General Comment: Please note that throughout this document, the use of the "strikethrough" is intended to indicate deleted wording; the use of the "double underline" is meant to indicate inserted wording.

Terrestrial Animal Health Standards Commission Report

September 2009

CHAPTER 7.X.

USE OF ANIMALS IN RESEARCH AND EDUCATION

Preamble

The purpose of this chapter is to provide advice and assistance for OIE Members to follow when formulating regulatory requirements, or other form of oversight, for the use of live *animals* in research ~~,~~ and education [1]. A system of animal use 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~~ guidelines in formulating a regulatory framework that is appropriate to their local conditions. This framework may be delivered through a combination of jurisdictions at the level of the country, the region and/or the institution and both public sector and private sector responsibilities should be clearly defined.

- **Rationale:** If the purpose of this chapter is to provide, as stated, "advice and assistance" for OIE members, then the information contained therein should be referred to as "guidance" or "guidelines", rather than standards. In many countries, the use of the term "standard" implies setting requirements as opposed to providing advice.

The OIE recognises the vital role played by the use of live *animals* in research and education. The OIE Guiding Principles for Animal Welfare 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). The OIE also recognizes the International Guiding Principles for Biomedical Research Involving Animals which were developed by the Council for International Organizations of Medical Sciences (CIOMS, 1985)(Figure X/Annex XX). The OIE encourages countries to consider incorporating such principles into national policies for the humane care and use of laboratory animals in biomedical research. Most scientists and members of the public agree that the *animals* should only be used when necessary and ethically justified (thereby avoiding unnecessary duplication of animal based research); that the minimum number of *animals* should be used to achieve the scientific or educational goals; and that such use of *animals* should cause as little pain and/or distress as possible.

- **Rationale:** The CIOMS Principles are requested to be incorporated as an Annex, or alternatively as a Figure in the body of the text, as they represent an existing, internationally approved conceptual and ethical framework regarding the use of animals for scientific purposes. Reference to these Principles is inserted in other areas within this chapter for this reason.

The OIE emphasises the need for humane treatment of sentient *animals* and that good quality science depends upon good *animal welfare*. It is the responsibility of all involved in the use of *animals* to ensure that

[1] Wherever the term "research" is used, it includes basic and applied research, testing and the production of biological materials; "education" includes teaching and training.

they give due regard to these recommendations. In keeping with the overall approach to *animal welfare* detailed in the OIE Guiding Principles and the CIOMS Guiding Principles, the OIE stresses the importance of standards based on outcomes for the *animal*.

- **Rationale**: See above reference to CIOMS Principles.

The OIE recognises the significant role of *veterinarians* in animal based research. Given their unique training and skills, they are essential members 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 leads to high quality scientific and educational outcomes and optimum *welfare* for the *animals* used.

The OIE recommends that records on animal use should be maintained, as appropriate to the institution and project proposals and species used, on a regional or national basis. These records may be used to provide a degree of public transparency, without compromising personnel or animal safety, or releasing proprietary information.

Article 7.X.1

Definitions

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.

Biosecurity:

means a continuous process of *risk assessment* and *risk management* designed to minimise or eliminate microbiological *infection* with adventitious organisms that can cause clinical *disease* in the infected *animals* or humans, or make *animals* unsuitable for biomedical research. A comprehensive biosecurity programme not only seeks to prevent contamination but also to minimise the loss of *animals* and scientific data, and to limit the spread of unwanted microorganisms should contamination occur.

Biological containment or biocontainment

means the system and procedures designed to prevent the accidental release of biological material ~~including allergens~~. 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.

- **Rationale:** While allergens are a hazard to consider in the laboratory environment, they are not considered as having the same status as hazardous infectious agents. The principles of containment, as stated in *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), focus on fundamentals to protect laboratory workers, the environment and the public from infectious microorganisms.

Bioexclusion

means the prevention of the unintentional transfer of adventitious organisms with subsequent *infection* of *animals*, resulting in adverse effects on their health or suitability for research.

Cloned animal

means a genetic copy of another living or dead *animal* produced by somatic cell nuclear transfer or other reproductive technology.

Distress

means the state of an *animal*, that has been unable to adapt ~~completely~~ to stressors, and that manifests as abnormal physiological or behavioural responses. It can be acute or chronic and may result in pathological conditions.

- **Rationale:** Distress is not an "all or none" phenomena, therefore the use of a modifying term in the definition is not appropriate.

