# DRAFT GUIDELINES FOR THE USE OF

# ANIMALS IN RESEARCH

# AT RHODES UNIVERSITY

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**Definitions**:

**What is an Experimental Animal?**
"Experimental Animal" means any living non-human vertebrate, non-human vertebrate foetus, or any other animal species with in the opinion of the Ethical Standards committee, has a nervous system which is so sophisticated that it might be capable of experiencing pain in much the same way that any vertebrate might experience it.

**What is an animal experiment?**
An "Animal Experiment" is any procedure involving the use of live animals in which the aim is to test a hypothesis, collect information and advance, impart or demonstrate knowledge, test or collect a product, or register the effect of a certain procedure on an animal.

**Introduction**
Research using animals contributes to the quality of life by expanding knowledge about living organisms. This improvement in quality of life stems in part from progress towards ameliorating human disease and disability, in part from advances in animal welfare and veterinary medicine, and in part from the steady increase in knowledge of the abilities and potentialities of human and animal life. Continued progress in many areas of biomedical research requires the use of living animals in order to investigate complex systems and functions because, in such cases, no adequate alternatives exist. Progress in both basic and clinical research in such areas cannot continue without the use of living animals as experimental subjects. The use of living animals in properly designed scientific research is therefore both ethical and appropriate. Nevertheless, our concern for the humane treatment of animals dictates that we weigh carefully the benefits to human knowledge and welfare whenever animal research is undertaken. The investigator using research animals assumes responsibility for proper experimental design, including ethical as well as scientific aspects.

The scientific community shares the concern of society at large that the use of animals in research should conform to standards that are consonant with those applied to other uses of animals by humans. While it is unlikely that any particular set of standards will satisfy everyone, it is appropriate for scientific societies to formulate guidelines that apply to the humane use of laboratory animals in particular areas of research. Ideally, such guidelines should also be acceptable to society at large as reasonable and prudent.

Most of the more specific sections of this document were formulated with respect to research using warm-blooded vertebrates. As a general principle, however, ethical issues involved in the use of any species, whether vertebrate or invertebrate, are best considered in relation to the complexity of that species' nervous system and its apparent awareness of the environment, rather than physical appearance or evolutionary proximity to humans.

**Factors that Relate to the Design of the Experiments**
The primary factor used to evaluate humane treatment in animal research is degree of distress or

discomfort, assessed by anthropomorphic judgments made by reasonable and prudent human observers. *The fundamental principle of ethical animal research is that experimental animals must not be subjected to avoidable distress or discomfort.* This principle must be observed when designing any experiment that uses live animals.

Although most animal research involves minimal distress or discomfort, certain valid scientific questions may require experimental designs that inevitably produce these effects. Such situations, while uncommon, are extremely diverse and must be evaluated individually. It is critical that distress and discomfort be minimized by careful experimental design. It is also important to recognize that there is no difference between distress and discomfort that may be inherent in a valid experimental design and that which may occur as an unintended side effect. It is therefore incumbent on the investigator to recognize and to eliminate all *avoidable* sources of distress and discomfort in animal subjects. This goal often requires attention to specifics of animal husbandry as well as to experimental design.

Invasive procedures and paralytic drugs should never be employed without benefit of anesthetic agents unless there is a very strong scientific justification and careful consideration is given to possible alternatives. Advances in experimental techniques, such as the use of devices chronically implanted under anesthesia, can offer alternative approaches. If these are not feasible, it is essential to monitor nociceptive responses (for example, recordings of EEG, blood pressure and pupillary responses) that may indicate distress in the animal subject, and to use these as signals of the need to alleviate pain, to modify the experimental design, or to terminate the experiment.

When designing research projects, investigators should carefully consider the species and numbers of animals necessary to provide valid information, as well as the question whether living subjects are required to answer the scientific question. As a general rule, experiments should be designed so as to minimize the number of animals used and to avoid the depletion of endangered species. Advances in experimental methods, more efficient use of animals, within-subject designs, and modern statistical techniques all provide possible ways to minimize the numbers of animals used in research. This goal is completely consistent with the critical importance of replication and validation of results to true progress in science.

