Staff

5.1.1 A very important factor ensuring high standards of animal care is sufficient number of well-trained, knowledgeable and committed Staff. Staff working with animals should be appropriately instructed in the care and maintenance of those animals. They should appreciate their role in facilitating the well-being of the animals and the successful outcome of Projects.

5.1.2 Staff should be instructed in how to recognise at an early stage, changes in animal behaviour, performance and appearance.

5.1.3 New Staff should be appropriately instructed in their duties immediately.

5.1.4 Institutions must encourage and promote formal training of all Staff in animal science or technology.

5.2 Staff-in-charge

5.2.1 The Staff with overall supervision over general animal care is the Staff-in-charge. The Staff-in-charge must have the appropriate veterinary or animal care qualifications or experience in handling of the species concerned.

5.2.2 The Staff-in-charge must :

(a) be responsible for managing the day-to-day care of the animals, supervising the work of other Staff, and acting as liaison between Investigators and Staff;

(b) contribute to the development and maintenance of the Institution's animal care policies and procedures;

(c) ensure that there is reliable monitoring of the well-being of all animals by other Staff, and be knowledgeable regarding signs of pain, distress and illness specific to each species housed (Note : After animals are allocated to a Project, the Investigator has primary responsibility for ensuring adequate monitoring of the animals' well-being);

(d) ensure that ill or injured animals are treated promptly, and any cause of death investigated if the animal dies unexpectedly;

(e) ensure that Staff are provided with appropriate protective clothing, maintain high standards of personal hygiene and do not eat, drink or smoke in animal areas;

(f) document procedures used in the management and care of animals. These procedures should take into account the requirements of the species and the experiments being conducted. The procedures include transport, quarantine and disposal of animals, routine husbandry, prevention, diagnosis and treatment of disease, monitoring of health status and genetic constitution, and physical

environmental factors. These procedures should be made known to all Staff involved in the care and use of the animals and should be reviewed regularly.

(g) maintain a regular schedule of pen, cage, equipment and facility sanitisation to ensure that potential pathogens are kept at minimum levels in the environment.

(h) ensure that adequate records are maintained of:

(i) the source, care, allocation, movement between locations, use and disposal of all animals, and development of any diseases;

(ii) the fertility, fecundity, morbidity and mortality in animal breeding groups, in order to monitor the management of the groups, and assist in the detection of the origin and spread of disease; and

(iii) the health status, genetic constitution and the physical environment of the animals, when definition of these is required.

(i) ensure that records maintained must be made available to Investigators and IACUCs.

(j) ensure that Investigators are informed of any changes to the conditions under which animals are held as these may affect their experiments.

5.3 Training for Staff

5.3.1 The minimum training requirements for Staff and other training that is recommended are set out in the Training Guidelines.

CHAPTER 6: VETERINARY CARE

6.1 Attending Veterinarian

6.1.1 Each Institution shall have an Attending Veterinarian for its Housing and Research Facility(ies). The Attending Veterinarian shall advise on the appropriate care and use of animals and provide adequate veterinary care.

6.1.2 The Attending Veterinarian must be engaged under formal arrangements. The Attending Veterinarian can however be engaged on a part-time or full-time basis.

6.1.3 The formal arrangements must include a written programme of veterinary care to be provided. In the case of a part-time Attending Veterinarian, the formal arrangements must also set out regularly scheduled visits to the Housing and Research Facility(ies) of the Institution.

6.1.4 If the Attending Veterinarian is on leave or will be otherwise unavailable to provide any general or emergency veterinary care, interim arrangements must be made to ensure that there is always ready access to veterinary care.

6.1.5 The Attending Veterinarian or other veterinarians engaged on a full-time, part-time or adhoc basis must be persons with qualifications in veterinary science who are licensed by the AVA.

6.2 Components of veterinary care

6.2.1 The Staff-in-charge and their Staff managing the animals, as well as the Investigators, must have ready access to veterinary care for the animals at all times.

6.2.2 Institutions must establish and maintain adequate veterinary care, overseen by the Attending Veterinarian, that include:

(a) the availability of appropriate facilities, personnel, equipment, and services to comply with the Guiding Principles.

(b) the use of appropriate methods to prevent and control diseases (e.g. vaccination and other prophylaxis, disease monitoring and surveillance, quarantine and isolation), diagnose, and treat diseases and injuries.

(c) the availability of 24 hour emergency, weekend and holiday care.

(d) daily observation (or more frequently as necessary) of all animals to assess their health and well-being: The daily observation of animals may be accomplished by someone other than the Attending Veterinarian provided that there is a mechanism of direct and frequent communication between the Attending Veterinarian and the Staff concerned so that timely and accurate information on problems of animal health, behaviour, and well-being is conveyed to the Attending Veterinarian.

(e) guidance to Investigators and other personnel involved in the care and use of animals regarding handling, immobilisation, anaesthesia, analgesia, tranquillisation, and euthanasia.

(f) adequate pre-procedural, surgical, and post-procedural care in accordance with current established veterinary medical and nursing procedures.

6.2.3 The IACUC may direct that certain Manipulations or other tasks related to the care and use of animals shall be performed only by the Attending Veterinarian or a veterinarian.

6.3 Training for Veterinarians

6.3.1 The minimum training requirements for veterinarians and other training that is recommended are set out in the Training Guidelines.

CHAPTER 7: RESPONSIBILITIES OF INSTITUTIONS AND THE INSTITUTIONAL ANIMAL CARE AND USE COMMITTEES (IACUC)

7.1 Overview

7.1.1 The ultimate responsibility for ensuring compliance with the Guiding Principles and legislative mandates for the care and use of animals for Scientific Purposes rests with the CEO.

7.1.2 The CEO must establish one or more IACUCs to evaluate the care and use of animals. IACUCs are to report to the CEO, who is then responsible for acting on the IACUC's recommendation.

7.2 Responsibilities

7.2.1 Each Institution shall, through the CEO, :

(a) establish one or more IACUCs

(b) ensure, through the IACUC, that the care and use of animals for Scientific Purposes comply with the Guiding Principles and relevant legislation.

(c) provide the IACUC with facilities, powers and resources to fulfil its terms of reference and responsibilities. Resources include the purchase of educational materials, access to training courses for IACUC members and access to administrative assistance.

(d) refer to the IACUC for comment on all matters which may affect animal welfare including the building and modification of Housing and Research Facilities;

(e) review annually the operation of the IACUC. This review includes an assessment of the annual report from the IACUC and a meeting with IACUC Chairman. This annual review of the IACUC is to help ensure that the IACUC is adjusting its operations in light of their experiences and circumstances, and according to continuing developments in care and use of animals for scientific purposes.

(f) respond effectively to recommendations from the IACUC to ensure that the facilities for the housing, care and use of animals are appropriate for the maintenance of the health and well-being of the animals and that the disposal of the animals are appropriate.

(g) respond promptly and effectively to recommendations from the IACUC to ensure that all care of the animals and use of animals for Scientific Purposes remains in accord with the Guiding Principles and relevant legislation.

(h) provide all relevant Staff with details of the Institution's policy on the care and use of animals, and the relevant legal requirements.

(i) establish grievance procedures for IACUC members and Investigators who are dissatisfied with IACUC procedures or decisions.

(j) ensure that the IACUC develops guidelines for animal care and use within the Institution and that these are implemented, including those which ensure that emergencies are detected promptly and dealt with effectively.

(k) ensure that there are adequate numbers of Staff to care for the animals and that they are appropriately trained and instructed.

(l) ensure that appropriate veterinary care is available for the animals and that there is access to diagnostic services.

(m) ensure adequate record keeping and annual reporting to AVA.

(n) ensure that Investigators and personnel have appropriate qualifications or experience for conducting procedures on animals. Adequate arrangement shall be provided for in-service training, including the proper and humane care and use of the animals.

(o) ensure that appropriate corrective action is taken after the withdrawal of approval for a Project by the IACUC and, on request, to report on the corrective action taken with a full explanation to AVA and any funding agency of the Institution.

7.3 Membership of IACUC

7.3.1 An IACUC shall be comprised of at least 5 persons, including 4 persons, each of whom is appointed to represent one and only one of each of the following 4 categories:

(a) a veterinarian with training or experience in laboratory animal science and medicine and who has experience in routine care of 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 appropriate experience in the use of animals for scientific purposes.

(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 and is not a user of animals for any 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 non-scientific area (e.g. ethicist, lawyer, clergy).

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

7.3.3 The CEO is not to be appointed a member of the IACUC.

7.3.4 The Chairman of the IACUC shall be appointed by the CEO from amongst the members of IACUC. The Chairman should either hold a senior position in the Institution or if an

external appointee, be given a commitment by the Institution to provide the necessary support and authority to carry out his/her role.

7.4 Functions of the IACUC

7.4.1 IACUCs are to:

(a) review, at least once every 6 months, the Institution's programmes on the care and use of animals for Scientific Purposes using the Guiding Principles as a basis for evaluation. The review must include the procurement, transportation, production, housing, care, use and disposal of animals.

(b) inspect the Housing and Research Facility(ies), at least once annually, using the Guiding Principles as a basis for evaluation. The inspection must also cover satellite facilities where animals are housed for more than 24 hours.

(c) prepare reports of its evaluation and to submit the same directly to the CEO. The reports shall be maintained by the Institution and made available to AVA and any funding agency of the Institution upon request. The reports shall be reviewed and signed by a majority of the IACUC members and must include the following:

(i) minority views.

(ii) a description of the nature and extent of compliance with the Guiding Principles, identify specifically any departures from the Guiding Principles, and state reasons for each departure.

(iii) distinguish significant deficiencies from minor deficiencies. A significant deficiency is one that is or may be a threat to the health and safety of the animals. The reports shall contain a reasonable and specific plan and schedule for correcting each deficiency.

(d) determine the best means of conducting an evaluation of the care and use of animals, provided no member wishing to participate in any evaluation is excluded.

(e) invite adhoc consultants to assist in conducting the evaluation, but IACUC remains responsible for the evaluation and report.

(f) review and approve, subject to modification, or reject proposals for Projects involving the use of animals for Scientific Purposes. This includes proposals to significantly change the care and use of animals involved in on-going Projects. IACUC should approve only those proposals for which animals are essential and which conform to the Guiding Principles, taking into consideration ethical and welfare aspects as well as scientific or educational value.

(g) formally withdraw approval for any on-going Project or to suspend it if the IACUC determines that the Project is not being conducted in accordance with the description provided by the Investigator and approved by the IACUC.

(h) make recommendations to the CEO regarding any aspects of the programmes, facilities, or personnel training at the Housing and Research Facility(ies).

(i) review and investigate concerns involving the care and use of animals including public complaints or reports of non-compliance from Staff or Investigators.

(j) authorise the treatment or humane killing of any animal.

(k) maintain a register of Approved Projects.

(l) approved Projects of long duration and the long-term continuing use of individual animals shall be reviewed at least annually by the IACUC.

(m) perform all other duties required by the Guiding Principles.

7.5 IACUC considerations in reviewing Projects involving animals

7.5.1 In general, written proposals submitted to the IACUC on Proposed Projects or a significant change in an on-going Project involving animals must contain sufficient information to satisfy the IACUC that the proposed use of animals is justified and complies with the principles of Replacement, Reduction and Refinement.

7.5.2 The IACUC shall consider whether proposed Projects or significant changes in ongoing Projects meet the following requirements before granting approval for proposed Projects or significant changes to on-going Projects :

(a) Procedures will avoid or minimise discomfort, distress, and pain to the animals. The proposal must give a description of procedures designed to assure that discomfort, distress or pain to animals will be limited to that which is unavoidable for the conduct of scientifically valuable research.