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 non-injurious species-typical behaviours and reduce the expression of maladaptive behaviours, as well as provide cognitive stimulation.

Euthanasia

means the act of inducing *death* using a method that results in rapid loss of consciousness and minimum pain or distress to the *animal*.

Ethical review

means consideration of the validity and justification for using *animals* including: the potential ~~harms~~ for pain and/or distress to the *animals* and likely benefits of the use and how these balance; experimental design; implementation of the Three Rs; animal husbandry and care and other related issues such as staff training. Ethical judgements are influenced by prevailing societal attitudes.

- **Rationale:** The term "harm" is not used in the regulatory schemes of many countries, and no definition is provided in this document. Suggest substituting "pain and/or distress" as more widely recognized terms.

Endangered species

means a population of organisms which is at risk of becoming extinct because it is either few in numbers, or threatened by changing environmental or predation parameters.

Genetically altered animal (GA animal) (also genetically modified animal and genetically engineered animal)

means an *animal* that has had a random or targeted change in its nuclear or mitochondrial DNA, or the progeny of such an *animal(s)*, where they have inherited the change, achieved through a deliberate human technological intervention.

- **Rationale**: The United States suggests including in the definition the two other terms/phrases that are in common usage and are often regarded to be synonymous with "genetically altered animal", as this guidance will be read by a wide range of individuals who may be more familiar with these terms.

Humane endpoint

means the point in time at which an experimental *animal*'s pain and/or distress is avoided, terminated, minimised or reduced, by taking actions such as giving treatment to relieve pain and/or distress, terminating a painful procedure, removing the *animal* from the study, or humanely killing the *animal*. Ideal humane endpoints are those that can be used to end a study before the onset of pain and/or distress, without jeopardising the study's objectives. In consultation with the *veterinarian*, humane endpoints should be described in the Project Proposal and, thus, established prior to commencement of the study. They should form part of the ethical review. Endpoint criteria should be easy to assess over the course of the study. Except in rare cases, *death* (other than euthanasia) as a planned endpoint is considered ethically unacceptable.

~~*Harm-benefit analysis*~~

~~means the process of weighing the likely adverse effects (harms) to the *animals* against the benefits likely to accrue as a result of the proposed project. The benefits should be maximised and the harms, in terms of pain and distress, should be minimised.~~

- **Rationale**: The harm-benefit analysis is a tool used for the ethical evaluation of human studies. Research and teaching activities involving animals must be conducted humanely, but these activities are not necessarily undertaken to provide benefit to the individual animals in question. Suggest instead substituting the term "Ethical review" and its definition within this document.

The Three Rs

means the internationally accepted tenet, first described by ~~of~~ Russell and Burch (1959), for the use of *animals* in research and education. The Three Rs comprise the following alternatives:

- **replacement** ~~which~~ refers to the use of methods utilizing cells, tissues or organs of vertebrate animals (relative replacement), as well as those that do not require the use of vertebrate *animals* to achieve the scientific aims (absolute replacement);

- **reduction** ~~which~~ refers to the use of 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 the use of methods that prevent, alleviate or minimise ~~known and potential~~ pain, distress or lasting harm and/or enhance *welfare* for the *animals* used. Refinement includes the appropriate selection of species with a lesser degree of structural and functional complexity in their nervous systems and a lesser apparent capacity for experiences that derive from this complexity. Opportunities for refinement should be considered and implemented throughout the lifetime of the *animal* and include, for example, housing and transportation as well as procedures and euthanasia.

- **Rationale:** Inserted "the use of" as editorial suggestions for clarification. Added language from Russell and Burch to clarify the concepts of absolute and relative replacement. Lastly, an editorial clarification to delete the adjectives "known and potential" as the verbs "prevent, alleviate or minimise" already address these concepts.

Operant (Instrumental) conditioning

means the association that an *animal* makes between a particular response (such as pressing a bar) and a particular reinforcement that may be positive (for example, a food reward) or negative (e.g. a mild electric shock). 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).

Project Proposal (or Protocol)

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

- **Rationale:** Again recommend the term "quality" be deleted, as this could be open to various interpretations and may lead to inconsistent application of this definition.

Pain

Means an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It may elicit protective actions, result in learned avoidance and distress and may modify species-specific traits of behaviour, including social behaviour.

Article 7.X.2.

Scope

These standards apply to *animals* as defined in the *Terrestrial Code* (excluding bees) bred, supplied and/or used in research, ~~(including testing)~~ and ~~higher~~ education. *Animals* to be used for production of biologicals and/or 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* in implementing these standards.