**Factors that Relate to the Conduct of Experiments**

Research animals must be acquired and cared for in accordance with the guidelines published in the *South African Medical Research Council Guide for the Use and Care of animals for research*. The use of an animal scheduled for euthanasia by a pound or shelter saves the life of another; therefore, the use of pound or shelter animals is endorsed for research projects in which they are suitable subjects. In using animals acquired from a pound or shelter, as with all other aspects of research, investigators must adhere to the relevant local and national laws. The quality of research data depends in no small measure on the health and general condition of the animals used, as well as on the specifics of the experimental design. Thus, proper animal husbandry is integral to the success of any research effort using living animal subjects. General standards for animal husbandry (housing, food quality, ventilation, etc.) must be met. The experienced investigator can contribute additional specifics for optimum care for particular experimental situations, or for species not commonly

encountered in laboratory settings.

Surgery performed with the intent that the animal will survive (for example, on animals intended for chronic study) should be carried out, or directly supervised, by persons with appropriate levels of experience and training, and with attention to asepsis and prevention of infection. Major surgical procedures should be done using an appropriate method of anesthesia to render the animal insensitive to pain. Muscle relaxants and paralytics have no anesthetic action and should not be used alone for surgical restraint. Postoperative care must include attention to minimize discomfort and the risk of infection.

Many experimental designs call for surgical preparation under anesthetic agents with no intent that the animal should survive. In such cases, the animals ordinarily should be maintained unconscious for the duration of the experiment. At the conclusion of the experiment, the animal should be killed without regaining consciousness and death ensured before final disposition.

Certain experiments may require physical restraint, and/or withholding of food or water, as methodological procedures rather than experimental paradigms. In such cases, careful attention must be paid to minimize discomfort or distress and to ensure that general health is maintained. Immobilization or restraint to which the animals cannot be readily adapted should not be imposed when alternative procedures are practical. Reasonable periods of rest and readjustment should be included in the experimental schedule unless these would be absolutely inconsistent with valid scientific objectives.

When distress or discomfort are unavoidable attributes of a valid experimental design, it is mandatory to conduct such experiments so as to minimize these effects, to minimize the duration of the procedure and to minimize the numbers of animals used, consistent with scientific objectives of the study.

## WHAT RESEARCHERS SHOULD PREPARE

If your research requires the use of animals, there are several steps you should follow, regardless of whether or not you think your work may be questioned.

### Make Sure Your Research Complies with Applicable University Regulations

Every researcher using animals at Rhodes University should automatically comply with the appropriate following policies and regulations. These are cited below:

### Prerequisites for the use of animals in research at Rhodes University

- The main purpose of any animal experimentation must be to gain usable results and scientific information of high quality to the benefit of humans and animals. The experimentation must therefore not be purposeless or unnecessary.
- The experiment must be carefully and scientifically planned, based on the available knowledge of the disease or problem being studied and designed so that the expected results, wherever possible, will justify the experiment. A written protocol should

therefore be prepared (before each experiment) which clearly indicates the purpose of the experiment as well as all procedures to be carried out. No experiment on animals must start before the research protocol has been passed by the RUESC.

- All attempts should be made to keep the use of animals to a minimum. Care should be taken to ensure that the correct species is chosen and that animals with all the necessary genetic attributes and microbiological qualities are chosen to ensure reliable results.
  The application of *in vitro* biological systems, statistical analyses and mathematical models should be considered as alternatives to supplement or replace animal experimentation. These alternatives must not only be considered on the grounds of humane principles but also because they generally demand less time, space, equipment and funding.
- Where the experiment inflicts inescapable pain or more pain than the use of anaesthetics would cause, the proper use of analgesics or the administration of anaesthesia according to recognised veterinary practice is obligatory until the procedure is completed. The only exception to this principle is in cases where the administration of anaesthesia would nullify the aims of the experiment and the results could not be obtained by any other more humane method. If approved, the Committee must then appoint a veterinarian to take responsibility for the welfare of the animals subjected to those procedures. As a general guide, researchers should accept that any procedure which will cause pain to humans will also cause pain to other vertebrates.

