

# Terrestrial Animal Health Standards Commission Report

March 2009

## CHAPTER 7.X.

### **USE OF ANIMALS IN RESEARCH, TESTING OR TEACHING**

#### **Preamble**

The purpose of this Chapter is to provide standards for OIE Members to follow when formulating regulatory requirements for the use of live animals in research, testing or teaching<sup>1</sup>. It is the responsibility of all scientists using animals to ensure that they give due regard to these standards in designing and implementing their research protocols.

The OIE recognises the vital role played by the use of live animals in research. The OIE Guiding Principles state that such use makes a major contribution to the wellbeing of people and animals and emphasise the importance of the Three Rs of Russell and Burch (1959). Most scientists and members of the public agree that the use of animals in science should cause as little pain and/or distress to animals as possible, and those animals should only be used when necessary. The OIE also recognises the need for humane treatment of sentient animals and that good quality science depends upon good animal welfare. In keeping with the overall approach to animal welfare, as detailed in the Guiding Principles, the OIE emphasises the importance of standards based on outcomes for the animal.

A system of animal research oversight should be implemented in each country. The system will, in practice, vary from country to country and according to cultural, economic, religious and social factors. However, the OIE recommends that Members address all the essential elements identified in these standards in formulating a regulatory framework that is appropriate to their local conditions. This framework may be delivered through a combination of national, regional and institutional jurisdictions and both public sector and private sector responsibilities should be clearly defined.

The OIE recognises the central role of veterinarians in animal-based research. Given their unique training and skills, they are an essential member of a team including scientists and animal care technicians. This team approach is based on the concept that everyone involved in the use of animals has an ethical responsibility for the animals' welfare. The approach also ensures that animal use in science leads to high quality scientific outcomes and optimum welfare for the animals used.

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<sup>1</sup> Wherever the term “research” is used, it means “research, testing or teaching”.

## **Definitions**

### ***Animal Care and Use Committee (ACUC)***

means a committee responsible for overseeing the care and use of animals within an institution, including ethical considerations. It is also sometimes called Animal Care Committee, Animal Ethics Committee, Ethical Review Committee or Institutional Animal Care and Use Committee.

### ***Project Proposal***

or protocol, means a written description of a study or experiment, programme of work, or other activities that includes the goals, characterises the use of the animals, and includes ethical considerations. The purpose of the *Project Proposal* is to enable assessment of the quality and integrity of the study, work or activity.

### ***Operant (Instrumental) conditioning***

means the association that an animal makes between a particular response (such as pressing a bar) and a particular reinforcement (for example, a food reward). As a result of this association, the occurrence of a specific behaviour of the animal can be modified (e.g., increased or decreased in frequency or intensity).

### ***Biological safety or biosafety***

means the application of knowledge, techniques and equipment to prevent personal, laboratory and environmental exposure to potentially infectious agents or biohazards.

### ***Biological containment or biocontainment***

means the system and procedures designed to prevent the accidental release of biological material. The objective of biocontainment is to confine biohazards and to reduce the potential exposure of the laboratory worker, animals on other studies, persons outside of the laboratory, and the environment to potentially infectious agents.

### ***Bioexclusion***

means the prevention of the unintentional transfer of pathogenic organisms and subsequent infection of animals by human, vermin or other means.

### ***Humane endpoint***

means the point at which an experimental animal's pain and/or distress is terminated, minimized or reduced, by taking actions such as giving treatment to relieve pain and/or distress, terminating a painful procedure or humanely killing the animal.

### ***Genetically altered animal (GA animal)***

means an animal that has had a random or targeted change in its nuclear or mitochondrial DNA achieved through a deliberate human technological intervention.

### ***Harm-benefit analysis***

means the process of weighing the likely adverse effects (harms) on the animals against the benefits likely to accrue as a result of the proposed project. The analysis should require more than just establishing that the benefit is likely to exceed the harms. The benefits should be maximised and the harms, in terms of animal use and suffering, should be minimised.

### ***The Three Rs***

means the internationally accepted philosophy of Russell and Burch (1959) for the use of animals in research. The Three Rs comprise:

- **replacement** which refers to methods which do not require the use of animals to achieve the scientific aims;
- **reduction** which refers to methods that enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals;
- **refinement** which refers to methods that prevent, alleviate or minimise known and potential pain, distress, discomfort or lasting harm and/or enhance animal welfare for the animals used; or which replace higher animals with those of lower neurophysiological sensitivity which have less capacity to experience pain, distress, discomfort or lasting harm.