(b) The Investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources used to determine that alternatives were not available.

(c) The Investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments.

(d) The investigator has provided a description and justification for the end-points of the experiments.

(e) Procedures that may cause more than momentary or slight pain or distress to the animals will:

(i) be performed with appropriate sedatives, analgesics or anaesthetics, unless withholding such agents is justified for scientific reasons justified in writing, by the Investigator and will continue for only the necessary period of time;

(ii) involve, in their planning, consultation with the Attending Veterinarian;

(iii) not include the use of paralytics without anaesthesia;

(f) Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be humanely killed as soon as possible.

(g) Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures. Trainees must be under appropriate supervision.

(h) Projects that involve surgery include appropriate provision for pre-operative and post-operative care of the animals in accordance with established veterinary medical and nursing practices, including all survival surgery will be performed using aseptic procedures and aseptic techniques.

(i) No animal will be used in more than one experiment unless justified for scientific reasons by the Investigator, in writing, and that the repeated use of animals is in accordance with 8.4.4.

(j) Specify the species and the approximate number of animals to be used;

(k) The rationale for involving animals and the appropriateness of the species and numbers of animals to be used.

(l) A complete description of the proposed use of the animals.

(m) A description of any euthanasia method to be used.

7.6 IACUC Approval Process

7.6.1 All proposals must be approved by IACUC at a quorate meeting. A quorum consists of more than 50% of the members of the IACUC and must comprise members from Category 7.3.1 (c) and/or (d) member to ensure that IACUC remains reasonably balanced in membership representation. Decisions made by the quorum shall be by a majority vote.

7.6.2 No member may participate in the IACUC review or approval of a proposal in which that member has a conflict of interest such as where the member is involved in a competing Project.

7.6.3 The IACUC may invite consultants to assist in the review of complex issues arising out of its review of proposals. Consultants may not approve or withhold approval of a proposal, and may not vote with the IACUC.

7.6.4 The IACUC shall notify Investigators and the Institution in writing of its decision to approve or withhold approval of the proposed Project involving the use of animals, or of modifications required to secure IACUC approval. If the IACUC decides to withhold approval of an activity, it shall include in its written notification a statement of the reasons for its decision and give the Investigator an opportunity to respond in person or in writing.

The IACUC may reconsider its decision in light of further information provided by the Investigator.

7.7 IACUC Records

7.7.1 The CEO shall maintain the following IACUC records:

(a) Minutes of IACUC meetings, including records of attendance, activities of the Committee, and Committee deliberations.

(b) Records of proposals involving animals, including proposals for significant changes in on-going activities involving animals, and whether IACUC approval was given or withheld.

(c) Records of all IACUC reports and recommendations (including minority views).

7.7.2 All records and reports shall be maintained for at least three years. Records that relate directly to a Project, including proposals for significant changes in ongoing activities, reviewed and approved by the IACUC shall be maintained for the duration of the Project and for an additional three years after completion of the Project.

7.7.3 All records shall be available for inspection and copying by AVA and funding agency representatives.

7.8 Annual report by the CEO

7.8.1 The CEO shall prepare and sign an annual report covering the period 1 January to 31 December of each year. The information in the annual report shall include 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 were maintained or used at the Housing and Research Facility(ies).

(ii) Assure that each Investigator has considered alternatives to procedures which cause pain or distress to animals.

(iii) Assure that the Guiding Principles are being complied with by Investigators and Staff, and that it has required that exceptions to the Guiding Principles be specified and explained by the Investigators 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 the IACUC.

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

(iii) State the location of all facilities where animals are housed, used or held for scientific activities.

(iv) State the common names and the numbers of animals used for scientific activities at each facility 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 activities at each facility 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 activities at each facility 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 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 activities at each facility but not yet used for such purposes.

(viii) Indicate the dates of reviews and inspections by IACUC.

(ix) State the significant deficiencies identified in the 6-monthly programme reviews and annual facility 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.

7.9 Training for IACUC Members

7.9.1 The minimum training requirements for IACUC members and other training that is recommended are set out in the Training Guidelines.

7.10 Detailed Guidelines for IACUCs

7.10.1 Further and detailed guidelines on the operation of the IACUC and the standards that the IACUC should set are outlined in the Guidelines for Institutional Animal Care and Use Committee.

CHAPTER 8: RESPONSIBILITIES OF INVESTIGATORS

8.1 General

8.1.1 Investigators who use animals for Scientific Purposes have a moral and professional obligation to treat the animals humanely and consider their welfare when planning Projects and conducting experiments.

8.1.2 Investigators have direct and primary responsibility for all matters related to the welfare of the animals under their control, including the general husbandry and housing of those animals as well as the specific experimental Manipulations. They must act in accordance with the Guiding Principles. The responsibility of Investigators extends over all facets of the care and use of animals in Projects approved by the IACUC, beginning from the time the animal is allocated to the Approved Project to the end and disposal of the animal. Investigators are responsible for the standard of animal care and use by all other persons involved in the Approved Project. They should ensure that the extent of supervision is compatible with the level of competence of each person and the responsibilities they are given.

8.1.3 It is recognised however that in many Institutions, the responsibility of managing routine animal husbandry is delegated to Staff on a daily basis. Protocols must be in place for the Staff-in-charge to effectively communicate with the Investigator regarding animal welfare and research concerns.

8.1.4 Investigators have a legal and ethical responsibility to ensure that animals being studied are Manipulated using medical and surgical techniques, which are consistent with the principles of good practice and scientific knowledge in laboratory animal veterinary medicine. Investigators should consult with veterinarians whenever adverse effects occur, in order that standard veterinary care and treatment regimes are promptly implemented. This responsibility parallels the public's duty of care to seek veterinary management of any sick animals in their charge.

8.2 IACUC approval

8.2.1 Before any Project begins, Investigators must submit a proposal to the IACUC to demonstrate that the Project will comply with the Guiding Principles. Moreover, the Investigators must satisfy the IACUC of their competence to conduct the techniques described in the experiment.

8.2.2 Investigators must not begin experiments before written IACUC approval is obtained and must adhere to any requirements of the IACUC.

8.2.3 Investigators may obtain and hold, for acclimatisation or adaptation, species which are not normally readily available, prior to formal IACUC approval but only after providing the Chairman/IACUC in writing, a document which contains the intention to obtain and hold these species, with a justification and a timetable, and provided that their use for Scientific Purposes does not commence until approval is given.

8.2.4 Investigators must inform the IACUC in writing when each Project is completed or discontinued; and the outcome of each Project.

8.3 Planning projects

8.3.1 Choice of Animal

(a) Investigators must ensure that the choice of species is appropriate for the purpose of the Project.

(b) Requirements for known genetic constitution, freedom from specific diseases, documented health, nutritional and environmental histories, and other relevant factors should be taken into account.

(c) When the definition of the biological status of animals is necessary, Investigators must ensure that the supplier can provide adequate proof that all requirements can be met.

(d) Where relevant, species and individual animals should be chosen on the basis that the proposed experiments will result in the least pain and distress. In making this decision, all aspects of the biological nature of the animals, including their behavioural characteristics and cognitive development, should be taken into account.

8.3.2 Monitoring

(a) Investigators should ensure that all intensively managed animals are observed daily (or more frequently if circumstances require it) to assess their health and welfare.

(b) Investigators should ensure that satisfactory arrangements are made for contacting them and other responsible persons in the event of emergencies.

8.3.3 Record-keeping

(a) Investigators should ensure that their experimental research records include details of animal husbandry routine, environmental conditions, and other non-experimental variables which may potentially affect the study. Records must meet the statistical reporting requirements.

8.3.4 Consultation

(a) Investigators should consult other experienced scientists, veterinarians, or laboratory animal, livestock or wildlife specialists when necessary.

(b) The Attending Veterinarian must be consulted on the following in the planning of any practice or procedure which can cause pain to animals:

(i) the use of tranquillisers, analgesics, and anaesthetics

(ii) pre-surgical, surgical and post-surgical care by laboratory workers, in accordance with established veterinary medical and nursing procedures

(iii) the use of paralytics without anaesthesia

(iv) the withholding of tranquillisers, anaesthesia, analgesia, or euthanasia when scientifically necessary.

(c) The Attending Veterinarian must be consulted on the use of appropriate euthanasia.

8.3.5 Checklist

(a) When planning is completed, the Investigator should re-check the protocol to ensure that the following points have been adequately addressed:

(i) Is the Project justified ethically and scientifically?

(ii) Can the aims be achieved without using animals?

(iii) Are there any additional experiments that could be included which would reduce the number of animals used?

(iv) Are suitable holding facilities and competent Staff available?

(v) Have all Staff been informed of the planned experimental and other procedures?

(vi) Has the most appropriate species of animal been selected?

(vii) Is the biological status (genetic, nutritional, microbiological, general health) of the animals appropriate?

(viii) Is the environmental condition (including caging or pen type, noise, photoperiod, temperature, humidity, ventilation, density of housing and social structures) appropriate?

(ix) Are the experiments designed so that statistically valid results can be obtained or the educational objectives achieved using the minimum necessary number of animals?

(x) If the scientific activity could cause the animals any pain or distress, what will be done to minimise or avoid this?

(xi) Do all key project personnel have the skills and experience to perform these procedures?

(xii) Does this project involve students and are they appropriately supervised?

(xiii) What arrangements will be made to monitor the animals adequately, in terms of their general health and welfare and response to manipulation?

(xiv) If any of the experiments have been performed previously, why should they be repeated?

(xv) If any animals are to be used repeatedly, what will be done to minimise the cumulative effects of such use?

(xvi) Are there any permits that must be obtained for the importation, capture, use, destruction or release of the animals?

8.4 Conduct of experiments

8.4.1 Limiting pain and distress

(a) Pain and distress cannot always be adequately evaluated in animals and investigators must therefore assume that animals experience pain in a manner similar to humans. Decisions regarding their welfare in experiments must be based on this assumption unless there is evidence to the contrary.

(b) The Investigator should anticipate any potentially adverse effects of a manipulation and take all possible steps to avoid or minimise pain and distress. These steps should include:

(i) choosing the most appropriate and humane method for the conduct of the experiment;

(ii) ensuring the technical skills and competence of all persons involved in animal care and use are appropriate;

(iii) use of pre-emptive analgesia when pain is anticipated;

(iv) ensuring that animals are adequately monitored for evidence of pain and distress;

(v) developing a plan to manage any adverse effects of a manipulation;

(vi) acting promptly to alleviate pain and distress;

(vii) using anaesthetic, analgesic and tranquillising agents appropriate to the species and the experimental purposes;

(viii) developing study end-points that minimise pain and distress;

(ix) conducting projects over the shortest time practicable; and

(x) using appropriate methods of euthanasia.

(c) The use of local or general anaesthetics, analgesics or tranquillisers must be appropriate to the species, and should meet the criteria generally accepted in current medical, veterinary or laboratory animal practice.

(d) Experiments which are liable to cause pain of a kind and to a degree for which anaesthesia would normally be used in medical or veterinary practice must be carried out under anaesthesia.

(e) Distress can sometimes be avoided or minimised by non-pharmacological means. For example, before an experiment begins, animals should be appropriately conditioned to the experimental environment and procedures and familiarised with the animal care Staff.

(f) The monitoring of animals during and after experiments must at all times be adequate to prevent the occurrence of pain or distress, or allow prompt alleviation. Appropriate nursing procedures to minimise pain and distress and promote the well-being of the animals should be provided.

(g) If animals develop signs of severe pain or distress despite the precautions outlined above, they should have the pain or distress alleviated promptly or be killed humanely and without delay if the pain cannot be alleviated. Veterinarians involved in the animal care programme should be informed immediately. Alleviation of such pain or distress takes precedence over continuing or finishing the experiment. If in doubt, Investigators must always seek a professional veterinary opinion before continuing an experiment.