- **Rationale:** Editorial suggestion, as the term "testing" has been incorporated into "research" by the footnote on page 1 of this Chapter. Deleted "higher", as the title of this chapter refers only to "education", and no definition is provided for what is meant by "higher education".

Article 7.X.3.

The Oversight Framework

The role of a *Competent Authority* is to implement a system (governmental or other) for verification of compliance by institutions. This usually involves a system of authorisation (such as licensing or registering of institutions, scientists, and/or projects) and compliance which may be assessed at the level of the country, the region and/or the institution.

- **Rationale:** Editorial suggestion for clarification.

A requirement for keeping records on animal use, as appropriate to the institution, p*roject 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.

The oversight framework encompasses both ethical review of animal use and considerations related to animal care and *welfare*. This may be accomplished by a single body or distributed across different groups. Different systems of oversight may involve *animal welfare* officers, regional/local committees, or national bodies. Typically each institution utilises a local committee (often referred to as Animal Care and Use Committee, Animal Ethics Committee or Animal Care Committee) to deliver this oversight framework. Where the local committee does not perform ethical review, this may be undertaken by regional or national ethical review bodies. It is important that the local committee reports to senior management within the institution to ensure it has appropriate authority, resources and support. Such a committee should undertake periodic review of its own policies, procedures and performance.

In providing this oversight and ensuring the implementation of the Three Rs, 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 such *animals*.

- one public member to represent general community interests who is independent of the institution and is not involved in the use of *animals* in research.

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, in teaching institutions, to involve a student representative.

Oversight responsibilities include three key elements:

1. Project Proposal Review

   Project Proposals, or significant amendments to these, should be reviewed and approved prior to commencement of the work, should identify the person with primarily responsibility for the project and should include a description of the following elements, where relevant:

   a) the scientific or educational aims, including consideration of the relevance of the experiment to human or animal health, the environment, or the advancement of biological knowledge;

   b) an informative, non-technical (lay) summary may enhance understanding of the project and facilitate the ethical review of the proposal by allowing full and equitable participation of members of the local committee who may be dealing with matters outside their specific field. Subject to safeguarding confidential information, such summaries may be made publicly available.

   c) the experimental design, including justification for choice of species, source and number of *animals*, including any proposed reuse;

   d) the experimental procedures;

   e) methods of handling and restraint and consideration of refinements such as animal training and operant conditioning;

   f) the methods to avoid or minimise pain, discomfort, distress or lasting impairment of physical or physiological 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 general health, husbandry and care of the species proposed to be used, including environmental enrichment and any special housing requirements;

   i) ~~ethical~~ Considerations such as the application of the Three Rs and ~~a harm/benefit analysis~~ an ethical review;
      - **Rationale**: See recommended change to "Definitions", Section 7.x.1.

   j) an indication of any special health and safety risks; and

k) resources/infrastructure necessary to support the proposed work (e.g. facilities, equipment, ~~qualified~~ staff trained and found competent to perform the procedures described in the proposed project).

- **Rationale:** Clarification to distinguish between generally qualified staff and those whose credentials must be considered in terms of the specific procedures that are proposed.

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. This process is often referred to as post approval monitoring. Such monitoring may be achieved through animal observations made during the conduct of routine husbandry procedures; observations made by the veterinary staff during their rounds; or by inspections by the local oversight committee, *animal welfare* officer, compliance/quality assurance officer or government inspector.

2. Facility inspection

There should be regular inspections of the facilities, at least annually. These inspections should include the following elements:

a) the *animals* and their records, including cage labels and other methods of animal identification;

- **Rationale**: As mentioned in our previous comments, a variety of methods (e.g., tattoos, microchips), in addition to cage labels, are appropriately used to identify animals. The most appropriate method will depend on animal type and housing design, and should not be limited to only cage labels.

b) husbandry practices;

c) maintenance, cleanliness and security of the facility;

d) type and condition of caging and other equipment;

e) environmental conditions of the *animals* at the cage and room level;

f) procedure areas such as surgery; necropsy and animal research laboratories.

g) support areas such as washing equipment; animal feed, bedding and drug storage locations.

h) 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 review

The animal care and use programme–reflects the policies and practices of the institution. It should include the functioning of the local oversight committee; training and competency of staff; veterinary care; husbandry and operational conditions, including emergency plans; sourcing and final disposition of *animals*; and occupational health and safety. The programme should be reviewed regularly and should be

included in relevant regulations to empower the *Competent Authority* to take appropriate action to ensure compliance.