### ***Environmental enrichment***

means increasing the complexity (e.g., with toys, cage furniture, foraging opportunities, social housing, etc.) in a captive animal's environment to foster the expression of species-typical behaviours and reduce the expression of aberrant behaviours, as well as provide cognitive stimulation.

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### **Scope**

These standards apply to animals as defined in the *Terrestrial Code* (excluding bees) bred, supplied and/or used in research, testing or teaching. Animals to be humanely killed for harvesting their cells, tissues and organs for scientific purposes are also covered. Members should consider both the species and the developmental stage of the animal.

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### **The Oversight Framework**

The role of *Competent Authorities* is to implement a system (governmental or other) for verification of compliance by institutions. This usually involves a system of approval (such as licensing or registering of institutions, scientists, and/or projects) and compliance may be assessed at the institutional, regional and/or national level.

The framework for compliance should comprise three key elements:

1. Project Proposal review,
2. Facility Inspections; and
3. Animal Care and Use Programme (ACUP) Review.

Different systems of oversight may involve animal welfare officers, regional/local committees, or national bodies. One common system is for each institution using live animals for research to have

an Animal Care and Use Committee (ACUC) that is responsible, at the institutional level, for ensuring compliance with applicable requirements regarding the use of live animals as well as cells, tissues and organs derived from live animals. It is important that an ACUC should report to a senior individual within the institution to ensure the committee has an appropriate level of authority and support. An ACUC should undertake periodic review of its own policies, procedures and performance.

In providing this oversight, the following expertise should be included, as a minimum:

- one scientist with experience in animal research, whose role is to ensure that protocols are designed and implemented in accordance with sound science;
- one veterinarian, with the necessary expertise to work with research animals, whose specific role is to provide advice on the care, use and welfare of the animals.

Additional expertise may be sought from the animal care staff, as these professional and technical staff are centrally involved in ensuring the welfare of animals used.

Other participants may include statisticians, information scientists and ethicists and biosafety specialists, as appropriate to the studies conducted.

It may be appropriate to involve representatives of the community (general public) or, in teaching institutions, a student representative. This increases public confidence in the oversight process.

#### 1. Project Proposal Review

*Project Proposals* should be reviewed and approved prior to commencement of the research and should include a description of the following elements:

- a) the scientific aims;
- b) the experimental design, including statistics where appropriate;
- c) the experimental procedures;
- d) methods of handling and restraint and consideration of alternatives such as animal training and operant conditioning;
- e) the application of the Three Rs;
- f) the methods to avoid or minimise pain, discomfort, distress or lasting impairment of physical or physiologic function,, including the use of anaesthesia and/or analgesia;
- g) application of humane endpoints and the final disposition of animals, including methods of euthanasia;
- h) consideration of the husbandry and care of the species proposed to be used, including environmental enrichment and any special housing requirements;

- i) consideration of the relevance of the experiment to human or animal health or the advancement of biologic knowledge;
- j) an assessment for any occupational health and safety risks; and
- k) resources/infrastructure necessary to support the proposed work (e.g. facilities, equipment, qualified staff).

The provision of a non-technical (lay) summary may enhance understanding of the project.

The oversight body has a critical responsibility in determining the acceptability of *project proposals*, taking account of the animal welfare implications, the advancement of knowledge and scientific merit, as well as the societal benefits, in a risk-based assessment of each project using live animals.

Following approval of a project proposal, consideration should be given to implementing an oversight method to ensure that animal activities conform with those described in the approved project proposal.

## 2. Facility inspection

There should be regular inspections of the facilities. These inspections should include the following elements:

- a) the animals and their records, including cage labels;
- b) husbandry practices;
- c) maintenance and cleanliness and security of the facility;
- d) type and condition of caging and other equipment;
- e) environmental conditions;
- f) occupational health and safety concerns.

Principles of risk-management should be followed when determining the frequency and nature of inspections.

## 3. Animal Care and Use Programme (ACUP) Review

Critical elements of the Animal Care and Use Programme (ACUP) should be included in relevant regulations to empower the government authority to take appropriate action to ensure compliance. The ACUP should be reviewed regularly to include the following:

- a) training and competency of all staff;
- b) the programme of veterinary care;



- c) husbandry and operational conditions;
- d) sourcing and final disposition of animals; and
- e) occupational health and safety programme;

A requirement for keeping records on animal use, as appropriate to the institution, project proposal and species, should be included. It may be appropriate to maintain such records on a regional or national basis and to provide some degree of public access without compromising personnel or animal safety, or releasing proprietary information.