(h) Unexpected deaths occurring during a Project must be properly investigated by a veterinarian or other qualified person who will determine the cause and initiate remedial action. If the deaths are due to manipulations, these must cease. The IACUC must be notified of all unexpected deaths and the Project protocol resubmitted with appropriate modification

8.4.2 Animal welfare monitoring of pain or distress

(a) Investigators should be familiar with the normal behaviour patterns of the animal species chosen, be knowledgeable of signs of pain or distress specific to that species, and must monitor their animals for these signs.

(b) Deviations from normal behaviour patterns are often the first indications that animals are experiencing pain or distress. Any changes in patterns of sleeping, feeding, drinking, grooming, exploratory behaviour, performance in learning or discriminatory tasks, reproduction or social behaviour should be noted, assessed and acted on if appropriate.

(c) Animals must be monitored appropriately for clinical signs of acute pain or distress. These may include one or more of the following:

(i) aggressive and/or abnormal behaviour (some species may become unduly submissive);

(ii) abnormal stance or movements;

(iii) abnormal sounds;

(iv) altered cardiovascular and/or respiratory function;

(v) abnormal appetite;

(vi) rapid decline in body weight;

(vii) altered body temperature;

(viii) vomiting and

(ix) abnormal defecation or urination.

(d) Indicators of sustained pain or distress may include:

(i) loss of body weight or failure to gain weight;

(ii) failure to display normal grooming behaviour;

(iii) failure to thrive;

(iv) impaired reproductive ability; and

(v) reduced resistance to disease.

(e) Animal welfare monitoring score sheets can be useful for documenting the observations and collection of data listed above. General observations for signs of pain or suffering in the animal should be conducted daily or more often as needed during the immediate post-operative period for surgical manipulations. Sample monitoring sheets are set out at **Appendix V**.

8.4.3 Study end-points

(a) The Investigator should develop humane study end-points when preparing a Project application.

(b) Death as an end-point is generally ethically unacceptable and should be fully justified. When Death as an end-point cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible.

(c) Best practice indicates that end-points earlier than the moribund condition should always be used. For the purpose of the Guiding Principles, animals can generally be considered to be in a moribund state when:

(i) they have lost more than 20% of their pre-study body weight; or

(ii) they have lost more than 10% in 24hrs; or

(iii) a tumour grows to more than 10% of the animal's weight; or

(iv) abscesses develop; or

(v) body temperature falls below a pre-set level (as determined by pilot studies which indicate that the level set is predictive of death); or

(vi) animals self-mutilate; or

(vii) animals become obviously incapacitated and are not able to eat, rest or perform normal activity.

(d) All animals found in a moribund state must be euthanised unless there is specific justification to do otherwise.

8.4.4 Repeated use of animals in experiments

(a) Individual animals should not be used in more than one experiment, either in the same or different Projects, without the express approval of the IACUC. However, it is noted that appropriate re-use of animals may reduce the total number of animals used in a Project, result in better design of experiments, and reduce stress or avoid pain to other animals.

(b) When approving experiments involving the re-use of animals, the IACUC should be satisfied of the following:

(i) none of the procedures cause the animals pain or distress; or

(ii) the second and subsequent studies produce little or no pain or biological stress to the animals (e.g. modifying diet, taking a succession of blood samples, repeated non-invasive recording procedures).

(c) Animals that are used in more than one experiment must be permitted to recover fully from the first experiment before the subsequent experiment is performed.

8.4.5 Duration of experiments

(a) Experimental duration should be limited to that just sufficient to achieve the objective of the experiment.

(b) Experiments, particularly those which involve any pain or distress, should be as brief as practicable. IACUC approval must be sought for the continued long-term use of individual animals. The decision to continue must be based on the well-being of the animal and the absence of aversion to the experimental situation.

8.4.6 Handling and restraining animals

(a) Animals should be handled by competent individuals trained in methods that cause minimal distress and injury.

(b) The use of restraint devices is sometimes essential for the welfare of the animal and safety of the handler. Restraint devices should be used to the minimum extent, for the minimum period required to accomplish the purpose of the experiment, and be appropriate for the animal.

(c) Tranquilisers or anaesthetics may aid restraint but may prolong recovery from the procedure. When these agents have been used, recovery of the animals should be monitored.

(d) Periods of prolonged restraint should be avoided. Where animals are in prolonged restraint, consideration should be given to their biological needs, including their behavioural requirements and the need for appropriate exercise. They should be monitored regularly by a veterinarian or other qualified person not participating in the Project. If any ill effects are apparent, the animal should be removed from the restraint or the method modified.

8.4.7 Completion of Projects

(a) Upon completion of the Project, animals should be returned promptly to either normal husbandry conditions or, if appropriate and permitted, to their natural habitat, or be euthanised (if appropriate under the Guiding Principles).

(b) Where practicable, Investigators should share with other Investigators tissue from animals being euthanised.

8.4.8 Euthanasia

(a) When it is necessary to kill an animal, humane procedures must be used. These procedures must avoid distress, be reliable and produce rapid loss of consciousness without pain until death occurs.

(b) The appropriate means must be readily at hand.

(c) The procedures should be performed only by persons who have demonstrated to a veterinarian or designated by a veterinarian that they are competent in the methods to be used.

(d) Animals should be killed in a quiet, clean environment, and preferably away from other animals.

(e) There must be no disposal of the carcass until death is established.

(f) Dependent neonates of animals being killed must also be killed or provision made for their care.

(g) When fertilised eggs are used, the method of disposal must ensure the death of the embryo.

8.4.9 Post-Mortem Examination

(a) A post-mortem examination should be performed when animals die unexpectedly. Investigators should consider the value of a post-mortem examination for such animals. Post-mortem evaluation may identify one or more non-experimental variables which could compromise the remaining research subjects.

(b) Records of post-mortem examination should be kept. Records of digital images of post-mortem findings are encouraged.

8.4.10 Pre-operative planning

(a) Surgical success can be improved by careful attention to the following.

(i) The use of healthy, disease-free animals will ensure more reliable research data. Investigators should consult the Attending Veterinarian or other qualified person to assist in obtaining such animals.

(ii) Pre-operative physical examination can often identify potential problems, such as increased anaesthetic risk, which may compromise the surgical procedure. Sick animals should be rejected.

(iii) Pre-surgical fasting should be considered where appropriate for the species to minimise complications of anaesthetic administration.

(iv) Pre-operative antibiotic administration should be considered. This can ensure maximal blood levels of drug during the surgical procedure. Additional post-operative antibiotic treatment may be required.

(v) Surgical time can frequently be reduced by practice on cadavers. This enables Investigators to familiarise themselves with anatomical landmarks and streamline the experimental surgical procedures, thereby reducing the quantity of anaesthetic required. This will reduce the duration of post-operative recovery and promote animal well-being.

(vi) Pre-operative analgesia should be routinely used. Such pre-emptive use of analgesics can reduce the quantities of general anaesthetic agents required and prevent the induction of sensitisation of the central nervous system.

(vii) Post-operative pain is best managed by pre-operative analgesic administration, followed by additional analgesics after surgery.

8.4.11 Surgery

(a) Surgical procedures should be carried out under appropriate local or general anaesthesia. There should be adequate monitoring of the depth of anaesthesia and effects such as hypothermia, and cardiovascular and respiratory depression.

(b) The choice and administration of anaesthetic, analgesic and tranquilising agents should be suitable for the species and appropriate for the purpose of the experiment. The use of such agents should conform to current medical, veterinary or laboratory animal practice.

(c) Investigators should consider the value of a limited anaesthetic trial to familiarise themselves with new anaesthetic or analgesic drug combinations. Species and strain variation in drug metabolism can result in unexpected morbidity and mortality when dosages are extrapolated from published data. A limited trial, when combined with a non-survival surgical practice session, can provide invaluable information and promote surgical success and animal well-being in subsequent study animals.

(d) Anaesthesia and surgery should be performed by competent staff with appropriate training and experience. All tissues should be handled with care and particular attention should be given to haemostasis. Instruction in surgical or anaesthetic techniques should be under the direct and constant supervision of such persons.

(e) When more than one surgical procedure is to be performed the animal must have recovered to good general health before the next procedure. Every effort should be made to reduce the total number of procedures and the IACUC should be informed specifically of the need for more than one procedure.

(f) When the animal is not to recover from the surgery, it must be unconscious for the whole procedure, either by continuing the administration of the general anaesthetic or by inducing brain death.

(g) When the animal is to recover from the anaesthetic, surgical procedures must conform to accepted standards in veterinary and laboratory animal practice. Aseptic technique should be used for all survival surgery. Aseptic technique includes aseptic preparation of the surgical field, use of sterilised instruments, wearing of sterile surgical gloves, gowns, caps, and face masks. The use of post-operative antibiotics should not be a substitute for correct aseptic technique.

8.4.12 Post-operative care

(a) Consideration of and attention to pain relief is paramount in post-operative care.

(b) Investigators should ensure that adequate monitoring, treatment and care of post-operative animals is provided. They should ensure that they, or other experienced personnel, are fully informed of the animals' condition. The duties of all Staff must be clearly defined and ways of dealing with emergencies established.

(c) The comfort of animals must be promoted throughout the post-operative period. Attention should be given to warmth, hygiene, fluid and food intake, and control of infection. The use of analgesics and tranquilisers may be needed to minimise post-operative pain or distress. Care should be taken that animals recovering from anaesthesia are housed to prevent injury and that conditions are such that they are not disturbed, attacked or killed by other animals in the same enclosure.

(d) Regular observation of surgical wounds is essential to check the progress of healing. Any problems must be attended to promptly.

(e) Any post-operative animal observed to be in a state of severe pain or distress which cannot be alleviated quickly must be killed humanely without delay and a veterinarian informed immediately.

8.4.13 Implanted devices

(a) Investigators should be aware of the need for strict attention to aseptic technique when foreign bodies are surgically implanted. Contamination of prosthetic devices frequently requires their removal after antibiotic therapy has failed.

(b) Skilled and specialised attention is required in the care of animals following an operation in which monitoring or sampling devices have been implanted, or a fistula created. Regular observation is essential to determine signs of distress, pain or infection, which must be treated promptly.

8.4.14 Neuromuscular paralysis

(a) Neuromuscular blocking agents must not be used without adequate general anaesthesia or an appropriate surgical procedure which eliminates sensory awareness.

(b) Immobilisation of an animal solely with a neuromuscular blocking agent is not acceptable. When these agents are used with an anaesthetic, special care must be taken to ensure the maintenance of an adequate plane of anaesthesia. Since criteria such as character of respiration and corneal and flexor withdrawal reflexes cannot be used, continuous or frequent intermittent monitoring of physiological variables such as heart rate, blood pressure, oxygen saturation, pupil size and electroencephalogram is necessary, together with the effects on these of mild sensory stimuli. Care is required to ensure that drugs used in the experiments do not interfere with this monitoring.

8.4.15 Electro-immobilisation

(a) Electro-immobilisation must not be used as an alternative to analgesia or anaesthesia.

8.4.16 Animal models of disease

(a) The scientific validity of an animal model of human diseases rests in part on how closely it resembles a particular human disease. An animal should be used only if the disease in the animal can serve as a reliable model for investigation into the human disease.

(b) It must be assumed, unless there is contrary evidence, that the attendant pain and distress of the human disease will also occur in the animal. The Investigator must therefore take special care to ensure that any pain or distress is minimised and the IACUC is informed of the potential effects of the disease on the animals.