Article 7.X.4.

Assurance of Training and Competency

An essential component of the animal care and use programme 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, including ethical considerations. A system (at the level of the country, the region and/or the institution) to assure competency should be in place, which includes supervision during the training period. Continuing professional and paraprofessional educational opportunities should be made available to relevant staff. Senior management, given their overarching responsibility for the animal care and use programme, should be knowledgeable about related issues.

1. Scientific staff

   Researchers using *animals* have a direct ethical ~~and legal~~ responsibility for all matters relating to the *welfare of the animals* in their care. 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 and institutional policies. The laboratory animal *veterinarian* is often a resource for this and other training. Scientific staff should have demonstrated competency in procedures related to their research (e.g. surgery, anaesthesia, sampling and administration, etc.).

   - **Rationale:** It is beyond the scope of the OIE and this Article, specifically, to recommend legal structure for animal welfare oversight. This will vary according to individual Member country's needs.

2. Veterinarians

   It is important that *veterinarians* working in an animal research environment have veterinary medical knowledge and experience in the species used, including normal behaviour, and they should understand research methodology. Relevant approvals issued by the *Veterinary statutory body* and appropriate national or regional schemes (where these exist) should be adopted as the reference for veterinary training.

3. Animal Care Staff

   Animal care staff should receive training that is consistent with the scope of their work responsibilities and have demonstrated competency in the performance of these tasks.

4. Students

   Students should learn scientific and ethical principles using nonanimal methods (videos, computer models, etc) when such methods can effectively reduce or replace the use of *animals* and still meet learning objectives. 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).

5. Members of the local oversight committee or others involved with oversight

Continuing education about the use of *animals* in research and education, including associated ethics, regulatory requirements and their institutional responsibility, should be provided.

Occupational health and safety training for research animal related risks should be provided as part of the assurance of training and competency for personnel. This might include consideration of human infectious *diseases* which may infect research *animals* and thus compromise research results, as well as possible zoonoses. Personnel should understand that there are two categories of hazards, those that are intrinsic to working in an animal facility and those associated with the research. Specific training may be required for particular species, for specific procedures, and for the use of appropriate protective measures for personnel who may be exposed to animal allergens. Research materials, such as chemicals of unknown toxicity, biological agents and radiation sources, may present special hazards

Article 7.X.5.

Provision of Veterinary Care

Adequate veterinary care includes responsibility for promoting an *animal*'s health and *welfare* before, during and after research procedures and providing advice and guidance based on best practice. Veterinary care includes attention to the physical and behavioural status of the *animal*. The *veterinarian* must have authority and responsibility for making judgements concerning *animal welfare*. Veterinary advice and care should be available at all times.

Rationale: It is useful to place a clear emphasis on both health care and welfare. As outlined under the section on clinical responsibilities below, having access to a veterinarian to provide such care, not just advice, emphasizes the need for the veterinarian to be able to assess a clinical situation and develop a diagnosis with potential courses of treatment.

1. 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. Controlled drugs prescribed by the veterinary staff must be managed in accordance with applicable regulations.

2. Post mortem examinations

   In the case of unexpected *disease* or *deaths*, the *veterinarian* should provide advice based on post mortem examination results. As part of health monitoring, a planned programme of post mortem examinations may be considered.

3. Veterinary Medical Records

   Medical records, including post mortem records, are considered to be a key element of a programme of adequate veterinary care for *animals* used in research and education. Application of performance standards within the medical record programme allows the *veterinarian* to effectively employ professional judgment, ensuring that the *animal* receives the highest level of care available.

4. 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 minimise 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, appropriate disinfection procedures, 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.

- **Rationale**: Suggest including "appropriate disinfection procedures" as another very relevant example.

5. 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 providing advice concerning preoperative procedures, aseptic surgical techniques, the competence of staff to perform surgery and the provision of postoperative care. Veterinary oversight should include the detection and resolution of emerging patterns of surgical and post procedural complications.

6. Advice on analgesia, anaesthesia and euthanasia

Adequate veterinary care includes providing advice on the proper use of anaesthetics, analgesics, and methods of euthanasia.

7. Advice on humane endpoints

Humane endpoints should be established prior to commencement of a study in consultation with the *veterinarian* who also plays an important role in ensuring that approved humane endpoints are followed during the course of the study. It is essential that the *veterinarian* have the 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 and the ethical evaluation.