- The scientist in charge of any animal experiment must be prepared to terminate it if it becomes clear that the continuation thereof will cause unwarranted pain and suffering. If the procedure causes serious injury, the animal should be killed before recovery from anaesthesia. If it becomes clear that an animal will suffer unwarranted pain or discomfort after an experimental procedure, it should be killed in a humane manner. The veterinarian must have an overriding discretion as to when animals shall be killed or withdrawn from an experiment for humane reasons.
- The clinical care of experimental animals before, after and during the application of the experimental procedure must be of high standard and according to accepted veterinary practice so that pain, discomfort and any detrimental effects, caused by the procedure, can be eliminated.
- If it becomes necessary to kill an experimental animal it must be done in a humane manner and according to accepted principles which ensure immediate death. It is preferable that only personnel with experience in the application of euthanasia are responsible for this task. No animal may be disposed of before there is absolute certainty that it is dead.
- Animals already used in an experimental procedure should not be subjected to it for a second time, unless the first procedure was harmless or non-invasive and left the animal in good health.
- No animal should be subjected to more than one procedure that causes significant pain.

**Care**

- The care of experimental animals should be under the direct control and supervision of a technician, preferably one with experience in animal experimentation. The supervisory personnel should also include the services of other technical staff and workers with experience and/or training in laboratory animal science.
- High standards should be maintained in the daily care of experimental animals. Special consideration should be given to regular feeding, adequate and clean water, hygienic surroundings, adequate ventilation and the elimination of excessive heat, cold or noise in the animals' environment. Care should be taken to eliminate disease, injury, overpopulation and stress factors and to safeguard the animals from endo- and ectoparasites. Careful and thorough supervision of the welfare of the animals is absolutely essential.
- Experimental animals should be kept under optimal conditions at all times. This includes good housing, correct environmental conditions with acceptable space for movement and opportunity for social inter-action except where non-compatibility or the requirements of the experiment prevent it. The animal holding cages as well as the premises in which the cages are housed should therefore meet with accepted minimum standards.
- Wild animals which are captured in their natural habitat, for research purposes, should be trapped in cages that meet with the standards of the nature conservation authorities. The traps should be visited regularly, preferably daily, to prevent animals being left without food and water for long periods.
- It is the duty of the head of the research department/institute to ensure that all researchers who use experimental animals have the necessary training and experience to do so correctly. In-service training programmes should be established at research departments/institutes to ensure that this requirement can be met.

**Transport**

- Experimental animals must be transported according to the recognised minimum standards and regulations for the transportation of animals.
- During transportation special care should be taken for the provision of good ventilation, the elimination of discomfort, excessive cold or heat and the spread of diseases.
- Provision must be made during long journeys for regular provision of food and water.
- Animals must be unloaded as quickly as possible on arrival at an airport, harbour or railway station. At their ultimate destination they must be removed from their transport cages immediately and placed in suitable permanent accommodation.
- Appropriate veterinary care must be given to animals found to be diseased, injured or in a poor state during travel or on arrival.

**Develop and Maintain and Animal Use Research Project File**

In addition to the files normally maintained for various aspects of your research project, you should start and regularly update a file that contains background material that would be useful in case there

were an enquiry into the use and care of animals used for your research. Specifically, this file should contain the following:

- Approved research grant documentation;
- Rhodes University Ethical Standards Committee-approved protocol and any other related documents;
- List of all research grants, fellowships, honors and awards received by researchers working on the project;
- Brief description, in non-technical terms, of your research projects goals and accomplishments. This statement should be prepared so that it could be given to the press or used in discussions with local groups. It should describe the nature of your research, why it is being conducted, why the use of animals is necessary, how the research will benefit humans and animals (either directly or in the long run).
- References that demonstrate your procedures are humane and necessary;

Every project that uses animals should have a separate file that includes the above information/documents.

**Coordinate with the Rhodes University Ethical Standards Committee**

Rhodes University should have a plan of action to respond to complainants. The plan should contain the following:

- Names and responsibilities of key people within the institution who should be contacted immediately if an incident occurs, e.g. security, administrative representative, veterinarian, animal care and use staff;
- Name of the individual who will be the official spokesperson;
- Lines of communication;
- Security procedures;
- Public relations procedures;
- Support groups within the community to contact;
- Other organizations to contact nationwide.

Ideally, the person designated to be the official spokesperson should not be a scientist who is working on the project, but rather someone who understands both the institution's animal care and use program and is accustomed to talking to the press and groups of people.

SOURCES:
1. Guidelines on Ethics for Medical Research, SA Medical Research Council (1993)
2. Handbook for the use of Animals in Neuroscience Research, Society for Neuroscience (USA)