THE ETHICAL USE OF LABORATORY ANIMALS FOR MEDICAL RESEARCH

10.1 REGULATIONS & RESPONSIBILITIES

Background

Animal research needs to be carefully regulated just like human research. Animals may benefit from the information gained through animal experiments and some research involving animals is conducted specifically for the purpose of improving animal health (e.g. veterinary medicine and animal husbandry research). But most animal research is conducted primarily for the benefit of humans, not animals. Moreover, unlike humans, animals cannot consent to participate in experiments or comment on their treatment, creating special needs that should be taken into consideration in their care and use.

Regulatory, Institutional and Voluntary (Local and/or Overseas) Oversight

Where animal research is involved, research institutions would be required to adhere to the local regulatory and/ or voluntary oversight.

- Animal & veterinary Service, Animal & Birds (Care and Use of Animals for Scientific Purposes) Rules (https://www.nparks.gov.sg/avs/resources/legislation)
- National Advisory Committee for Laboratory Animal Research, Guideline on the Care and Use of Animals for Scientific Purposes (2004) (Animal & Veterinary Service (a cluster of National Parks)
- Institutional guideline(s)

Responsibilities of Institutions

Institutions should assure that researchers adhere to the regulations and guidelines for the responsible care and use of animals. There may be an Institutional Officer, who in turn appoints a mandated Institutional Animal Care and Use Committee (IACUC), and administers institutional matters relating to the care and use of animals at the institutions.

The IACUC would oversee and evaluate all aspects of the institution's animal programme, procedures and facilities. Its members may include veterinarians, scientists, non-scientists and members who are not affiliated with the institution. Many IACUCs also have a researcher who does not use animals or a member who has expertise in ethics.

IACUC members are appointed by their institution and their responsibilities include:

- Reviewing and approval of all research protocols using animals
- Reviewing the institution's animal care programme
- Inspecting the institution's animal facilities (at least twice a year)
- Receiving and reviewing concerns raised about the care and use of animals

- Submitting reports to the Institutional Official

IACUCs, like that of the Institutional Review board; also have independent authority to suspend research projects if they determine that they are not being conducted in accordance with applicable requirements and/or regulations.

Research institutions with large animal research programmes generally have centralized animal care and use units that provide veterinary support, training in procedures and advice on analgesics, anesthesia, euthanasia and occupational health and safety. The staff employed in these units cannot approve research protocols nor make decisions specifically assigned to the institutions' IACUCs. However, they as animal professionals are an excellent source of information about the responsible care and use of animals in research.

Responsibilities of Researchers

Researchers intending to use animals in their research should:

- Know what activities are subject to regulation(s)
- Understand and follow the rules for research approval
- Obtain appropriate training
- Accept continuing responsibility for compliance through all stages of the research

In addition, regardless of the level of invasiveness on the use or study of living animals in a research, researchers should familiarize themselves with their responsibilities and check with someone in a position of authority before making any plans or undertaking any work.

Responsibilities of a research facility

Under the Animal & Birds (Care and Use of Animals for Scientific Purposes) Rules (Animals and Birds Act, Chapter 7, Section 80, 2007 Edition), any research facility that uses animals for scientific purposes must obtain a licence from the Animal & Veterinary Service (a cluster of National Parks). For Application Procedure & Conditions of Licensing, please click here.

As part of the licensing requirements, a research facility must comply with the Guidelines set forth by NACLAR for the proper care and use of animals for scientific purposes and allow the Animal & Veterinary Service to carry out inspections of its facilities.

10.2 PRINCIPLES FOR THE RESPONSIBLE USE OF ANIMALS IN RESEARCH

Before deciding whether to conduct an experiment on animals, researchers must decide whether it is ethically acceptable to use the animal in the experiment, given the purpose of the study, the experimental design, the methods used and the species of the animal. If it is decided that the animal has some moral value and that the experiment would harm the animal in some way (e.g. by causing pain, suffering, disability or death), then the experiment must be ethically justified given the expected benefits.

Researchers can conduct experiments on animals provided that sufficient moral justifications for the experiments are provided. Because many different animal species may have some degree of moral value, the moral burden of proof rest with researchers who intend to conduct experiments on animals; researchers do not have a moral free ticket regarding animal experimentation. Moreover, because animal species may differ with respect to their moral worth, an experiment can be morally acceptable in one species but not in a different species. For example, it may be morally acceptable to create a transgenic mouse that is prone to various forms of cancer instead of a chimpanzee or monkey as they have a greater moral value than mice by virtue of their higher degree of similarity to human beings.