(c) Investigators must not allow the experiments to proceed to the painful or distressful or lingering death of animals unless no other experimental end-point is feasible and the goals of the experiments are the prevention, alleviation, treatment or care of a life-threatening disease or situation in human beings or animals.

(d) Investigators must avoid using Death as an end-point whenever possible. When Death as an end-point cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible.

8.4.17 Modifying animal behaviour

(a) Procedures used to modify an animal's behaviour or to induce it to perform specific tasks depend on motivating the animal. The preferred inducement is positive reinforcement.

(b) If the inducement by necessity has to be some form of biological stress, it should be as mild as possible. Severe water, food, social or sensory deprivation should not be used. Painful or noxious stimuli should be limited to those which do not distress human beings and must be used for the minimum time necessary.

(c) Behaviour can usually be modified using procedures that involve no more of a stressor than that normally experienced by the species.

(d) When noxious stimuli are used to modify behaviour, the animal must be able to escape from the stimuli.

8.4.18 Toxicological experiments

(a) Investigation into the safety of agents intended for use in human beings, animals, the household or the environment, or investigation of naturally occurring toxins, should be performed by persons with appropriate training. If suitable non-animal tests are available, they must be used. In particular, *in vitro* methods should be used as an initial screening test wherever possible.

(b) The end-point of such experiments must be as early as is compatible with reliable assessment of toxicity, and must minimise the extent of any pain and distress.

(c) When Death as an end-point cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible.

8.4.19 Experiments involving hazards to humans or animals

(a) Hazards may arise from sources that include:
(i) viruses;
(ii) bacteria;
(iii) fungi;
(iv) parasites;
(v) radiation;
(vi) radioactivity;
(vii) corrosive substances;
(viii) toxins;
(ix) allergens;
(x) carcinogens;
(xi) recombinant DNA;
(xii) anaesthetic gases; and
(xiii) physical injuries.

(b) Experiments involving hazards to humans or animals shall be in accordance to the guidelines and requirements of the National Biosafety Committee, Ministry of Health and the Ministry of Manpower.

(c) Protocols submitted to the IACUC should include a description of any intended use of hazardous compounds or organisms. They should describe specific safety measures and disposal protocols used to prevent contamination of caging, other animals, research personnel and students.

(d) Animals being administered infectious organisms should be isolated as appropriate, taking into account risks to other animals and to people.

(e) Investigators must not allow the experiments to proceed to the painful or distressful or lingering death of animals unless no other experimental end-point is feasible and the goals of the experiments are the prevention, alleviation, treatment or care of a life-threatening disease or situation in human beings or animals. When Death as an end-point cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible. The Investigator must also ensure that the animal's suffering or pain is minimised and use appropriate sedation, analgesia, or anaesthesia to relieve the animal's suffering or pain.

(f) Precautions, security and emergency plans to contain hazardous agents should be appropriate to a "worst-case" situation.

8.4.20 Experimental manipulation of animals' genetic material

(a) Such experiments shall be in accordance with the 'Singapore Biosafety Guidelines for Research on GMOs as set out by the Genetic Modification Advisory Committee.

(b) All proposals to manipulate the genetic material of animals, their germ cells or embryos must be submitted to the IACUC for approval.

(c) The manipulation of the genetic material of animals has the potential to affect the welfare of the animals and their offspring adversely. Investigators must inform the IACUC of the known potential adverse effects to the well-being of the animals.

(d) The clinical status of animals in which the genetic material has been manipulated experimentally must be monitored for unusual or unexpected adverse effects, and such effects reported to the IACUC.

(e) There are examples of strains of animals in which pathological conditions can be generated by normal breeding procedures. Expert care should be available to look after the welfare of such animals.

8.4.21 Experimental induction of neoplasia

(a) The site for induction of tumours must be chosen carefully. Subcutaneous, intradermal and flank sites should be chosen wherever possible. Prior to the use of footpad, brain and eye sites, specific justification as to the lack of any other alternative should be made to the IACUC.

(b) Investigators should monitor their animals regularly for signs of pain or distress, especially sudden changes in body weight.

(c) Animals with experimentally induced tumours should be euthanised whenever possible before predictable death occurs, cachexia becomes advanced, or the tumour becomes large enough to cause ulceration or severe limiting of normal behaviour.

(d) With ascitic tumours, including hybridomas, Investigators should ensure that the volume of ascitic fluid does not cause gross abdominal distension, and the volumes of solid tumours and cachexia do not become distressful to the animals.

(e) In tumour therapy experiments, the end-points chosen should be as early as possible and be compatible with reliable assessment of the therapy. Weight changes should be monitored closely. Death from the tumour should not be chosen as an experimental end-point unless no other experimental end-point is feasible and the goals of the study are the alleviation, treatment or cure of life-threatening disease situations in human beings or animals. When death as an endpoint cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible.

8.4.22 Lesions of the central nervous system

(a) Anatomical or chemical lesions of the central nervous system have been widely used to study its structure and function in health and disease. These experiments demand special consideration when the lesion produces loss or impairment of limb or trunk movements, loss of sensibility to touch, temperature or pain, impairment of the animal's awareness of its surroundings or impairment of appetite or injury mechanisms.

(b) Special animal care, caging and other facilities may be needed and the condition of the animals must be closely monitored.

8.4.23 Withholding food or water

(a) Experiments involving the withholding or severe restriction of food or water should produce no continuing detrimental effect on the animals. In these experiments, the fluid balance and/or body weight must be monitored, recorded and maintained within the limits approved by the IACUC.

8.4.24 Foetal experimentation

(a) When foetal experimentation or surgery compromises the ability of the neonate to survive and not experience pain or distress, it must be euthanised before or immediately following birth unless such pain or distress can be relieved.

(b) Unless there is specific evidence to the contrary, Investigators must assume foetuses have the same requirements for anaesthesia and analgesia as adult animals of the species.

(c) During surgery of the mother, consideration must be given to any special requirements for anaesthesia of the foetus.

(d) Eggs must be destroyed before hatching, unless hatching is a requirement of the experiment. The IACUC must approve the arrangements made for hatchlings.

8.4.25 Research on pain mechanisms and the relief of pain

(a) For experiments in which unanaesthetised animals are to be subjected to stimuli designed to produce pain or when pain is to be inflicted on animals as part of normal management, Investigators must satisfy the IACUC that their choice of the measurement of pain is appropriate.

(b) Investigators should:

(i) ensure that the pain stimuli limit pain at all times to levels comparable to those which do not distress human beings;

(ii) ensure that the animals are exposed to the minimum pain necessary for the purpose of the experiment; and

(iii) provide treatment for the relief of pain, or allow self-administration of analgesics, or escape from repetitive, painful stimuli whenever possible.

8.4.26 Animal welfare and animal health research

(a) When studying ways of improving the health and welfare of animals, Investigators may need to design experiments that replicate conditions such as injury, trauma, nutritional disorder, physical exertion, disease or environmental stress. Thus the attendant pain and distress may also be replicated. When such experiments are necessary, the Investigator must ensure that:

(i) the principal aim of the Project is to improve animal health or welfare;

(ii) alternative methods, such as the use of animals naturally inflicted with the condition, are not possible;

(iii) all possible steps are taken to minimise any pain or distress; and

(iv) the experiments do not proceed to the painful or distressful or lingering death of animals unless no other experimental end-point is feasible and the goals of the experiments are the prevention, alleviation, treatment or care of a life-threatening disease or situation in human or animals. When Death as an end-point cannot be avoided, the experiments must be designed to result in the deaths of as few animals as possible.

8.5 Training for Investigators

8.5.1 The minimum training requirements for Investigators and other training that is recommended are set out in the Training Guidelines.

CHAPTER 9: RESPONSIBILITIES OF TEACHERS

9.1 Teaching at tertiary levels

9.1.1 When animals are being used to achieve educational objectives, the person in charge of the class must:

(a) accept responsibility for ensuring that the care and use of the animals is in accordance with all relevant legislation and these Guiding Principles;

(b) have relevant training and qualifications;

(c) consider whether alternative teaching methods can be used;

(d) obtain prior IACUC approval for use of all animals for the entire course;

(e) instruct students appropriately in the care and use of animals before the students participate in experiments with live animals;

(f) ensure that there is close, competent supervision of all students;

(g) allow students to anaesthetise animals or carry out surgery only if it is essential for their training; and

(h) be responsible for the humane killing of the animals, if required, bearing in mind that it is good practice to segregate manipulated animals from animals held under normal living conditions.

9.1.2 Persons supervising students who are training in research must ensure that the students are appropriately instructed prior to using animals and must be responsible for the welfare of animals used by students.

9.1.3 No student should be forced to use an animal against his will.

9.2 Teaching at non-tertiary levels

9.2.1 Non-tertiary schools using animals for teaching are encouraged to refer to the Guiding Principles.

9.2.2 No student should be forced to use an animal against his will.

9.2.3 It should be noted that students in primary schools are more impressionable and at an age that makes them more prone to suffering the long-term effects of mental and emotional traumatic experiences. As the use of animals for teaching could have such negative impact on these students, animals should preferably not be used for teaching at this level of education.

APPENDIX I: REFERENCE MATERIALS

GENERAL

Handbook of Laboratory Animal Science, 2nd Edition, Volume 1: Essential Principles and Practices, J. Hau and G. L. Van Hoosier, Jr., CRC Press, 2002.

Handbook of Laboratory Animal Science, 2nd Edition, Volume 2: Animal Models, J. Hau and G. L. Van Hoosier, Jr., CRC Press, 2002.

Management of Laboratory Animal Care and Use Programmes, M. A. Suckow, F. A. Douglas and R. H. Welchbrod, CRC Press, 2001.

UFAW Handbook on the Care and Management of Laboratory Animals, 2 volumes, T. B. Poole (editor), 7th Edition, Blackwell Science, 1999.

Guide for the Care and Use of Laboratory Animals: National Research Council, National Academy Press, 1996.

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Handbook of Facilities Planning, Laboratory Animal Facitilies, T. Ruys (editor), Van Nostrand Reinhold, 1991.

Laboratory Animal Medicine, J. G. Fox, B. I. Cohen and F.M. Loew, editors, Academic Press, 1984.

Institutional Animal Care and Use Committee Guidebook, 2nd Edition, Applied Research Ethics National Association (ARENA) and Office of Laboratory Animal Welfare (OLAW), 2002.

Australian code of practice for the care and use of animals for scientific purposes, 6th Edition, National Health and Medical Research Council, 1997.

Live Animals Regulations. International Air Transport Association, 2004. (www.iata.org)

PAIN & DISTRESS

Appendix I of the New Zealand “Good Practice Guide for the Use of Animals in Research, Testing and Teaching” entitled “Pain: Some Concepts and Definitions”.

Chapter X of the Canadian Council on Animal Care “Guide to the Care and Use of Experimental Animals”, Volume 1, 2nd Edition, 1993.

Recognising and Assessing Pain, Suffering and Distress in Laboratory Animals – A Survey of Current Practice in the UK with Recommendations by Penny Hawkins, Research Animals Department, RSPCA.

EUTHANASIA

Monograph entitled “Euthanasia of Animals used for Scientific Purposes” by the Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART), 1993.

Chapter XII of the Canadian Council on Animal Care “Guide to the Care and Use of Experimental Animals”, Volume 1, 2nd Edition, 1993.

2000 Report of the AVMA Panel on Euthanasia, American Veterinary Medical Association, Journal of the American Veterinary Medical Association, 218(5):669-696, 2001.

NON-HUMAN PRIMATES

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Report of the European Commission Scientific Committee on Animal Health and Animal Welfare on “The Welfare of Non-Human Primates used in Research”, 17 December 2002.

