

TERRESTRIAL ANIMAL HEALTH STANDARDS COMMISSION REPORT - MARCH 2008

ANNEX

OIE GUIDELINES ON RESEARCH ANIMAL WELFARE

Preamble

The purpose of this Annex is to provide a conceptual framework for OIE Members to consider when formulating regulatory requirements for the use of live animals in research, testing and teaching.

The OIE recognises the vital role played by the use of live animals in research, testing and teaching. As stated in the OIE Guiding Principles, such use makes a major contribution to the wellbeing of people (and animals). The OIE also recognises the status of animals as sentient beings and the OIE Guiding Principles for animal welfare emphasise the importance of the Three Rs of Russell and Burch.

The system used in practice will 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 Guidelines in formulating a regulatory framework that is appropriate to their conditions. This framework may be delivered through a combination of national, sub-national and local jurisdictions and both public sector and private sector responsibilities should be clearly defined.

The OIE recognises the central role played by veterinarians not only for their training and specialist skills but also as a 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.

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 from the animal's perspective rather than inputs from a 'systems-design' perspective. At the institutional level the Animal Care and Use Committee plays a critical role in determining the acceptability and protocols for animal use, taking account of the animal welfare implications, the scientific merit and the societal benefit, in a risk-based assessment of each project using live animals.

Definitions (to be developed)

Animal Care and Use Committee (ACUC)

Project Proposal

Operant conditioning

Biocontainment

Bioexclusion

Humane endpoint

Genetically altered animals (GA animals)

Scope

These guidelines apply to the use of animals as defined in the Terrestrial Animal Health Code (the *Terrestrial Code*) (excluding bees) in procedures in research, testing and teaching. Animals killed for the primary purpose of harvesting their cells, tissues and organs for use in scientific procedures are also covered. These recommendations are directed to:

All terrestrial vertebrate species, including foetal/embryonic developmental stages from the last third of the developmental period (refer AHAW Report).

In developing an appropriate regulatory framework, member countries should consider both the species and the developmental stage of the animal.

Note: the *ad hoc* Group also recommended that these Guidelines also address aquatic animals, including fish, some amphibians, and some invertebrate species (eg cyclostomes, Cephalopoda and decapod crustaceans) (refer AHAW Report). Given that the OIE's standard setting work in relation to these animals falls under the auspices of the Aquatic Animal Health Standards Commission, the OIE will forward the report of *ad hoc* Group to the this Commission for consideration.

Preamble

The *Terrestrial Code* states that the internationally recognised 'Three Rs' (reduction in numbers of animals, refinement of experimental methods and replacement of animals with non-animal techniques) provide valuable guidance for the use of animals in science.

Most scientists and governments agree that animal testing should cause as little pain and/or distress to animals as possible, and those animal tests should only be performed where necessary. The "Three Rs" of Russell and Burch (1959) (http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm) are guiding principles for the use of animals in research, testing and training. They comprise:

- Reduction 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.
- Replacement refers to the use of non-animal methods over animal methods, or a lower order species, whenever it is possible to achieve the same scientific aim.
- Refinement refers to methods that prevent, alleviate or minimise potential pain and/or distress and enhance animal welfare for the animals still used.

It is the responsibility of all researchers using animals to ensure that they give due regard to these principles in designing and implementing their research protocols.

Animal Care and Use Programme

Each facility using live animals for research, testing and teaching should have an Animal Care and Use Committee (ACUC) that is responsible, at the institutional level, for ensuring compliance with government requirements for the use of live animals and, in particular, their welfare.

The role of Competent Authorities is to implement a system (governmental or other) of verification of compliance by institutions. This often involves a system of approval (such as licensing of institutions, scientists, and projects) and compliance is assessed by a variety of methods

Critical elements of the Animal Care and Use Programme (ACUP) should be the subject of legislation to empower the government to take appropriate action to ensure compliance with requirements. In some countries, transparency is an important element in the ACUP and is desirable to support public confidence in the regulatory framework. Likewise, a requirement for keeping records on animal use as appropriate to the institution should be included. It may be appropriate to maintain such records on a regional or national basis and to provide some form of public access to such records in order to provide public transparency and confidence.