Many animal welfare organisations find that some scientifically necessary experiments is acceptable, however, it should be kept to a minimum and conducted on animals low on the phylogenetic scale in ways that minimize pain and suffering. Should extensive animal experimentations be necessary and moral, sound scientific practices utilizing quality animal care, along with minimization of pain and distress should be justified. The Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research and Training is a guiding principle for researchers and IACUCs to make decisions about the responsible and appropriate use of animals in research. These principles specify the requirements for planning and conducting research and are useful for investigators and IACUCs. Apart from these principles, local regulations, and institutional guidelines provide further criteria for researchers and IACUCs to consider in assessing protocols.

Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research and Training:

- Follow the rules and regulations for the transportation, care and use of animals;
- Design and perform research with consideration of relevance to human or animal health, the advancement of knowledge or the good of society;
- Use appropriate species, quality and the minimum number of animals to obtain valid results, and consider non-animal models;
- Avoid or minimize pain, discomfort, and distress when consistent with sound scientific practices;
- Use appropriate sedation, analgesia or anesthesia;
- Painlessly kill animals that will suffer severe of chronic pain or distress that cannot be relieved;
- Feed and house animals appropriately and provide veterinary care as indicated;

- Assure that everyone who is responsible for the care and treatment of animals during the research is appropriately qualified and trained, and
- Defer any expectations to these principles to the appropriate IACUC.

The NACLAR Guidelines on the Care and Use of Animals for Scientific Purposes covers all aspects of the care and use of animals for scientific purposes including their use in teaching, field trials, environment studies, research diagnosis, product testing and the production of biological products. The NACLAR Guidelines aims to promote humane and responsible care and use of animals for scientific purposes. Further practical advice on ways to assure appropriate respect for animals are based on the principles of the 3Rs – Replacement, Reduction and Refinement.

- Replacement – When it is possible to answer a research question without using an animal, replace the animal with a methodology that does not use animals, such as cell studies or computer modeling. When it is possible to answer a scientific question using a morally "lower" species of animal, replace the "higher" species with a lower one.

- Reduction – When it is possible to answer a research question using a smaller number of animals, reduce the number of animals used.

- Refinement – Wherever possible, refine research methods, techniques, concepts and tolls to reduce the need for animals in research and to reduce harms to animals.

The 3Rs can be justified on the grounds that they minimize harm to animals and promote animal welfare within the context of animal experimentation. These 3Rs make sense only if one believes that the research protocols are likely to yield results with scientific, medical or social value. Thus, a fourth R should also apply to animal research:

- Relevance – Research protocols that use animals should address questions that have some scientific, medical or social relevance; all risks to animals need to be balanced against benefits to humans and animals.

According to Shamoo and Resnik (2009) a fifth R is also important (which plays a key role in the U.S. animal research regulations):

- Redundancy avoidance – Avoid redundancy in animal research whenever possible. Make sure a thorough literature search is carried out to ensure that the experiment has not already been done. If it has been done, provide good justification for repeating the work.

Avoiding redundancy is important to avoid using animals unnecessarily and wasting research resources.

Discussions about the responsible use of animals in research are not likely to dissipate in the near future. If animals are essential to the research and cannot be replaced; if researchers cannot reduce the experiment; and if researchers cannot further refine their methods to reduce pain and suffering, then presumably researchers have done all they can to meet their responsibility. However, do not forget that society does not have to permit the use of animals in research. It can seek to protect animals through complex and expensive regulations if it loses confidence in the research community's ability to regulate itself.

[The following chapter was adapted from the ORI Introduction to the Responsible Conduct of Research, U.S. Department of Health and Human Services (HHS), Steneck, N 2007.]

10.3 REFERENCES & ACKNOWLEDGEMENT: THE WELFARE OF LABORATORY ANIMALS

1) Animal & Veterinary Service, Animals in scientific research https://www.nparks.gov.sg/avs/animals/animals-in-scientific-research/naclar-guidelines/naclar-guidelines
2) Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International
3) National Parks Board Animals and Birds Act, Chapter 7, Section 80
4) National Advisory Committee on Laboratory Animal Research (NACLAR) Guidelines
5) National Institute of Health, Office of Laboratory Animal Welfare – Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animal (Policy)
6) National Parks: NACLAR Guidelines
7) National University of Singapore, Office of the Deputy President (Research & Technology) IACUC
8) Office of Laboratory Animal Welfare (OLAW)
9) Office of Research Integrity – Introduction to the Responsible Conduct of Research: The Welfare of Laboratory Animals
10) Responsible Conduct of Research – Chapter 11: The Use of Animals in Research, 2nd Edition, Adil E. Shamoo and David B. Resnik – 2009