Policy on the Care and Use of Non-Humane Primates for Scientific Purposes, Animal Welfare Committee, National Health & Medical Research Council, Australia

FISH

“Guidelines for the Care and Use of Fish in Research" - Louis J. DeTolla, S. Srinivas, Brent R. Whitaker, Christopher Andrews, Bruce Hecker, Andrew S. Kane and Renate Reimschuessel; Journal of the Institute of Laboratory Animal Resources; 1995 Volume 37(4), 159-173

“Guide to the Care and Use of Experimental Animals” - Canadian Council on Animal Care, Vol 2 1984

UFAW Handbook on the Care and Management of Laboratory Animals: Amphibious and Aquatic Vertebrates and Advanced Invertebrates (Cephalopod Molluscs and Decapod Crustaceans) v.2, Poole T (ed) 1987

"The Care and Use of Amphibians, Reptiles and Fish" - Scientists Center for Animal Welfare (SCAW), Schaeffer, Kleinow & Krulisch (eds) 1992

Ross, L.G. & Ross, B. 1984. Anaesthetic and Sedative techniques for fish, Institute of Aquaculture Handbook. University of Stirling. pp45. ISBN 0-901636-52-5.

Ross, L.G., & Ross, B. 1983. Principles and practice of fish anaesthesia. Proceedings of the Association of Veterinary Anaesthetists. No 11, 154-189.

Ross, L.G. 2001. Restraint, anaesthesia and euthanasia. In: Veterinary practice and procedures for ornamental fish. Ed. W Wildgoose. British Small Animal Veterinary Association. London. UK.

Ross, L.G. & Ross, B. 1999. Anaesthetic and Sedative techniques for Aquatic Animals. Second edition. Fishing News Books. Blackwell Science. Oxford, pp 176. ISBN 0-632 05252X

APPENDIX II: STANDARDS FOR HOUSING AND ENVIRONMENTAL CONDITIONS

A. MOUSE, RAT, HAMSTER, GUINEA PIG, GERBIL

ANIMAL	WEIGHT / gm	FLOOR AREA / cm^2	HEIGHT / cm
MOUSE	< 10	38	12
	Up to 15	51	12
	Up to 25	77	12
	>25 [a]	>96	12
RAT	<100	109	17
	Up to 200	148	17
	Up to 300	187	17
	Up to 400	258	17
	Up to 500	387	17
	>500 [a]	>451	17
HAMSTER	<60	64	15
	Up to 80	83	15
	Up to 100	103	15
	>100 [a]	>122	15
GUINEA PIG	≤350	387	17
	>350 [a]	>651	17
GERBIL	-	116	15

[a] Larger animals might require more space to meet performance standards.

B. RABBIT, CAT, DOG, PIGEON, QUAIL, CHICKEN, NON-HUMAN PRIMATE

ANIMAL	WEIGHT / kg	FLOOR AREA / m^2	HEIGHT / cm
RABBIT	<2	0.135	35
	Up to 4	0.27	35
	Up to 5.4	0.36	35
	>5.4[a]	>0.45	35
CAT	≤4	0.27	60
	>4 [a]	≥0.36	60
DOG[b]	<15	0.72	-
	Up to 30	1.08	-
	>30 [a]	≥2.16	-
PIGEON[c]	-	0.072	-
QUAIL[c]	-	0.0225	-
CHICKEN[c]	<0.25	0.225	-
	Up to 0.5	0.045	-
	Up to 1.5	0.09	-
	Up to 3.0	0.18	-
	>3.0 [a]	≥0.27	-
MONKEY[de] (including the baboon)	Up to 1	0.144	50
	Up to 3	0.27	76
	Up to 10	0.387	76
	Up to 15	0.54	81
	Up to 25	0.72	91

ANIMAL	WEIGHT / kg	FLOOR AREA / m^2	HEIGHT / cm
	Up to 30	0.9	116
	>30 [a]	1.35	116
APE[e]	Up to 20	0.9	139
	Up to 35	1.35	152
	>35 [a]	2.25	213

[a] Larger animals might require more space to meet performance standards.
[b]These recommendations might require modification according to body conformation of individual animals and breeds.
[c] Cage height should be sufficient for the animal to stand erect and stretch its wings.
[d] Callitrichidae, Cebidae, Cercopithecidae, and *Papio*. Baboons might require more height than other monkeys.
[e] For some species (e.g. *Brachyteles*, *Hylobates*, *Symphalangus*, *Pongo* and *Pan*), cage height should be such that an animal can, when fully extended, swing from the cage ceiling without having its feet touch the floor. Cage-ceiling design should enhance brachiating movement.

C. GOAT, SHEEP, SWINE, CATTLE, HORSE, PONY

ANIMAL	WEIGHT / kg	FLOOR AREA[a] / m^2	HEIGHT / cm
GOAT	<25	0.9 / 0.765 / 0.675	-
	Up to 50	1.35 / 1.125 / 1.017	
	>50[b]	1.8 / 1.53 / 1.35	
SHEEP	As for goat		
SWINE	<15	0.72 / - / -	-
	Up to 25	1.08 / 0.54 / 0.54	
	Up to 50	1.35 / 0.9 / 0.81	
	Up to 100	2.16 / 1.8 / 1.62	
	Up to 200	4.32 / 3.6 / 3.24	
	>200 [b]	≥5.4 / ≥4.68 / ≥4.32	
CATTLE	<75	2.16 / 1.8 / 1.62	
	Up to 200	4.32 / 3.6 / 3.24	
	Up to 350	6.48 / 5.4 / 4.86	
	Up to 500	8.64 / 7.2 / 6.48	
	Up to 650	11.16 / 9.45 / 8.37	
	>650 [b]	≥12.96 / ≥10.8 / ≥9.72	
HORSE	-	12.96	
PONY	- (1 – 4 / pen)	72	
	≤200 (> 4 / pen)	60	
	>200 [b] (> 4 / pen)	≥72	

[a] Floor area per animal is given according to grouping sizes of 1, 2 to 5 and >5.
[b] Larger animals might require more space to meet performance standards.

D. TEMPERATURE, HUMIDITY, VENTILATION AND LIGHTING

The recommended temperature ranges for the different animals are as provided in the table below.

ANIMAL	**DRY-BULB TEMPERATURE °C**
Mouse, rat, hamster, gerbil, guinea pig	18 – 26
Rabbit	16 – 22
Cat, dog, non-human primate	18 – 29
Farm animals & poultry	16 – 27

The relative humidity should be 30 – 70%.

The ventilation should be 10 – 15 fresh air changes per hour. In some situations, the use of such a broad ventilation guideline might over-ventilate an enclosure that contains few animals or under-ventilate an enclosure that contains many animals. To determine more accurately the ventilation required, the minimal ventilation rate required to accommodate heat loads generated by animals can be calculated with the assistance of mechanical engineers. The minimal required ventilation is then determined by calculating the amount of cooling required to control the heat load expected to be generated by the largest number of animals to be housed in the enclosure plus any heat generated by non-animal sources and heat transfer through room surfaces.

Lighting of 325 lux about 1.0 metre above the floor should be provided.

APPENDIX III: ADDITIONAL INFORMATION ON THE CARE AND USE OF NON-HUMAN PRIMATE FOR SCIENTIFIC PURPOSES

1 Non-human primates (NHP) are recognised as having highly developed mental and emotional capacities, more so than most other animals. In many ways, they are similar to humans and exhibit many similar external manifestations of emotions such as facial expressions, vocalisations, postures, gestures, and reactions. They have been known to react in ways similar to humans under comparable situations, e.g. compare captive NHP and institutionalised humans.

2 Given the greater complexity of the NHP, when managing and caring for them, besides providing a physical environment conducive to their well-being, emphasis should therefore be placed on enhancing their social and behavioural well-being through enrichment of their environment.

3 Researchers should acquaint themselves with the animal's distinctive characteristics and needs. They should be able to recognise abnormal behaviour patterns such as stereotypes, appetite disorders, abnormal social behaviours, etc and take necessary steps to treat or ameliorate them. They should be familiar with the literature on animal cognition and perception and conduct frequent routine observation of every animal in order to be in a position to provide optimal care and handling of the animals. NHP that are housed improperly or treated inhumanely are likely to yield unreliable data due to the effects of behavioural stress. This can introduce unwanted variables.

4 Most primate species, including the majority of those used in laboratories, are highly social, live in complex social groups and establish long-term bonds, although such bonds may not necessarily be permanent. Because of the bonding, social isolation is likely to adversely affect individual animals. Animals raised in total social isolation could suffer from social deprivation and become withdrawn and develop aberrant social, sexual and exploratory behaviour. It is therefore important to provide the company of compatible conspecifics or other NHP species, and if this is not possible, increased human company.

5 Group or paired housing is preferred but the potential for problems such as wounding, disease transmission, dominance hierarchies, social distress, and undernourishment of a lower-ranking partner should be kept in mind. When groups are being formed, observers must adjust group composition so the units show minimal aggression. Where single housing is necessary, the role of the animal care technician takes on added importance. Familiarity with the handler, surrounding and procedure can significantly reduce anxiety. NHP should never be housed in a restraint chair but the restraint chair may be used to the extent necessitated by the nature of an experiment.

6 NHP form coalitions through which they establish their dominance ranks and compete for food and sexual partners. Removing a monkey from its group may disrupt the existing network of alliances and induce rank changes, which may be associated with vicious fighting resulting in injuries. Animals that are to be reintroduced should be kept away from the group for as short a time period as possible.

7 While enclosure size is an important variable, the primary emphasis should be on providing the animal with the option for species-appropriate activities. Besides providing social peers, an animal's environment can also be enriched by providing food gathering activities, devices such as perches, shelves and swings and artificial appliances, such as audiovisual

devices (radio, video, television). These latter appear to be useful in enhancing the well-being of NHP, especially if the NHP can turn the equipment on and off at will. It has been reported anecdotally that monkeys are particularly fascinated by visuals depicting their natural environment, animals that are found in their natural habitat or videos of themselves.

8 Most primates show vertical flight reactions. This should be taken into account when arranging their housing. Attempts should be made to cater to their preferred vertical limits in the wild. Because of the importance of vision to the NHP, particularly *M. nemestrina*, cages should be positioned so that the monkeys can see animals of like species. Solid-sided caging prevents visual contact. If physical contact is possible, there must be assurance that the animals are compatible.

9 Interaction between the NHP and the researcher or technician is encouraged but it should not be forced. The interaction, however, must not involve handling other than what is necessary for the maintenance of the animal or for investigational procedures. Direct physical contact between humans and NHP should be evaluated from facility to facility. In many instances it should be kept to a minimum to avoid problems that may arise, for example from breaking of the human / animal bond when staff changes occur or when an animal must be euthanised, as well as the hazards posed by zoonotic diseases. Some of the most significant diseases associated with NHP are *Cercopithecine herpesvirus I* (formerly *Herpesvirus simiae*) infection and infectious haemorrhagic fever viruses.

10 Many NHP have extreme physical strength in relationship to body size and can inflict serious injury on personnel. Humans can also transmit infectious diseases to primates, e.g. measles, tuberculosis. It is recommended therefore that personnel exposed to NHP be provided with such protective items as gloves, arm protectors, masks and face shields. They should be routinely screened for tuberculosis and a procedure established for ensuring medical care for bites and scratches.

