

Research with Animals

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Objectives

- Describe situations when animals may be research subjects
- Identify laws and regulations that protect animals as research subjects in the U.S.
- Assess systems to protect animals as research subjects in institutions.



Why Use Animals in Medicine, Biology and Biomedical Research?

- Animals as parts
- Animals as factories
- Animals as models for human disease
- Animals as test subjects



Why Use Animals in Medicine, Biology and Biomedical Research?

- Animals to study basic physiology principles and integration of systems
- Animals for the study of animals and the environment
- Animals to study basic principles in biology
- Animals for the study of disease



3. Justification of use of animals in research, responsible conduct in research

- The use of animals in biomedical research has always played an important role in the acquisition of scientific knowledge for understanding basic biological processes and for improving the quality of life of humans and animals.
- Recently, the development and use of genetically modified animals have also given scientists the opportunity to better study the role of specific genes, and this has created new perspectives in combating and treating diseases such as gene therapy.
- Despite all the benefits, the use of animals in biomedical research continues to be a subject of debate with respect to its true value.
- Opponents on the use of animals in any kind of research believe that animal experimentation should be abolished immediately (Festing and Wilkinson, 2007).



- On the other hand, there are legal requirements that oblige scientists who conduct animal-based research to ensure that their experiments are conducted humanely in order to satisfy societal concerns and to ensure the quality of their experimental results (European Council, 1986).
- Ethical Justification: For many years, scientists justified the use of animals in their experiments solely by referring to their scientific value in human health and welfare.
- Aside from a purely anthropocentric perspective, ethical concerns about the compromised animal welfare in animal experimentation cannot be tempered by human benefits alone (Olsson et al., 2007).
- It is equally important that the benefits of the experiment are achieved with minimal negative consequences to the animals.



RCR includes Animal Research

- In US, laws protect animal research
 - US Department of Agriculture (USDA) Animal Welfare Regulations
 - US Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (OLAW)
 - “Guide” for the Care and Use of Laboratory Animals
 - Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International
 - American Veterinary Medicine Association (AVMA) Guidelines on Euthanasia



In US, laws protect animal research

- Facility inspection/approval required for animal research
- Institutional Animal Care and Use Committee (IACUC)
 - University committee that assures compliance with federal laws
 - Review and approve proposals that use animal subjects in research
 - Animal model and number are appropriate
 - Procedures are appropriate and minimize pain
 - Living conditions appropriate
 - Researchers are qualified to conduct research



Euthanasia

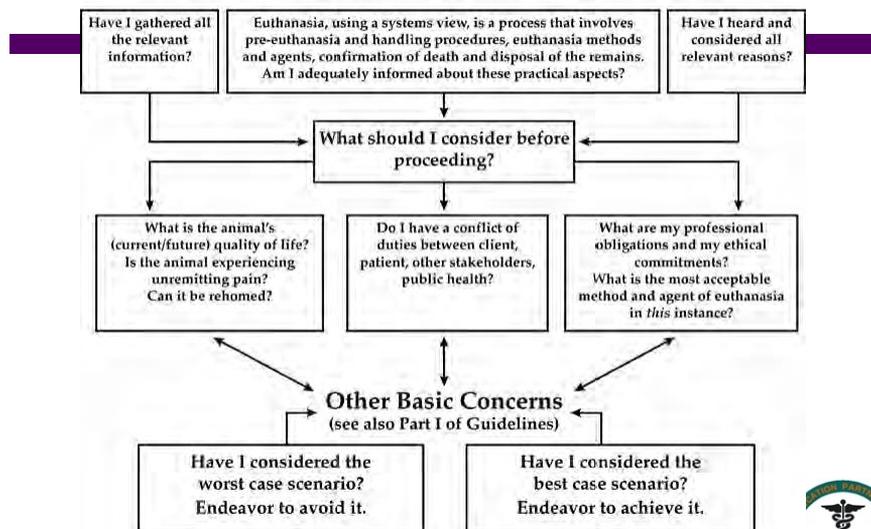
- When euthanasia is appropriate, either as a requirement of the research or because it constitutes the most humane form of disposition of a nonhuman animal at the conclusion of the research:
 1. Euthanasia must be accomplished in a humane manner, appropriate for the species and age, and in such a way as to ensure immediate death, and in accordance with procedures outlined in the latest version of the "AVMA (American Veterinary Medical Association) Guidelines on Euthanasia (2007)," available from http://www.avma.org/issues/animal_welfare/euthanasia.
 2. Disposal of euthanized laboratory animals must be conducted in accord with all relevant legislation, consistent with health, environmental, and aesthetic concerns, and as approved by the IACUC.
 - No animal shall be discarded until its death is verified



- Humane disposition reflects the veterinarian's desire to do what is best for the animal and serves to bring about the best possible outcome for the animal. Thus, euthanasia as a matter of humane disposition can be either intent or outcome based.
- Euthanasia as a matter of humane disposition occurs when death is a welcome event and continued existence is not an attractive option for the animal as perceived by the owner and veterinarian.
- When animals are plagued by disease that produces insurmountable suffering, it can be argued that continuing to live is worse for the animal than death or that the animal no longer has an interest in living.
- The humane disposition is to act for the sake of the animal or its interests, because the animal will not be harmed by the loss of life. Instead, there is consensus that the animal will be relieved of an unbearable burden.