Article 7.X.6.

Source of animals

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

1. Animal procurement

Animals must 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.-In the case of farm *animals*, non traditional breeds and species, and *animals* captured in the wild, non purpose bred *animals* are often used to achieve specific study goals. The use of wild caught nonhuman primates is generally discouraged.

2. Documentation

Relevant documentation related to the source of the *animals*, ~~including~~ such as health and other veterinary certification, breeding records, genetic status and animal identification, should accompany the *animals*.

- **Rationale:** Suggested change for clarification, as not all of these types of records may be available for the animals.

3. 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.

4. 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~~ DNA assays. Detailed and accurate documentation of the colony breeding records must be maintained

- **Rationale:** Today, biochemical or immunological markers are seldom used for genetic monitoring. Instead, a variety of DNA assays have become the most common means of monitoring for genetic authenticity. The use of the phrase "DNA assays" is more technically appropriate.

5. Genetically altered or cloned animals

If genetically altered or cloned *animals* are used, such use should be conducted in accordance with relevant regulatory guidance. ~~With such *animals*, as well as harmful mutant lines arising from spontaneous mutations,~~ Consideration should be given to addressing and monitoring special husbandry and *welfare* needs associated with abnormal phenotypes. ~~Records should be kept of~~ Information regarding biocontainment and bioexclusion requirements, genetic information, and phenotypic information related to individually identified animals ~~individual identification, and be communicated~~ should be provided by the animal provider to the recipient. Archiving and sharing of genetically altered lines is recommended to facilitate the sourcing of these customised *animals*.

- **Rationale:** Editorial changes suggested for clarification, and to add more examples of useful information regarding these types of animals.

6. 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. Field studies have the potential to cause disturbance to the habitat thus adversely affecting both target and non-target species. The potential for such disturbance should be assessed and minimised. The effects of a series of stressors, such as trapping, handling, transportation, sedation, anaesthesia, marking and sampling, can be cumulative, and may produce severe, possibly fatal, consequences. An assessment of the potential sources of stress and management plans to eliminate or minimise distress should form part of the Project Proposal.

7. Endangered species

Endangered species should only be used in exceptional circumstances where there is strong scientific justification that the desired outcomes cannot be achieved using any other species.

8. 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.

9. Risks to biosecurity

~~To reduce risks to biosecurity 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.~~ In order to minimise the risk of contamination of animals with unwanted infectious microorganisms or parasites that may compromise the health of animals or make them unsuitable for use in research, the microbiological status of the animals should be determined and regularly assessed. Appropriate biocontainment and bioexclusion measures should be practised to maintain their health status and, if appropriate, measures taken to prevent their exposure to certain human or environmental commensals.

- **Rationale**: It is important to understand the microbiological status of animals acquired for biomedical research purposes—most commonly by setting up an exclusion list and assessing for organisms of concern. There should be some regular assessment of the microbiological status in order to assure that status has not changed making the animals unsuitable for their intended purpose. The wording of the original paragraph implies that exposure to humans necessarily is associated with an unacceptable biosecurity risk. In fact, depending upon the genotype and phenotype of the animals in question, there may be certain issues with infection with human and environmental commensals that might not be of concern with other genotypes and phenotypes.

Article 7.X.7.

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 designed 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.

Important environmental parameters to consider include ventilation, temperature and humidity, lighting and noise:

1. Ventilation

The volume and physical characteristics of the air supplied to a room and its diffusion pattern influence the ventilation of an *animal*'s primary enclosure and are thus important determinants of its microenvironment. Factors to consider when determining the air exchange rate include range of possible

heat loads; the species, size, and number of *animals* involved; the type of bedding or frequency of cage changing; the room dimensions; and the efficiency of air distribution from the secondary to the primary enclosure. Control of air pressure differentials is an important tool for biocontainment and bioexclusion.

2. Temperature and humidity

   Environmental temperature is a physical factor which has a profound effect on the *welfare* of *animals*. Typically, animal room temperature should be monitored and controlled. The range of daily fluctuations should be kept to a minimum to avoid repeated large demands on the *animals*' metabolic and behavioural processes to compensate for changes in the thermal environment. Relative humidity may also be controlled, but not nearly as narrowly as temperature.

3. Lighting

   Light can affect the physiology, morphology and behaviour of various *animals*. In general, lighting should be diffused throughout an animal holding area and provide appropriate illumination for the *welfare* of the *animals* while facilitating good husbandry practices, adequate inspection of *animals* and safe working conditions for personnel. It may also be necessary to control the light/dark cycle.