APPENDIX IV: ADDITIONAL INFORMATION ON THE CARE AND USE OF FISH FOR SCIENTIFIC PURPOSES

1 There are about 20,000 species of fish worldwide, constituting about half of all living species of vertebrates. As fish vary significantly in size, taxonomy, morphology, genetics, behaviour, physiology and ecology, it is not possible to derive a set of comprehensive guidelines on housing, management and husbandry that can apply equally to all and every species of fish. However, some general principles for the care and use of fish in research can be used and these are briefly highlighted below. The principles are adapted from two main publications – the article "Guidelines for the Care and Use of Fish in Research" in the Institute of Laboratory Animal Resources (ILAR)'s Journal Volume 37(4) 1995 and the "Guide to the Care and Use of Experimental Animals" by the Canadian Council on Animal Care, Vol 2 1984. These publications (with the references contained therein) and a few others on the use of fish in research are listed as reference materials in Appendix II.

Choice of species

2 The choice of fish species – whether marine, freshwater or brackish water – will determine much of the life support system needed. Ease of maintenance, space requirements and hardiness of the species are other considerations.

Sources, procurement and permits

3 The Investigator should obtain fish only from legal sources. If wild-caught fish are to be used or field trials conducted, permission must be obtained from the relevant authorities, including the Agri-Food & Veterinary Authority, National Parks Board and Public Utilities Board. Catching / trapping fish from the wild or using them in field trials should be done according to acceptable standards of capture and handling.

Transportation and handling

4 Care should be taken to reduce the stress associated with transportation. In the US and Canada, it has been recommended that food be withheld two to four days prior to transportation to reduce fouling of the water, and that food deprivation be continued for a similar period after arrival followed by a gradual return to normal feeding. Under our local conditions, withholding food one to two days before and after transport may be sufficient. Transportation standards set by the International Air Transport Association (IATA) should be followed where appropriate.

5 The Investigator and his assistants should be proficient and equipped to handle the fish properly so as to minimise stress and injury to the fish. Where appropriate, chemical restraint should be judiciously and correctly used. Fish should be handled as little as possible. Nets should be soft and only equipment that causes minimal damage to the skin of the fish should be used for handling fish.

Acclimatisation

6 Proper acclimatisation should be done upon introduction of the fish to the facility. Ideally the temperature of the water of the tank in which the fish is kept on arrival should be the same as that of the water in which the fish originated and was transported. However, as temperature change may be unavoidable, a gradual transition to the fish' preferred temperature should be made to minimise shock. In general, fish will tolerate a reduction in temperature better than they

will an increase. They should be disturbed as little as possible during their first few days in their new tank.

Quarantine

7 New batches of fish should be held separately from existing stock, regardless of whether they were from the same source. Complete separation of water supplies should be practiced. To minimise the possibility of introduction of pathogens, some form of sterilisation may need to be carried out. For dangerous pathogens, appropriate chemical sterilisation, ozonisation or ultraviolet light treatment may be used.

Facilities – design and construction

8 The tanks in which the fish are to be kept should be properly designed and constructed to meet the needs of the fish. Proper choice of materials (concrete, plastic or fibre) is crucial to ensure that the best and safest environment for the fish is provided. Care should be taken to ensure that concrete structures are properly treated so that there is minimal leaching and salt deposition. Construction materials should not contain copper, nickel, cadmium or brass. If polyvinyl chloride pipes are used, they should be flushed to eliminate acetone, methylethylketones and tetrahydrofurans that are released following gluing.

Water quality

9 For a closed water system, all four major processes of biological filtration, mechanical filtration, chemical filtration and disinfection should be used to maintain good water quality. Close daily monitoring of pH, hardness, dissolved oxygen, nitrogen, ammonia, carbon dioxide, salinity and suspended solids should be done.

Water temperature

10 The health, nutrient requirements, performance, reproduction and well-being and survival of fish are dependent on the temperature of the water. Temperature requirements vary among species as well as between estuarine and freshwater species. Gradual equilibration of water temperature is crucial during the acclimatisation period.

Illumination

11 Both photoperiod and light intensity are important and requirements vary among species. Although most species do well with a cycle of 12 hours of light and 12 hours of darkness, 8 – 10 hours of light is generally adequate for most fish, while 12 – 14 hours is appropriate for tropical fish. A timer can be used to actuate the light cycles. Fluorescent lamps, which are commonly used in aquaria, can be used as source of lighting.

Stocking density and water flow

12 Different species of fish have different space requirements and allowing them as much space as possible may not necessarily be in their best interest. Optimum stocking densities depend on many factors, including water quality, flow rates and temperature. At higher temperatures, water oxygen levels decrease while the requirements of the fish increase, necessitating a reduction in stocking density. Water current should not be so great that the fish have difficulty swimming.

Diet and feeding

13 Some species are herbivorous, some carnivorous and some omnivorous. Since nutritional requirements vary, an appropriate diet should be selected. Specially prepared diets are desirable as a food supply. Commercially prepared pellets can be used, where available. Feeding once or twice a day for the five working days is adequate, although fry require more frequent feeding and should include feeding on the weekends. Feeding by hand, with the appropriate hygiene measures undertaken, is preferable as it encourages frequent inspection of the fish so that problems can be detected early.

Health programme and disease control

14 A proper health and disease control programme should be put in place. It should be under the supervision of a veterinarian or qualified person with expertise in fish medicine. Staff should be trained and the facility equipped to detect and deal with health problems in species of fish being used for the research.

Analgesia, anaesthesia and invasive procedures

15 The Investigator and his assistants must be familiar with the use and application of analgesic and anesthetic agents that can be used to sedate, immobilise and anesthetise fish. Such agents are useful and should be considered for all procedures that are likely to cause stress and pain to the fish, especially invasive ones. During recovery from anesthesia, the fish can be placed in a well-oxygenated, anaesthetic-free environment. Propelling the fish head first in the water will hasten recovery.

Euthanasia

16 Euthanasia, where required, should be humane. Methods of euthanasia that can be used include hypothermia, electrocution, overdosing with Tricaine Methanesulfonate (Finquel, MS-222) or carbon dioxide, or a sharp blow to the head. Of these, MS-222 administered at 500 mg/L has been found to cause the least stress and pain. Where chemicals may alter experimental data, cranial concussion followed by some other physical method may be employed. The report of the American Veterinary Medical Association Panel on Euthanasia should be consulted.

Dangerous species and zoonoses

17 Working with any animal can expose Investigators and their Staff to the risk of physical injury or contraction of zoonotic disease. The Investigator should ensure that appropriate safety measures are put in place to minimise these risks.

A. APPENDIX V: SAMPLE ANIMAL WELFARE SCORE SHEET

(Acknowledgement: This score sheet is adapted from the one used by Professor David B. Morton, Centre for Biomedical Ethics, University of Birmingham UK as contained in Appendix III of the New Zealand "Good Practice Guide for the Use of Animals in Research, Testing and Teaching")

Animal Species: _____ **Date of Procedure:** _____
IACUC Ref: _____

Starting Body Weight: _____ **Investigator:** _____
Wt. Of Water Bottle: _____

DATE												
DAY												
TIME												
VISUAL INSPECTION												
Inactive												
Hunched posture												
Coat rough												
Breathing rate												
Breathing pattern[a]												
HANDS-ON INSPECTION												
Bodyweight /gm												
% bodyweight change												
Alert & Inquisitive												
Diarrhoea												
Dehydration												
Vocalisation												
Seizures / convulsions												
FOOD & WATER												
Food intake[b]												
Wt of full water bottle												
Wt of water bottle today												
SITE OF INVASIVE PROCEDURE												
Wound[b]												
Bleeding												
Other discharges[c]												
Sutures / clip[b]												
POST-PROCEDURAL SUPPORT												
Pain medication used												
Dose												
Subcut. fluids / ml.												
STAFF'S INITIALS												

APPENDIX V: SAMPLE ANIMAL WELFARE SCORE SHEET (continue)

Scoring details:

[A] Breathing pattern: R = rapid, S = shallow, L = laboured, N = normal
[b] Write in "OK" if normal
[c] Other discharges: C = clear discharge, P = pus

How to use the Animal Welfare Score Sheet:

Key points:
- One score sheet per animal
- The 12 boxes across the page can be used for 12 different time points on different days
- For critical post-op cases, animals should be checked every 4 hrs (i.e. three times a day)
- A pre-procedural examination of the animal should be made before anaesthesia. This is time zero in the first box
- Look for evidence of red discharge from nose or eyes. This is a non-specific sign of stress
- Look at the coat. It should be smooth and shiny. A rough coat has fur standing on end and indicates that the animal is too sick to groom itself
- Look for dehydration. If the skin can be gently pulled away from the body and remains that way, the animal is significantly dehydrated
- Look at the breathing and note if it is rapid, laboured or shallow
- Listen to the breathing and note any respiratory noises
- Look at the colour of the ears and feet. They should be pink
- Look at the behaviour of the animal when handled. It should be alert and inquisitive
- Record the weight of the water bottle before the procedure

Use this form to score and record:
- Physical observations of clinical condition- This can be done in 2 ways (for example for nose discharge):
    - example 1: Score presence (+) or absence (-) of nose discharge or dehydration
    - example 2: Graded score from 0 to 5 (0 = no discharge, 5 = max discharge)
- Changes in physical condition with time after the procedure- When several animals are used simultaneously, it is difficult to remember how any individual animal looked the previous day
- Administration of pain medication- The volume of water consumed is a good indicator of animal well-being. If the animal is not drinking up to 10% of body wt per 24 hrs, it is probably in pain. Pain medication should be increased and additional fluid administered by subcutaneous injection. Seek veterinary advice on this
- Administration of subcutaneous fluids
- Condition of the sites of invasive procedures- Look for blood or other discharges
- Body weight of the animal- Body weight should be maintained. Significant weight loss is used as a humane end-point

Humane End-points:

1. Weight loss of 10% or more over 24 hrs
2. Weight loss of 20% or more plus one other clinical sign compared with control group
3. Weight loss of 25% compared with control group

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

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CHAPTER 4: EVALUATION OF ANIMAL CARE AND USE CONCERNS

CHAPTER 5: RECORD KEEPING AND COMMUNICATIONS

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 for scientific purposes.

(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 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 for scientific purposes 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 and annual inspection of Housing and Research Facility(ies) as a means of overseeing the care and use of animals by the Institution. This puts the IACUC in an advisory role to the CEO. In its programme and facility review 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 Proposals independent of the CEO. The CEO cannot overrule an IACUC decision to withhold approval of a Proposal. However, if an IACUC approves a Proposal, the Institution is not required or obligated to conduct the research activity. An Institution may subject Proposals or protocols to additional Institutional review (e.g. department head, bio-safety 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 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 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. The Chairman should hold a senior position in the institution appropriate to the oversight of the IACUC, of if an external appointee, be given a commitment by the Institution to provide the necessary support and authority to carry out their role. 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 approval of proposals and suspension/withdrawal of approval for a Project.

1.9.2 “Quorum” is defined as more than 50% of the members of the IACUC and must include at least one representative from either category (c) or (d). Therefore:

(a) a proposal is approved only if a quorum is present at a convened meeting, and if more than 50% of the quorum votes in favor.

(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 11 members, at least 6 undisqualified members must be present at a convened meeting to constitute a quorum and approval of a protocol would require a minimum of 4 votes whether or not there were abstentions.

1.10 Facility Review Functions of the IACUC:

1.10.1 Review, at least once 6 months the Institution's programme for the care and use of animals, using the Guiding Principles as a basis for evaluation.

1.10.2 Inspect, at least once every year, all of the Institution's Housing and Research 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. Areas in which surgical manipulations are performed must always be included.

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 safety and health
(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 fulltime 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 in 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 and inspect the Housing and Research Facility(ies) annually, 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 safety and health 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 anesthetics and analgesics, and euthanasia procedures.

2.3 Facility Review

2.3.1 All Housing and Research Facilities must be inspected in the 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.