I. Animal Care and Use Committee (ACUC)

a) Roles and Responsibilities (To be developed)

i) Project Proposal Review

- Review – All projects should undergo an evaluation comprising of:
 - assessment of the scientific aims;
 - consideration of experimental design including statistics where appropriate;
 - consideration of the husbandry and care of the species proposed to be used;
 - incorporation of the Three Rs – replacement, reduction and refinement;
 - assignment of a severity class,
 - an assessment of any health and safety risks;
 - an assessment of the harm-benefit analysis, and
 - an assessment of methods of restraint and alternatives to restraint such as animal training and *operant conditioning*.
- The review might also include a non-technical summary of the project proposal

ii) Facility inspection

- The ACUC should perform regular inspections of the facilities, some of which should be unannounced. Principles of risk-management should be followed when determining the frequency and nature of inspections.
- The inspection team should include more than one member of the ACUC.

iii) ACUP Review

- The ACUC should be responsible for review of the overall ACUP including :
 - Training and competency of all staff;
 - The programme of veterinary care;
 - The physical facility and environmental conditions;

- Husbandry and operational conditions;
 - Sourcing of animals;
 - Staff Occupational Health and Safety programme; and
 - Collection of accurate statistics on the use of animals within the facility to meet government requirements.
- Reporting structure. It is important that the ACUC should report to a senior individual within the institution who has the authority to implement the Committee's recommendations.

b) Committee Composition

The ACUC should include:

one or more scientists, whose role is to ensure that protocols are designed and implemented in accordance with sound science, that the research is appropriate and valuable, and to ensure compliance with regulatory requirements relevant to research conducted at the establishment.

one or more veterinarians, preferably with competence to work with research animals, whose specific role is to provide advice on the care, use and welfare of the animals.

In addition, it is important to include a member of the animal care staff in the ACUC as these professionals are centrally involved in ensuring the welfare of animals used at the establishment.

Other participants in the ACUC may include statisticians, information scientists and ethicists as appropriate to the studies conducted at the establishment.

It may be appropriate to include representatives of the community (general public) in which the facility is located. This can help to support public confidence that the establishment management takes its responsibilities seriously and that the establishment consistently complies with regulatory requirements.

II. Assurance of Training and Competency

An essential component of the animal care and use program is the assurance that the personnel working with the animals are appropriately trained and qualified to work with the species used and to support the research mission. A system (e.g., institutional, regional, national, etc.) to assure competency should be in place. Continuing professional education opportunities should be made available to relevant staff.

- a) Scientists. Due to the specialised nature of animal research, focused training should be offered to supplement educational and experiential backgrounds of researchers (including visiting scientists) before initiating the study. The laboratory animal veterinarian often is a resource for this focused training. Competency in performance of procedures related to their research (e.g., surgery, anaesthesia, dosing, 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 have a working knowledge of 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 (also see Annex 2).

- c) Animal Care Staff. Animal care staff should be offered 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 about animal research 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 oversight in the use of animals until such time that they have demonstrated competency in the related procedure(s).

III. Provisions of Veterinary Care

Adequate veterinary care includes responsibility for the promotion and monitoring of an animal's welfare before, during and after experimentation or testing. Animal welfare includes both physical and psychological aspects of an animal's condition evaluated in terms of environmental comfort, freedom from pain and distress and appropriate social interactions, both with conspecifics and with man. The veterinarian must have the authority and responsibility for making determinations concerning animal welfare and assuring that animal welfare is adequately monitored and promoted.

- a) Clinical Responsibilities. Preventive medicine programmes such as vaccinations, ecto- and endoparasite treatments and other disease control measures should be initiated according to currently acceptable veterinary medical practices appropriate to the particular 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 disease. The veterinarian must have authority to use appropriate treatment or control measures, including euthanasia if indicated, following diagnosis of an animal disease or injury. If possible, the veterinarian should discuss the situation with the principal investigator to determine a course of action consistent with experimental goals. The veterinarian has the responsibility to ensure that controlled drugs 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 research animals poses a risk of the transmission of zoonotic disease (e.g., 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 of government officials. It is important that the veterinarian be aware of, and comply, with these requirements.
- d) Advice on surgery and postoperative care. A programme of adequate veterinary care includes the review and approval of all preoperative, surgical and postoperative procedures by a qualified veterinarian. A veterinarian's inherent responsibility includes monitoring and providing recommendations concerning preoperative procedures, 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 assure that appropriate methods of handling and restraint are being used and to ensure proper use of anaesthetics, analgesics, tranquilizers, and methods of euthanasia. Written guidelines regarding the selection and use of anaesthetics,

analgesics and tranquilizing drugs and euthanasia practices for all species used must be provided and periodically reviewed by the veterinarian.