Making a Decision Regarding Euthanasia



EVALUATING EUTHANASIA METHODS

- In evaluating methods of euthanasia, the POE considered the following criteria:
 - (1) ability to induce loss of consciousness and death with a minimum of pain and distress;
 - (2) time required to induce loss of consciousness;
 - (3) reliability;
 - (4) safety of personnel;
 - (5) irreversibility;
 - (6) compatibility with intended animal use and purpose;



- (7) documented emotional effect on observers or operators;
- (8) compatibility with subsequent evaluation, examination, or use of tissue;
- (9) drug availability and human abuse potential;
- (10) compatibility with species, age, and health status;
- (11) ability to maintain equipment in proper working order;
- (12) safety for predators or scavengers should the animal's remains be consumed;
- (13) legal requirements; and
- (14) environmental impacts of the method or disposition of the animal's remains.



Case Study 1: Untimely Death

A new lecturer is starting his first totally independent research project at a large biomedical research institution. This project is an outgrowth of the work he did previously. The project will examine the comparative efficacy and safety of two different types of bone implants with regard to their capacity to promote the healing of fractures. The study will be carried out in dogs.

He has submitted a protocol review form to the Institutional Animal Care and Use Committee (IACUC) and has obtained IACUC approval of the study. Twenty dogs are randomly assigned to either Group 1 or Group 2 and implanted with one of two devices. After eight weeks, the dogs will be sacrificed and the bones will be tested.

At six weeks, several animals in Group 2 die. The cause of death is unknown, but the animals appear anxious and uncomfortable at the time of death. The time course of the experiment is almost up, and he wants to continue with the hope that at least some of the animals in Group 2 will live to eight weeks.

As an alternative, he is considering sacrificing all animals at six weeks



Case Study 2: A Question of Sacrifice

- A second year graduate student in a neurosciences program. Is planning a research project. Having just completed his course work, he must design his own project of research. His special area of interest is in studying the effects of methamphetamine and related compounds on brain activity. These compounds are commonly abused as recreational drugs and, although many are illegal, new "designer drugs" or slightly different chemical variations, are developed on a regular basis by illicit drug manufacturers.
- One of his first considerations in designing his project is to find an appropriate animal model. In his review of the literature, he finds that cats are an adequate model because their brains are physiologically and anatomically similar to those of humans. Rhesus monkeys, however, have brains even closer to those of humans with more complex patterns of brain wave activity. His protocol would entail restraining the animal, hooking up electrodes, measuring brain activity both before and after administration of the drug, then sacrificing the animal to examine any physiological and anatomical changes in the brain tissue.
- He is concerned that any sedatives, anesthetics, or analgesics administered before sacrificing the animal could possibly alter the brain chemistry and consequently the results. Yet, as a humane and compassionate person, he is concerned that the animals not experience any unnecessary pain or suffering.



A Question of Sacrifice

- The initial phase of the study, restraint and brain wave monitoring is not painful for the animal, though the animal will generally resist the limitations on its physical movement. Nonetheless, he believes that not providing any pain-reducing substances at this point is entirely appropriate. He is less certain when it comes to sacrificing the animal. Are there humane ways to sacrifice the animal without providing anesthetics or analgesics? How might he deal with this issue?
- Assume that for purposes of his study, it is not necessary to sacrifice the animal in the end. The protocol, which then only entails restraint and attachment of electrodes and administration of the drug under study, is rather noninvasive. Is it appropriate to use the animals (either cats or monkeys) for other, unrelated experimental procedures afterward? What if the initial experiment involved a surgery from which the animal would survive? Should the availability or species of the animal weigh in this decision?



Case Study 3: The New Hip

- A design engineer, Louise Chandler has developed a new design for a hip prosthesis. The new designer represents a major departure from previous designs; the shape and the materials are innovative and have not been used before. Dr. Chandler wants to test the implant in an animal before it is used in humans. After reviewing the literature, she finds that dogs have been used previously to test joint replacements. For most designs, results in dogs were subsequently shown to be very similar to results in humans.
- However, there is one case that is troubling; several years ago, another innovative design was tested in dogs and it performed very well. The failure rates were very low, there was no loosening of the implanted material, and there was very little wear on the artificial joint surface. The orthopedic community was excited and proceeded to implant this design in humans. Unfortunately, the prostheses had a very high failure rate in patients.



The New Hip

- Dr. Chandler also finds many reports in the literature of machines that simulate joints to test new prosthesis designs. She does not have these sophisticated pieces of equipment available to her.
- Should Dr. Chandler test her new design in dogs, despite the one troubling study from the literature?
- What considerations do you think Dr. Chandler should use to aid her in this decision?
- What alternatives might Dr. Chandler have?



A PI wants to identify individual mouse pups at 10 days of age and is proposing to use a technique involving the clipping of the mouse's toe(s). Toe clipping is considered to be a potentially painful procedure.

What questions should we ask this PI?



Case Study 4: Water Deprivation

A PI who uses non human primates does recording experiments in both the cerebellar nuclei and primary motor cortex in the awake behaving monkey. In order to motivate the monkeys to perform behavioral tasks they are water restricted.

What questions should we ask this PI?



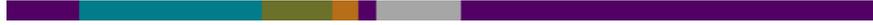
Case Study 5: Paralysis

PI induces a relapsing autoimmune encephalomyelitis in mice (model for multiple sclerosis) which causes paralysis in the mice for a period of time. Some strains of mice recover from the paralysis and other strains have a persistent paralysis.

What questions should we ask this PI?



University Policies and Procedures



Questions & Discussion