(c) Animal study areas (where animals are held more than 12 hours)

(d) 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 IACUC 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 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 safety and health concerns

(i) 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 IACUC 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 Written reports of the semi-annual programme review and annual 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 behavior and minimises stress–induced behaviors. 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 behavioral 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 :

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

0(ii) 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:

(a) Cage cards

(b) Subcutaneous transponders

(c) Ear notches and tags

(d) Collars

(e) Coloured stains

(f) 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:

(a) Source of the animal

(b) Strain or stock

(c) Names and locations of responsible investigators

(d) Pertinent dates

(e) Protocol number

(b) Feeding

(i) All animals should receive food that is:

(a) Palatable

(b) Free from contamination

(c) 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:

(a) Bags should be stored off the floor

(b) The milling date should be known (the date or code is usually stamped on each bag)

(c) 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.

(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 odor 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) Frequencies and methods for cleaning and sanitation of facilities, equipment and accessories should ensure that animals are maintained and in a clean, dry environment, free from exposure to harmful contamination and excessive animal odors.

(iii) Cleaning agents that mask animal odors 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 "relevant biosafety standards and legislation".

(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 sterilisation, 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 Behavioral Management for Laboratory Animals

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

2.11.2 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.)

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

2.11.4 Oversight

(a) The IACUC should provide oversight of the behavioral 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 behavioral 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 behavioral 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 Institution. 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 anesthetic 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 Safety and Health 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 Safety and Health

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 in Occupational Safety and Health

(a) The IACUC should participate in the Occupational Safety and Health Programme of the institution by 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 The Occupational Safety and Health programme must conformed to the relevant biosafety standards and safety and health legislation.

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 fulfill the Institution'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 safety and health 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:

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

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

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

(d) 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:

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

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

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

(d) Regarding the intent and requirements of the appropriate Act(s). Training programmes should also include information on occupational safety and health.

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 CEO), 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 follows.

(b) Some key points include:

(i) Determine facility vulnerability.

(a) Look at the research facilities with a "public eye."

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

(c) 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.

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

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

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

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

(iii) Check storage of research data.

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

(b) Review research protocols for confidential information.

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

(iv) Organise a security plan.

(a) Consult with local police to establish procedures.

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

(c) Maintain a list of research projects and scientists.

(d) Identify ongoing investigations by regulatory agencies.

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

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

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

(h) 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 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. The veterinarian or animal facility manager could be part of the official Institutional response team. Facilities should 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 and annual inspection of facilities.

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); and

(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 semi-annual 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.

(c) 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 labor 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 refueling 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.

2.16.11Conclusion

(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 semi-annual 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.

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.

(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 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.

3.1.7 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.

3.1.8 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) 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.

3.1.9 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.

3.1.10 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.

3.1.11 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 following kinds of significant changes 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.

3.1.12 Frequency of Review of Approved Protocols

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

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 analyze 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 :

Method	**Examples**
Rational selection of group size	Pilot studies to estimate variability and evaluate procedures and effects
Careful experimental design	Appropriate choice of control groups
	Standardising procedures to minimise variability
	Maximising use of animals
	Performing several terminal procedures per animal
	Animals euthanised by one investigator used for tissue needed by another
Correct choice of model	Use of healthy, genetically similar animals decreases variability

Minimising loss of animals	Good post-operative care
	Avoid unintended breeding
	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 practiced of the 3 Rs, although it is not always recognised as one of the applications.

(i) 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.

(n) 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 anesthetics, analgesics, or other measures, such as anti-inflammatory agents, antibiotics, or sedatives.

(o) 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.

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

(q) 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

(a) 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.

(b) IACUC should 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 anesthetics (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) Chloral hydrate, chloroform and cyanide

(ii) Decompression

(iii) Neuromuscular blockers

(iv) Various pharmacological and physical methods

(v) Dry ice-generated CO_2

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

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 anesthesia.

(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 labored 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 tumor 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 tumor development is necessary to allow for appropriate intervention before significant deterioration or death.

(b) Effective monitoring systems and endpoints should include limits on tumor size and severity of tumor-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

Endpoint	**Characteristics**	**Applications**
Tumor growth or effects	Tumor exceeds 10% of normal body weight; necrosis, infection, ulceration, interference with ambulation or eating /drinking	Subcutaneous or intraperitoneal tumors and hybridomas
Prolonged inappetence/ Cachexia	Rapid loss of weight (>20% of normal body weight) and/ or condition	Metastatic disease, chronic infectious disease
Inability to ambulate	Prolonged recumbency	Many

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 anesthesia;

(ii) criteria for timely intervention, removal of animals from study, or euthanasia if painful or stressful outcomes are anticipated; and

(iii) details of post-procedural 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) tumor 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 behavioral 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.

(d) While there are no generally accepted criteria for distress, there are a number of metabolic, physiologic and behavioral 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.

(e) 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 behavior.

(f) 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

(a) 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.

(b) 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.

(c) 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.

(d) 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.

(e) The responses of different species to different anesthetics, analgesics or tranquilisers 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.

(f) 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.
Anesthesia	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 behavior.
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.
Tranquilisation	A state of mental calming, decreased response to environmental stimuli, and muscle relaxation. No sleep, analgesia or anesthesia is present, even at increased dosage.

From: *American College of Laboratory Animal Medicine.* 1997. *Anesthesia and Analgesia in Laboratory Animals*. D.F. Kohn, S.K. Wixson, W.J. White and G.J. Benson, eds. Academic Press.

(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

(g) Signs, Degree and Length of Surgically Produced Pain*

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

*Based on observations of dogs.

Reprinted with permission from *Recognition and Alleviation of Pain and Distress in LaboratoryAnimals*. Committee on Pain and Distress in Laboratory Animals, Institute of Laboratory AnimalResources, Commission on Life Sciences, National Research Council. National Academy Press, Washington, DC. 1992.

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 safety and health 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 semi-annual 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 theProject.

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 theuse of pre-anesthetic drugs where indicated, and appropriate anesthetic 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/anesthetics

(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 safety and health (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 fiber.

(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:

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

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

(c) 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 fiber 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 fiber 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 fiber 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 titers 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 Center, 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.

(i) 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 fetuses, the protocol should indicate the number of eggs, embryos or fetuses 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 fetuses. 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 behavioral 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 semi-annual 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 guide lines 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.

(i) 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 behavior 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 behavioral 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 feces 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 behavior or physiology by surgery or drugs. Any invasive surgery, such as organ removal or implanting transmitters, should be done using aseptic technique.

(viii) The use and choice of anesthesia will be affected by field conditions because some agents are difficult to transport or use in field conditions. Anesthetics 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.

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

(j) Conclusion

(i) 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.

(ii) 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 judgment of experienced professionals in the field and the IACUC should feel free to seek advice or consultation if necessary.

3.5.5 Hazardous Materials

(a) 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.

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

(c) Radiation Safety Committees (RSCs) and Institutional Biosafety Committees (IBCs) 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 safety and health issues, including information on working with hazardous materials in research animals.

(e) Radioactive Materials

(i) RSCs 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 US Office of Health and Safety Guidelines on Biosafety in Microbial and Biomedical Laboratories 4th Edition, provide a valuable source of reference for assessing 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:

(a) chemical storage and disbursement,

(b) dosage preparation and challenge procedures, and

(c) waste management and disposal practices.

(ii) It is also necessary to determine whether the chemicals will be present in feed, feces 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 tumors 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 anesthesia 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 anesthetics, 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 behavioral 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 biobehavioral 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) Behavioral 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 behavioral 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 behavioral 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 behavior 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 anesthesia.

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

(c) Reviewing Protocols for Surgical Procedures

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

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

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

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

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

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

(f) personnel occupational safety and health 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 judgment 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:

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

(b) he 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

(c) under other special circumstances which have been approved

(d) The provisions of the Guiding Principles 8.4.4 are not breached

(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 anesthesia.

(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:

(a) a pre-surgical assessment;

(b) adequate monitoring of depth of anesthesia and animal homeostasis during the surgical procedure;

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

(d) monitoring and support during anesthetic recovery; and

(e) 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).

(g) Recordkeeping

(i) Recordkeeping is an essential component of peri-operative care. For major surgical procedures on non-rodent mammals, an intra-operative anesthetic 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.

(h) Occupational Safety and Health

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

(a) use of inhalation anesthetics,

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

(c) 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 ('knocked-in'). 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 'knockedout' 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<b>) and short ear (Bmp5<se>) 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<hpg>) and 'little' (Ghrhr<lit>) 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.

(n) 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 Annual Inspection

(a) During the Annual 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 honored 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 war-ranted. 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 safety and health 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 counseling 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 deter-mine 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 nonInstitutional 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 con-duct 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 circum stances, 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) counseling;

(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.

CHAPTER 5: RECORD KEEPING AND COMMUNICATIONS

5.1 Introduction

5.1.1 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 reports of and recommendations from semi-annual programme reviews and annual facility inspection 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 Annual Facility Inspections and Semi-annual Programme Evaluations

(a) The Guiding Principles requires that the IACUC evaluate the Institution's animal programme every 6 months, inspect the facilities annually 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 semi-annual evaluation. To be used as the semi-annual report, the report must include all the information required, and be approved by vote of the IACUC.

(e) Annual 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) 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 CEO 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 1Jan 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 standard 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 locations

(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 semi-annual programme reviews and annual facility 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.

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NATIONAL ADVISORY COMMITTEE FOR LABORATORY ANIMAL RESEARCH
THE TRAINING GUIDELINES

Contents Page

CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 These Training Guidelines are to aid Institutions in implementing an educational and training programme (Training Programme) that will meet the expectations of the Guiding Principles of the National Advisory Committee For Laboratory Animal Research (NACLAR).

1.1.2 In particular, these Training Guidelines are intended to assist institutional officials and Institutional Animal Care and Use Committees (IACUCs) or any others assigned the responsibility for coordinating Training Programmes (Training Coordinators) in determining the scope and depth of such programmes that will meet both institutional needs and the requirements of NACLAR.

1.1.3 It must be emphasised that a strong Training Programme on the use of laboratory animals goes beyond the involvement of scientists, research technicians and animal care personnel. To promote understanding of the scientific process and minimise misunderstandings, it is suggested that administrators, nonscientific members of the IACUCs, support staff, and other nonscientific personnel indirectly involved in activities using live animals be included in the programme.

1.1.4 The IACUC and Training Coordinators are responsible for developing clear objectives for each phase of the Training Programme. These objectives must meet both the Guiding Principles as well as institutional requirements. The methods for presenting material will depend on the audience, the objectives that have been set, the nature of the content, and the resources available.

1.1.5 It is recognised that people who provide day-to-day animal care (Laboratory Animal Care-takers) require additional training that may extend beyond the scope and content proposed in these Training Guidelines. Reference is made to existing programmes offered by the "Federation of European Laboratory Animal Science Associations (FELASA). Additionally, for Laboratory Animal Technicians, Managers, Veterinarians and Researchers, existing programmes from the American Association for Laboratory Animal Science (AALAS), Institute of Animal Technology (IAT), American College of Laboratory Animal Medicine (ACLAM) and the Academy of Surgical Research (ASR) are referred to as well.

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

1.2 Scope of the Training Guidelines

1.2.1 These Training Guidelines encompass all staff caring for and working with live laboratory animals for scientific purposes. It is to ensure that these personnel are educated, trained and qualified to use animals in a manner that would be humane and ethical.

1.2.2 Training and education of all staff concerned is mandatory, with oversight by the IACUC and financial assistance from the Institution.