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#### **Assurance of Training and Competency**

An essential component of the ACUP is the assurance that the personnel working with the animals are appropriately trained and qualified to work with the species used and the procedures to be performed. A system (institutional, regional or national) to assure competency should be in place. Continuing professional and paraprofessional education opportunities should be made available to relevant staff.

- a) Scientists. Due to the specialised nature of animal research, focused training should be undertaken to supplement educational and experiential backgrounds of scientists (including visiting scientists) before initiating a study. Focused training may include such topics as the national and/or local regulatory framework, institutional policies and ethical considerations. The laboratory animal veterinarian is often a resource for this and other training. Competency in performance of procedures related to the scientist's research (e.g., surgery, anaesthesia, sampling and administration, etc.) should be verified.
- b) Veterinarians. It is important that veterinarians working in an animal research environment have veterinary medical knowledge and experience in the species used and they should understand research methodology. Relevant approvals issued by the *Veterinary statutory body* and appropriate national schemes (where these exist) should be adopted as the reference for veterinary training.
- c) Animal Care Staff. Animal care staff should receive training that is consistent with the scope of their work responsibilities and their competency in the performance of these tasks should be verified.
- d) Students. Wherever possible, students should learn scientific and ethical principles using non-animal methods (videos, computer models, etc). Wherever it is necessary for students to participate in classroom or research activities involving animals, they should receive appropriate supervision in the use of animals until such time that they have demonstrated competency in the related procedure(s).

## Provision of Veterinary Care

Adequate veterinary care includes responsibility for promoting and monitoring an animal's welfare before, during and after research. Veterinary care includes attention to the physical and behavioural status of the animal. The veterinarian must have the authority and responsibility for making judgements concerning animal welfare.

- a) Clinical Responsibilities. Preventive medicine programmes that include vaccinations, ectoparasite and endoparasite treatments and other disease control measures should be initiated according to currently acceptable veterinary medical practices appropriate to the particular animal species and source. Disease surveillance is a major responsibility of the veterinarian and should include routine monitoring of colony animals for the presence of parasitic, bacterial and viral agents that may cause overt or sub clinical diseases. The veterinarian must have the authority to use appropriate treatment or control measures, including euthanasia if indicated, and access to appropriate resources, following diagnosis of an animal disease or injury. Where possible, the veterinarian should discuss the situation with the scientist to determine a course of action consistent with experimental goals. The veterinarian has the responsibility to ensure that controlled drugs prescribed by the veterinary staff are managed in accordance with applicable regulations.
- b) Veterinary Medical Records. Medical records are considered to be a key element of a programme of adequate veterinary care for animals used in research, teaching, and testing. Application of performance standards within the medical record program allows the veterinarian to effectively employ professional judgment, ensuring that the animal receives the highest level of care available.
- c) Advice on zoonotic risks and notifiable diseases. The use of some species of animals poses a significant risk of the transmission of zoonotic disease (e.g., some nonhuman primates). The veterinarian should be consulted to identify sources of animals that minimize these risks and to advise on measures that may be taken in the animal facility to minimize the risk of transmission (e.g., personal protective equipment, air pressure differentials in animal holding rooms, etc.). Animals brought into the institution may carry diseases that require notification to government officials. It is important that the veterinarian be aware of, and complies with these requirements.
- d) Advice on surgery and postoperative care. A programme of adequate veterinary care includes input into the review and approval process of preoperative, surgical and postoperative procedures by an appropriately qualified veterinarian. A veterinarian's inherent responsibility includes monitoring, and providing recommendations concerning, preoperative procedures, aseptic surgical techniques, the qualifications of institutional staff to perform surgery and the provision of postoperative care.
- e) Advice on analgesia and anaesthesia. Adequate veterinary care includes providing guidance to animal users and monitoring animal use to ensure that appropriate methods of handling and restraint are being used as well as the proper use of anaesthetics, analgesics, tranquilizers, and methods of euthanasia for all species.
- f) Advice on humane endpoints and euthanasia. Endpoints are established for both experimental and humane reasons. An experimental endpoint is chosen to mark the planned end of an experimental manipulation and associated data gathering. In experiments with unrelieved or

unanticipated pain/or distress, humane endpoints are criteria that indicate or predict pain, distress, or death and are used as signals to end a study early to avoid or terminate pain and/or distress. Ideal endpoints are those that can be used to end a study before the onset of pain and/or distress without jeopardizing the study's objectives. However, in most cases, humane endpoints are developed and used to reduce the severity and duration of pain and/or distress.

The veterinarian and the ACUC where applicable, have a key role in ensuring that approved humane endpoints are followed during the course of the study. It is essential that the veterinarian have the responsibility and authority to ensure euthanasia is carried out as required to relieve pain and distress unless the *Project Proposal* approval specifically does not permit such intervention on the basis of the scientific purpose.