- f) Advice on humane endpoints and euthanasia. Humane 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 has a key role in ensuring that humane endpoints, as approved by the ACUC, are followed during the course of the study. It is essential that the veterinarian have the responsibility and authority to ensure euthanasia is administered as required to relieve pain and distress in research animals, provided such intervention is not specifically precluded in protocols reviewed and approved by the ACUC.

IV. Physical Facility and Environmental Conditions

A well-planned, well-designed, well-constructed, and properly maintained facility is an important element of good animal care and use, and it facilitates efficient, economical, and safe operation. 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. An animal facility should be designed and constructed in accordance with all applicable building standards. Animals should be housed in facilities dedicated to or assigned for that purpose and should not be housed in laboratories merely for convenience. Security measures (e.g., locks, fences, cameras, etc.) should be in place to protect the animals. For many species (e.g., rodents, , environmental conditions should be controllable to minimize physiological changes in the animals due to the stress of accommodating to changing temperature, humidity, light, noise, etc.

V. Husbandry

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

- a) Acclimatisation. Regardless of the duration of quarantine, newly received animals should be given a period for physiological, psychological, and biochemical stabilization before their use. The length of time for stabilization will depend on the type and duration of animal transportation, the species involved, country of origin, and the intended use of the animals.
- b) Enrichment. Animals should be housed with a goal of maximizing species-specific behaviors and minimizing stress-induced behaviors. 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 or interfere with the research goals.
- c) Normal Behavior. The housing environment and husbandry practices should take into consideration the normal behavior of the species to minimize stress and facilitate the production of sound research data.

VI. Source of animals

Animals to be used for research, testing and teaching should be of high quality to ensure reproducibility of research and testing accordingly.

- a) Legal and humane procurement. The acquisition of animals should be made legally. It is preferable that animals are purchased from recognized institutions producing high quality research animals.

It is desirable to use purpose bred animals where these are available. The use of animals that are not bred for the intended use should be avoided if possible.

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) Animal health status. Animals should have appropriate health profiles for their intended use. Health status of animals should be known before initiating research.
- c) Genetically altered animals. If genetically altered animals have to be used, relevant legislation should be observed. Records of biocontainment requirements, genetic information, and individual identification should be kept and communicated between the provider and recipient.
- d) Animals captured in the wild. If wild animals need to be used, the capture technique should be humane with due regard to human and animal health and safety.
- e) Reuse of animals. If animals have to be reused, the approval of the ACUC should be obtained. All animals to be reused should have a good health status. JM to provide further advice
- f) Transport, importation and exportation. Animals should be transported under conditions that are appropriate to their physiological and behavioural needs and microbiological status, with care to ensure appropriate containment (see OIE Appendix on transport of animals)
- g) Biosecurity risks. To reduce biosecurity risks related to research animals, the microbiological status of research animals should be confirmed and appropriate biocontainment and bioexclusion should be provided. Biosecurity risks to animals arising from exposure to humans should also be addressed.

VII. Occupational Health and Safety (To be developed -scratch, biting kicking, physical, chemical and radiation risks Study related risk)

Institutional measures for occupational health and safety should be extended to the animal care and use programme. Appropriate measures should be taken to protect animal users, animal care staff and students and others who may be exposed to animals or animal by products. An educational program for occupational health and safety should be implemented.

- a) Infectious diseases including zoonotic diseases. To protect the staff in research settings, infectious diseases including zoonotic diseases should be identified. Appropriate health protection measures should be effected.
- b) Allergies. Risks can be minimised by the occupational health and safety programme, including facility ventilation, biocontainment, appropriate equipment and health protection measures (e.g. mask, eye protection, gown, gloves).

VIII. Importance of post approval monitoring and validation

Following the approval of a protocol, a post approval monitoring system should be implemented to ensure the consistency of procedures and the validation of results.

List of references (To be developed)