1.2.3 The following categories of personnel must be involved:

(a) Animal Facility Staff

(i) Laboratory Animal Care-takers

(ii) Laboratory Animal Technicians

(iii) Laboratory Animal Managers

(iv) Laboratory Animal Veterinarians

(b) Research Staff

(i) Principal Investigators

(ii) Research Fellows

(iii) Post-doctoral and post-graduate students

(iv) Research Technicians

(c) IACUC Members

(d) Service Personnel

(e) Teachers at Tertiary Institutions (Training for teachers at non-tertiary level is to be determined by the Ministry of Education.)

1.2.4 The Training Guidelines are not intended to cover training in safety matters and handling biohazards. It does, however, recommend certain areas where staff dealing with such biohazardous agents should be trained before undertaking procedures that may have bio-safety implications. The training on safety matters and the handling of biohazards should be fully dealt with by Institutions through Institutional Safety Officers or other designated personnel.

CHAPTER 2: ANIMAL FACILITY STAFF

2.1 Laboratory Animal Care-takers

2.1.1 In-house classes and on-the-job training for these staff should be conducted by senior management e.g. experienced Laboratory Animal Technicians, Manager and/or Veterinarian.

2.1.2 Topics to be covered:

(a) Guidelines, Laws and Ethical issues that impact on the care and use of research animals.

(b) Recognising Pain and Distress

(c) Responsibilities of Care-takers and other Animal Facility Staff members

(d) Species-specific Husbandry and Care

(e) Impact of the Environmental Factors on Research Animals

(f) Personal Hygiene, Safety and Protection

(g) Basic Handling of Biohazardous Materials

(h) Handling Laboratory Equipment, and Facility Layout

(i) Compliance with SOPs

2.1.3 Instructors may refer to the "Federation of European Laboratory Animal Science Associations (FELASA) recommendations on the education and training of persons working with laboratory animals: Category A – Persons taking care of animals" (http://www.lal.org.uk/pdffiles/lafel7.pdf). It describes activities and responsibilities of Laboratory Animal Care-takers. Levels 1 and 2 would be suitable for these personnel.

2.2 Laboratory Animal Technicians

2.2.1 The Laboratory Animal Manager, Veterinarian or Director should instruct on the following:

(a) National Laws and Guidelines

(b) Institutional Policies for the care and use of laboratory animals

(c) Institutional Safety and Health Programme

(d) Management of Biohazardous Materials

(e) Local Cultural and Religious Views on Laboratory Animal Research

2.2.2 The "Federation of European Laboratory Animal Science Associations (FELASA) recommendations on the education and training of persons working with laboratory animals: Category A – Persons taking care of animals" (http://www.lal.org.uk/pdffiles/lafel7.pdf) is a reference for activities and responsibilities of Laboratory Animal Technicians. Level 3 would be suitable for these personnel.

2.2.3 Laboratory Animal Technicians should enroll (on-line) to American Association for Laboratory Animal Science (AALAS) www.aalas.org for continuing education.
3 levels are available:

(a) Assistant Laboratory Animal Technician (ALAT),

(b) Laboratory Animal Technician (LAT), and

(c) Laboratory Animal Technologist (LATG).

2.2.4 Continued registration as members of the ALAT, LAT and LATG programmes are encouraged.

2.2.5 Technicians should be encouraged to attend other courses of interest, e.g. micro-manipulation techniques, cryopreservation, micro-surgery, tissue preservation, husbandry for exotic animals, etc.

2.2.6 All Laboratory Animal Technicians are to participate in the course on "Responsible Care and Use of Laboratory Animals" as described in Chapter 3.

2.3 Laboratory Animal Managers

2.3.1 Laboratory Animal Managers must be certified at least at Assistant Laboratory Animal Technician (ALAT) level or equivalent (Institute of Animal Technologists (IAT) Certificate level – see www.iat.org.uk/).

2.3.2 The Laboratory Animal Manager should be encouraged to enroll and obtain certification from Institute for Laboratory Animal Management (ILAM). ILAM is an AALAS educational programme developed to provide instructional management concepts that are applicable to the laboratory science industry and to enhance communication, team building, and networking among colleagues with mutual interests. The programme includes 64 classroom hours of instruction over a 2-year period. The following are class titles provided in past years:

(a) Managing an AAALAC-site visit

(b) AALAS Orientation and Interactions

(c) Bioethics

(d) Facility Technology

(e) Leadership and managing diversity

(f) Stress management

(g) Institutional Policies and Public Relations

(h) Performance Appraisal

(i) Regulatory Compliance issues

(j) Financial Management

2.3.3 The Laboratory Animal Manager must participate in the course on "Responsible Care and Use of Laboratory Animals" as described in Chapter 3.

2.4 Laboratory Animal Veterinarians

2.4.1 The veterinarian must be licensed by the AVA to practice in Singapore.

2.4.2 Laboratory Animal Veterinarians must participate in the course on "Responsible Care and Use of Laboratory Animals" as described in Chapter 3.

2.4.3 Veterinarians who specialise in laboratory animal medicine and science should be encouraged to attend and participate in relevant conferences, scientific meetings and workshops.

2.4.4 Obtaining higher degrees, recognition as specialists, and certification through American College of Laboratory Animal Medicine (ACLAM) would be particularly significant achievements. Certification at being trained as FELASA Category D (Specialist) would be recognised as a specialist qualification.

2.4.5 Residency training will reinforce didactic study and provide an opportunity to acquire work experience. A good residency programme will include the following major activities:

(a) Animal Facilities Administration and Management

(b) Clinical Medicine

(c) Necropsy and Histopathology

(d) Clinical Pathology

(e) Experimental Surgery and Radiography

(f) Research Training

(g) Participation in Education and Training of Research Personnel and Students

CHAPTER 3: RESEARCHERS

3.1 "Responsible Care and Use of Laboratory Animals"

3.1.1 The aim of this course is to provide an understanding of basic animal experimentation requirements, highlighting correct animal handling and responsibilities of researchers. All users of animals for scientific purposes e.g. Principal Investigators, Collaborators, Research Fellows, Post-doctoral and Post-graduate students, as well as Research Technicians, must first attend and pass this "Responsible Care and Use of Laboratory Animals" course before commencing any work on animals.

3.1.2 Only institutes of higher learning (i.e. all Polytechnics and Universities), Hospitals from the 2 Healthcare groups and institutes for A*STAR may conduct this course. The course conducted at the National University of Singapore may be used as a guide for minimum standards required.

3.1.3 The "Responsible Care and Use of Laboratory Animals" course at each Institute must comply with NACLAR Guidelines on the care and use of animals.

3.1.4 The course should be conducted by suitably qualified senior staff of animal research facilities, e.g. the Director, Laboratory Animal Veterinarian or Laboratory Animal Manager, but not by researchers.

3.1.5 This course will comprise the following lecture topics:

(a) Biomedical research regulations, NACLAR guidelines and you

(b) The IACUC – Responsibilities, functions and animal protocol submissions.

(c) The 3Rs, Ethical Responsibilities of a Researcher and the Use of Alternatives.

(d) Occupational safety and health in biomedical research

(e) Animal handling and blood collection

(f) Laboratory animal disease and diagnosis

(g) Basic laboratory animal anaesthesia and analgesia, including recognising pain and distress in animals.

(h) Introduction to surgery, post-operative care and euthanasia.

3.1.6 A hands-on exercise on the 4 basic laboratory animal species (mice, rats, guinea pigs and rabbits) should be provided:

(a) Identification, restraint and handling

(b) Routes of injection

(c) Blood sampling and gavage

(d) Euthanasia.

3.1.7 The FELASA recommendations on the education and training of persons carrying out animal experiments (Category B) is a resource for training material (http://www.lal.org.uk/pdffiles/lafel6.pdf). “Category B” is described by FELASA as those persons who are responsible for carrying out experimentation and other scientific procedures on living animals.

3.2 Responsibility for Level of Training

3.2.1 Principal Investigators are responsible for reporting to the IACUC (via animal protocol application) that they and their staff have sufficient qualifications and training in the procedures to be performed on animals. If not, IACUC will provide training for researchers in those particular areas.

3.3 Special Courses

3.3.1 It is acknowledged that “Advanced and Special” courses will need to be conducted depending on the complexity of the research programmes. For example, special training on the use of large animals like pigs, dogs, sheep, goats and non-human primates may be required. Courses for exotic animals (handling, anaesthesia, sampling methods, husbandry practices) fish and / or birds may also be required. Special modules on wound management and suturing techniques may also be of special interest to researchers.

3.3.2 The IACUC, in conjunction with the animal facility staff, should be responsible for setting up these special courses as and when the need arises. Specialists may be consulted to conduct these special courses.

CHAPTER 4: MEMBERS OF IACUC

4.1 ARENA (American Research Ethics National Association) IACUC 101

4.1.1 At least 50% of members of the IACUC must be trained in their respective roles and responsibilities. The training must introduce members to the role of IUCAC and its evolution, provide basic information necessary for IACUC members to discharge their responsibilities and to provide a forum for response to, and discussion of, members' concerns and questions.

4.1.2 Recommended syllabus:

(a) Criteria for membership to IACUC

(b) Authority of the IACUC

(c) Proposal (protocol) submission and review process

(d) Monitoring of approved protocols and reviewing amendments

(e) Record keeping

(f) Semi-annual reviews of animal care and use programmes and annual inspection of institutional animal facilities

(g) Handling animal welfare concerns

(h) Roles and relationships between IACUC, CEO of the Institution, AVA, Animal facility staff and animal care programme, project sponsor and community.

4.1.3 One excellent source is the ARENA IACUC 101. This is a full day didactic and interactive training course for new as well as seasoned IACUC members, IACUC affiliates and individuals responsible for their Institution's animal care programme. The sessions provide a basic yet comprehensive overview of the laws, regulations, and policies that govern the humane care and use of laboratory animals supplemented with examples and possible approaches for successful and effective administration. Current available resources to help IACUCs keep abreast of the latest information as well as take advantage of networking opportunities are also be covered.

4.2 Responsible Care and Use of Laboratory Animals

4.2.1 All members must participate in the course on "Responsible Care and Use of Laboratory Animals" as described in Chapter 3.

4.3 Continuing Education

4.3.1 All members should be encouraged to attend refresher courses to keep abreast with latest updated and reviews on the responsibilities of IACUC.

CHAPTER 5: SERVICE PERSONNEL

5.1 A general information sheet on the nature of facility that the service personnel are entering into, and any other safety aspects should be provided.

5.2 Service personnel should be briefed, especially if there is a need to enter into rooms where large animals (e.g. non-human primates, dogs) and/or any rooms where biohazards are used.

5.3 Service personnel entering an animal facility to service equipment should be accompanied by an animal care staff (caretaker or Technician) to ensure that the welfare of animals is not compromised.

CHAPTER 6: TEACHERS

6.1 Tertiary Level

6.1.1 The person-in-charge of the class must attend and pass the course on “Responsible Care and Use of Laboratory Animals” as described in Chapter 3.

6.2 Non-tertiary Level

6.2.1 The Ministry of Education is to decide on the level of training required.

CHAPTER 7: HANDLING BIOHAZARDS

7.1 The Training Guidelines are not intended to cover training in handling biohazards, but it is recommended that the training be provided to any staff and / or researchers prior to commencement of any biohazard-related work involving:

(a) Genetically Modified Organisms (recombinant genetic material)

(b) Radiation (x-ray, isotopes, etc)

(c) Chemicals (mutagens, carcinogens, etc)

(d) General hazards (fire, short-circuit, etc)

7.2 Institutional Offices of Safety and National bodies such as GMAC for health and environmental effects of genetically-modified organisms, the Health Sciences Authority (HSA), the Bio-safety Committee at Ministry of Health and the Safety Office(s) at Ministry of Manpower should be consulted for advice when necessary.