4. Noise

   Separation of human and animal areas minimises disturbance to animal occupants of the facility. Noisy *animals*, such as dogs, pigs, goats, and nonhuman primates, should be housed away from quieter *animals*, such as rodents, rabbits, and cats. Consideration should be given to insulating holding rooms and procedure rooms to mitigate the effects of noise sources. Many species are sensitive to high frequency sounds and thus the location of potential sources of ultrasound should be considered.

Article 7.X.8.

Husbandry

Good husbandry practices enhance the health and *welfare* of the *animals* used and contribute to the scientific validity of animal research. Animal care and accommodation should, as a minimum, demonstrably conform to relevant published animal care, accommodation and husbandry guidelines and regulations.

The housing environment and husbandry practices should take into consideration the normal behaviour of the species, including their social behaviour and age of the *animal*, and should minimise stress to the *animal*. During the conduct of husbandry procedures, personnel should be keenly aware of their potential impact on the *animals*' *welfare*.

1. Transportation

   Transportation ~~is a typically~~ can be a stressful experience for *animals* ~~should be transported~~. Every precaution should be taken to avoid unnecessary stress through inadequate ventilation, exposure to extreme temperatures, lack of feed and water, long delays, etc. Consignments of *animals* should be accepted into the facility without avoidable delay and, after inspection, should be transferred to clean cages or pens and be supplied with feed and water as appropriate.

   - **Rationale:** The use of the phrase "can be a" stressful experience more appropriately characterizes transportation of animals. Studies sponsored by DEFRA have shown in livestock that the process of loading and unloading appears to be the stressful components of transportation and not necessarily the journey itself. With respect to the phrase "should be transported", this appears to be a typographical error and has no relevance in this sentence.

2. 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 transportation, the age and species involved, place of origin, and the intended use of the *animals*. Facilities should be available to isolate *animals* showing signs of ill health.

3. Cages and pens

Cages and pens should be made out of material that can be readily cleaned and decontaminated. Their design should be such that the *animals* are unlikely to injure themselves. Space allocations should be reviewed and modified as necessary to address individual housing situations and animal needs (for example, for prenatal and postnatal care, obese *animals*, and group or individual housing). Whenever it is appropriate, social *animals* should be housed in pairs or groups, rather than individually, provided that such housing is not contraindicated by the protocol in question and does not pose an undue risk to the *animals*.

4. Enrichment

Animals should be housed with a goal of maximising species ~~specific~~ appropriate behaviours and avoiding or 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.

- **Rationale:** The term "specific" may not be well understood in this context, and suggest using the word "appropriate" as a substitution. We are again recommending deleting the use of a modifier such as "significant", as it may create confusion. Providing enrichment should not be an obstacle in achieving the scientific goals of the experiment.

5. Feeding

Provision should be made for each *animal* to have access to feed to satisfy its physiological needs. Precautions should be taken in packing, transporting, ~~and~~ storing and preparing feed to avoid chemical, physical and microbiological contamination, deterioration or destruction. Utensils used for feeding should be regularly cleaned and, if necessary, sterilised.

- **Rationale:** The addition of the word 'preparing' addresses another area of potential mishandling of the food.

6. Water

Uncontaminated potable drinking water should normally be available at all times. Watering devices, such as drinking tubes and automatic watering systems, should be checked daily to ensure their proper maintenance, cleanliness, and operation.

7. Bedding

Animal bedding is a controllable environmental factor that can influence experimental data and *animal welfare*. Bedding should be dry, absorbent, non-dusty, non-toxic and free from infectious agents, vermin or chemical contamination. Soiled bedding should be removed and replaced with fresh material as often as is necessary to keep the *animals* clean and dry.

8. Hygiene

The successful operation of a facility depends very much on good hygiene. Special care should be taken to avoid spreading *infection* between *animals* through fomites, including through personnel traffic between animal rooms. Adequate routines and facilities for the cleaning, washing, decontamination and, when necessary, sterilisation of cages, cage accessories and other equipment should be established. A very high standard of cleanliness and organisation should also be maintained throughout the facility.

9. Identification

Animal identification is an important component of record keeping. *Animals* may be identified individually or by group. Where it is desirable to individually identify *animals*, this should be done by a reliable and the least painful method.

General Comment: Strongly recommend that the list of references provided in the March 2009 draft document remain as a component of this document in its final form and that the references be organized by topic or application to assist utilization.