CHAPTER 4

ETHICS AND ALTERNATIVES

I.   Ethics:

The use of animals in research, teaching and testing is an important ethical and political issue. Much of the discussion about this issue revolves around the relative value, or 'moral value', of humans and animals. When the needs of animals and humans come into conflict which takes precedence? Today there exists a wide spectrum of views on this subject, ranging from those concerned with animal 'rights' to those who view animals only as a resource to be exploited. All of these viewpoints have contributed to the development of ethical principles of animal use. These in turn have shaped animal use regulations promulgated by the USDA and the PHS and echoed by organizations such as AAALAC International, AALAS and the AVMA.

Advances in biology that began in the 1800s have provided some of the strongest arguments for imbuing animals with an enhanced moral value. By recognizing that the nervous systems of all vertebrate animals are very similar, it is assumed that activities that will cause a human pain or distress will likewise cause pain or distress to other animals. It is for these reasons that current animal use regulations require the use of analgesics, anesthetics and sedatives for any procedures on animals that may cause more than momentary pain or distress.

What once had been a clear physical and mental distinction between humans and animals has become much fuzzier with the understanding that evolution represents a continuum. Likewise, the assumption that there is a clear moral distinction between humans and animals also has become fuzzier, and it suggests that perhaps gradations in moral value should be applied to animals. Current legislation on animal use emphasized the idea of replacement of "higher" animals with "lower" animals, and requires environmental enrichment or human contact for intelligent, social animals such as non-human primates, or dogs and cats.

Current legislation also recognizes that there are diverse viewpoints about the moral value of animals. Thus, all live animal use in research, teaching or testing must be reviewed by a committee with diverse membership. There is also an emphasis on minimizing the overall use of animals. Proposals for animal use are reviewed based on the potential for learning new information, or for teaching skills or concepts that cannot be obtained using an alternative. There are also provisions for ensuring that animal use is performed in as humane a manner a possible, minimizing pain, distress or discomfort. These provisions include a requirement for a veterinarian to be employed at each institution, so that the needs of the animals are looked after by someone trained in and sympathetic toward animals' needs. In addition to the requirements for analgesics, anesthetics and sedatives to be used where needed, it is also required that all personnel with animal contact be trained in appropriate handling techniques and they be skilled in any experimental procedures that will be performed. Finally, basic husbandry requirements are specified, ensuring that an animal's food, water and shelter are provided for in an optimal manner. Deviations from the

numerous requirements are granted only if adequate justification is given which shows that the proposed experiment is scientifically and socially important, and that any methods to alleviate or pain or distress would frustrate the experimental objectives.

II. Alternatives

An important ethical principle of animal use in biomedical research is that alternatives to live animals should be used whenever possible. There is a legal requirement for documentation of a search for alternatives and an explanation as to why these alternatives were not found to be suitable or how alternatives were incorporated into the experimental design. The current definition of alternative that has become pervasive in the biomedical research setting is the "3R's": replacement, reduction and refinement.

A. **Replacement** means replacing "higher" animals with "lower" animals, or replacing live animals with non-animal models such as dummies, computer simulation or in-vitro systems. Microorganisms, plants, eggs, fish, amphibians, reptiles and invertebrates may be used in some studies to replace warm-blooded animals. Alternatively, live animals may be replaced with non-animal models, such as dummies or mechanical or computer models, audiovisual aids, or in vitro modeling.

Advantages of replacement include utilizing pre-existing knowledge for teaching, applying known principles to new systems to look for similarities, and using less expensive animals or models to screen large numbers of agents for toxicity or mutagenicity.

Disadvantages to replacement chiefly stem from the fact that any models are dependent on pre-existing information. In a system as complex as a live organism, all of the variables in physiology and pathology are not known. Thus, any research on new biological processes must utilize a living organism at some point.

B. **Reduction** means minimizing the number of animals needed to perform an experiment or teach a concept. Methods to achieve this include:

1. Performing pilot studies to determine some of the potential problems in an experiment before numerous animals are used

2. Designing a study to utilize animals as their own controls

3. Gathering a maximum amount of information from each animal, perhaps gathering data for more than one experiment concurrently

4. Consulting with a statistician to use only the numbers of animals required to achieve significance.

5. Minimizing variables such as disease, stress, diet, genetic, etc. that may affect experimental results

6. Performing appropriate literature searches and consulting with colleagues to ensure that experiments are not duplicated.

7. Using the appropriate species of animal so that useful data is collected

C. **Refinement** means refining experimental protocols to minimize pain or distress whenever possible. Examples of refinement include:

1. Identifying pain and distress and making plans for preventing or relieving it.

2. Setting the earliest possible endpoint for the experiment. That is, if the necessary information can be gathered before the animal experiences any ill effects from the experiment, this should be defined as the endpoint and the animals subsequently euthanized

3. Receiving adequate training prior to performing a procedure

4. Using proper handling techniques for animals

5. Ensuring that drug doses are correct and that drugs are not expired

6. Ensuring that procedures to be performed on the animal are reasonable for that species

7. Using appropriate analgesics and anesthetics for potentially painful procedures

8. Performing surgeries and procedure aseptically to prevent infection

9. Performing only a single major survival surgery on any one animal whenever possible

10. Performing appropriate post-surgical care, including thermoregulation and fluid balance

III. Searching for Alternatives

The animal protocol form asks for methods used to search for alternatives to animal use and to procedures that may cause more than slight pain or distress to animals. Examples of these would be a literature search (indexes searched and keywords used should be listed), consultation with peers in the field, and consultation with the National Agricultural Library's Animal Welfare Information Center or the Johns Hopkins Center for Alternatives to Animal Testing. The Animal Care Program website has information on resources to use for alternative searches.