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### Physical Facility and Environmental Conditions

A well-planned, well-designed, well-constructed, and properly maintained facility should include animal holding rooms as well as areas for support services such as for procedures, surgery and necropsy, cage washing and appropriate storage. An animal facility should be designed and constructed in accordance with all applicable building standards. The design and size of an animal facility depend on the scope of institutional research activities, the animals to be housed, the physical relationship to the rest of the institution, and the geographic location. For indoor housing, non-porous, non-toxic and durable materials should be used which can be easily cleaned and sanitised. Animals should normally be housed in facilities dedicated to, or assigned for, that purpose. Security measures (e.g., locks, fences, cameras, etc.) should be in place to protect the animals and prevent their escape. For many species (e.g., rodents), environmental conditions should be controllable to minimise physiological changes which may be potentially confounding scientific variables and of welfare concern.

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### Source of animals

Animals to be used for research should be of high quality to ensure the validity of the data.

- a) Animal procurement. Animals should be acquired legally. It is preferable that animals are purchased from recognised sources producing or securing high quality animals.

Purpose bred animals should be used whenever these are available and animals that are not bred for the intended use should be avoided unless scientifically justified or the only available source. The use of non purpose bred animals, including farm animals, non-traditional breeds and species, and animals captured in the wild, is sometimes necessary to achieve study goals.

- b) Documentation. Relevant documentation related to the source of the animals, including health and other certification, breeding records, genetic status and animal identification, should accompany the animals.
- c) Animal health status. The health status of animals can have a significant impact on scientific outcomes. There also may be occupational health and safety concerns related to animal health status. Animals should have appropriate health profiles for their intended use. The health status of animals should be known before initiating research.

- d) Genetically defined animals. A known genetic profile of the animals used in a study can reduce variability in the experimental data resulting from genetic drift and increase the reproducibility of the results. Genetically defined animals are used to answer specific research questions and are the product of sophisticated and controlled breeding schemes which must be validated by periodic genetic monitoring, typically using biochemical or immunological markers. Detailed and accurate documentation of the colony breeding records must be maintained
- e) Genetically altered animals. If genetically altered animals are used, such use should be conducted in accordance with relevant regulatory guidance. Consideration should be given to addressing special husbandry and welfare needs associated with abnormal phenotypes. Records should be kept of biocontainment requirements, genetic information, and individual identification, and be communicated by the animal provider to the recipient.
- f) Animals captured in the wild. If wild animals are to be used, the capture technique should be humane and give due regard to human and animal health and safety. Endangered species should only be used in exceptional circumstances where there is strong scientific justification which cannot be achieved with any other species.
- g) Transport, importation and exportation. Animals should be transported under conditions that are appropriate to their physiological and behavioural needs and pathogen status, with care to ensure appropriate physical containment of the animals as well as exclusion of contaminants. The amount of time animals spend on a *journey* should be kept to a minimum. It is important to ensure that relevant documentation accompanies animals during transport to avoid unnecessary delays during the *journey* from the sender to the receiving institution.
- h) Biosecurity risks. To reduce biosecurity risks related to animals, the pathogen status of animals should be confirmed and appropriate biocontainment and bioexclusion measures should be practised. Biosecurity risks to animals arising from exposure to humans should also be addressed.

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### Husbandry

High standards of care and accommodation enhance the health and welfare of the animals used and contributes to the scientific validity of animal research. Animal care and accommodation should, as a minimum, demonstrably conform to relevant, published national or international animal care, accommodation and husbandry guidelines.

- a) Acclimatisation. Newly received animals should be given a period for physiological and behavioural stabilisation before their use. The length of time for stabilisation will depend on the type and duration of animal transportation, the species involved, place of origin, and the intended use of the animals.
- b) Normal Behaviour. The housing environment and husbandry practices should take into consideration the normal behaviour of the species and age of the animal and minimise stress to the animal.
- c) Enrichment. Animals should be housed with a goal of maximising species-specific behaviours and minimising stress-induced behaviours. One way to achieve this is to enrich the structural and social environment of the research animals and to provide opportunities for physical and

cognitive activity. Such provision should not compromise the health and safety of the animals or people, nor significantly interfere with the scientific goals.

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### Occupational Health and Safety

Institutional occupational health and safety programmes should be developed and implemented to protect personnel from workplace hazards. National or state legislation requires employers to provide a safe working environment for staff. In addition to national or state legislative requirements, particular precautions need to be in place for those involved in the care and use of animals. These measures should extend to animal users, animal care staff, students, and others who may be exposed to animals or animal by products.

Occupational health and safety training for animal related risks should be provided as part of the assurance of training and competency for personnel. Specific training may be required for particular species, and for specific procedures/studies involving animals.

a) Infectious diseases. To protect personnel, all infectious diseases or potentially infectious diseases within the institution, including zoonoses, should be identified.

i) Biological Hazards

Hazards can arise from pathogens that are endemic to the particular animals as well as from pathogens (bacteria, viruses, parasites, fungi, prions) that have been brought into an institution for research purposes. National or state regulations or guidelines for working with biological hazards (biohazards) must be followed. These should include requirements for biocontainment, laboratory design, personal hygiene and safety. Any biohazardous materials should be labelled as such. Necropsy of animals with highly infectious agents should be carried out in certified biological safety cabinets. Animals, animal waste and carcasses should be disposed of appropriately, depending on the pathogenicity of the organisms to which they have been exposed. Material contaminated with highly infectious agents should be decontaminated before disposal.

ii) Zoonoses

The institutional veterinarian(s) should be able to provide input to the occupational health and safety program concerning any zoonoses (infections that are secondarily transmitted from animals to humans) that might be contracted from the species used by the institution. He/she should also be able to provide advice on the measures needed to protect those involved with the animals. These may include personal protective equipment, vaccination, special restrictions for vulnerable employees (e.g., pregnant women). In general, the closer phylogenetically a species is to humans, the greater the likelihood of zoonoses.

Particular precautions should be taken when working with non-human primates

b) Allergies

Individuals exposed to laboratory animals run a risk of developing allergies. Protective measures should be in place for personnel who may be exposed to animal allergens. These should include:

Environmental control and air handling systems to control air flow and contain allergens in the areas where the animals are housed and/or used;

Personal protective equipment such as masks, gloves and clothing dedicated to animal rooms;

Equipment such as filtered bedding disposal units and ventilated hoods for carrying out procedures;

Use of filtered transfer cages when transporting animals.

c) Physical injuries

Injuries that can be incurred as a result of handling animals include: bites, scratches, or being kicked, stepped on or crushed by larger species. These injuries can be minimized by ensuring that all personnel are: competent to handle the animals; aware of the particular hazards associated with each species; familiar with the hazards of the experiment; are provided with a proper working area and protective clothing; and have access to and use the appropriate restraining equipment or drugs. A mechanism should be in place to deal with animal inflicted injury, including referral for further medical treatment. Cuts, bites, scratches or needle punctures acquired while working with non-human primates require particular attention and should be reported to the medical authority designated by the institution.

Other physical injuries can occur as a result of working in a laboratory animal facility (e.g. burns, injuries from lifting animals or heavy equipment, repetitive strain injuries). These should be minimized through the implementation of an occupational health and safety programme, which examines the workplace hazards and ensures that adequate safeguards are in place for personnel.

d) Chemical injuries

There are potentially hazardous materials involved in most animal-based studies. These include drugs; cleaning agents and chemical compounds used for research studies. All hazardous substances must be labelled appropriately. The relevant national or state authority should provide licences to veterinarians or scientists requiring access to drugs for animal based studies. Licence holders are thereby responsible and liable for the use of substances purchased by them. Drugs must be handled, stored and used according to the requirements of national or state legislation.

Material Safety Data Sheets should be made available to personnel who are likely to come into contact with hazardous materials. Personnel should also be trained to use hazardous materials safely.

e) Radiation

Where radioactive materials are to be used, the national authority responsible for nuclear safety should be informed. National authorities should require personnel to obtain a licence and should impose restrictions on the use of radioisotopes. A radiation safety officer should be designated within the institution to be responsible for radioactive material use and disposal. Strict measures should be in place to limit and contain radioactive contamination, including appropriate signage and limiting access to rooms containing radioactive material. Strict

measures should also be in place to protect personnel working with radioactive animals, and staff in the vicinity, from exposure to the animals, animal wastes and carcasses.

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### **Post Approval Monitoring**

The institution should ensure that a culture of compliance exists within the animal care and use programme. Key to that compliance is assuring that studies are conducted in accordance with the written description in the project proposals that has been approved by the oversight body (animal care and use committee, government agency, etc.). The focus of post approval monitoring is to determine what happens to the animals after approval of the work has been granted and the study is underway. Such monitoring may be achieved through animal observations made during the conduct of routine husbandry procedures; observations made by the veterinary medical staff during their rounds; or by inspections by an animal care and use committee, animal welfare officer, compliance/quality assurance officer or government inspector

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