RCR-i²
Responsible Conduct of Research internet instruction

A Product of the RCR Education Committee

Use of Animal Subjects

Background

The merits of animal research are widely accepted by scientists and largely appreciated by the general public. Major biomedical research institutions, professional societies, and research scientists have a shared understanding of the tremendous value gained from studies using animal subjects. Similarly, polls of the general public repeatedly show strong support for biomedical research, and an acceptance of the need to perform studies using animals. However, the apparent support for biomedical research is tempered by widespread misunderstanding about the nature of research as well as an impassioned opposition to any use of animals by some vocal action groups.

Opposition to the use of animals in research is well funded and has had a significant impact on biomedical research. Some in the animal rights movement rely on carefully reasoned, philosophical arguments that humans do not have the right to use animals for experiments, despite the fact that such studies might contribute important new knowledge about physiology and the mechanisms of disease in both humans and animals (Singer, 1975; Regan, 1983). Other animal rights organizations bypass these philosophical arguments and instead focus on claims that animals suffer needlessly in research, that current medical advances were or could have been derived without the use of animals, and that animal research has provided no useful data.

Except for a set of guidelines for animal use recommended by the National Institutes of Health (NIH) in 1935, animal research in the United States was conducted with relatively little public attention and virtually no oversight until the 1960s. A report entitled "Concentration Camps for Dogs", published in Life magazine in 1966, documented brutal conditions and lack of care by suppliers of dogs to research laboratories. Within the year, the first Animal Welfare Act was written and approved, calling for regulatory oversight of the suppliers of some animals. Within the next few years, the government and researchers approved further guidelines and regulations to reduce the risk that the privilege of working with animal subjects would be abused. One of the most important outcomes was the NIH Policy for Animal Care and Use for institutions supported by the Public Health Service (PHS).

Most, but not all, researchers recognize the need to employ animal subjects responsibly. Yet some investigators perform studies that deviate from approved protocol, some provide inadequate care or feeding for animal subjects, and some leave animals poorly attended during recovery from anesthesia and surgery. None of these lapses is acceptable, and while it is hoped that they happen only rarely, they can occur at the hands of a poorly trained or inexperienced investigator. Unfortunately, some instances of animal abuse have been far worse.

In 1984, head injury studies conducted with baboons at the University of Pennsylvania were found to exemplify the worst fears of those opposed to animal research. Apparently conscious baboons were restrained to test the effects of rapid, traumatic head injury. Surgery was performed under nonsterile

conditions. Researchers working with the baboons made comments suggestive of a callous, if not sadistic, attitude toward the experimental subjects. Videotapes documenting these abuses were obtained by an animal rights organization and were aired on national television.

Despite the potential importance of studies on traumatic injury, such incidents reflect badly not just on one group of researchers, but on all of research. Investigators who are irresponsible risk not just their own research project, but also the research of others at the same institution. Potentially, they also risk the public's willingness to support or allow research with animal subjects.

Regulations and Guidelines

The use of animal subjects is covered by numerous regulations. Although many federal agencies have relevant regulatory controls, the two most important for biomedical research are the Public Health Service (PHS) and United States Department of Agriculture (USDA). Institutions are given the responsibility to implement federal regulations primarily through the Institutional Animal Care and Use Committee (IACUC). The roles of these federal agencies and the institutional committee are summarized below.

Public Health Service

The Health Research Extension Act of 1985 ('Animals in Research') is the legislative basis for PHS policy on use of animal subjects. The policy covers uses of living vertebrate animals for any PHS-supported research, research training, and biological testing. In addition to the NIH, PHS agencies include the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), and several others.

United States Department of Agriculture

Animal Welfare Regulations, and specifically the Animal Welfare Act (AWA), are implemented by the Animal and Plant Health Inspection Service (APHIS) of the USDA. The AWA, first enacted in 1966 and amended periodically, covers the sale, handling, transport, and use of warm blooded, vertebrate animals. At present, birds, rats, and mice that are bred for research, but not those that are wild, are specifically exempted from the Animal Welfare Regulations. The AWA, as amended in 1985, incorporates a variety of requirements designed to promote animal welfare. These include minimization of pain and distress, consideration of alternative procedures, definitions of institutional responsibilities, and the establishment of IACUCs. In addition, institutions, businesses, or individuals covered under the AWA must be licensed or registered with APHIS. Facilities are inspected on an unannounced basis, and if deficiencies are not corrected by the subsequent inspection, consequences could include fines, or the suspension or revocation of licensing to use animals.

Institutional Animal Care and Use Committee

Although institutions are subject to federal oversight and inspection, the daily responsibility for complying with federal regulations is largely the responsibility of the Institutional Animal Care and Use Committee (IACUC). Under PHS policy, institutions are granted the provisional responsibility for self-regulation after approval of an Animal Welfare Assurance by the Office of Laboratory Animal Welfare (OLAW). If the institution fails to meet its regulatory responsibilities, then OLAW can restrict or withdraw the assurance.

Considerations

There is no presumption that animals may be sacrificed for research. Animals should only be harmed if there is a legitimate scientific advantage to doing so, and even then the harm should be as little as possible. Russell and Burch (1959) proposed three specific strategies for minimizing the pain and distress to animal subjects:

- *Replacement:* When possible, conscious animals should be replaced with insentient material in research, and higher animals should be replaced with lower ones.
- *Reduction:* Fewer animals should be used if doing so will not compromise the significance or precision of a study.
- *Refinement:* Procedures should be designed so as to minimize the incidence and severity of harm to the animal subjects.

Reduction, Replacement, and Refinement have an ethical basis, but they also have practical advantages. Research with animal subjects is expensive. If experiments can be conducted, for example, with mice rather than monkeys, with fewer animals, or without animals, then the cost of those studies will generally be reduced.

The scientific enterprise and the integrity of research depend on the responsible, humane treatment of animal subjects. Animal research has tremendous utility because an understanding of the complex interactions of molecular, biochemical, and physiological mechanisms ultimately depends on studies in intact, living organisms. To be performed, such studies depend on many genetic and environmental controls that are difficult, if not impossible, to achieve in studies with humans-- yet the studies only have value if these controls are carefully maintained. Furthermore, an experimental design that results in pain or suffering often decreases, if not eliminates, the scientific value of the experiment. Finally, irresponsible or inhumane treatment of animals harms the reputation of scientific institutions, endangers funding, and threatens the public image of science.

Summary

- Comply with regulations
  No use of animals for the purposes of research, teaching, or testing should be performed that is not explicitly part of an approved protocol.
- Critically evaluate the use of animals
  The spirit of the regulations and good science both require that individuals give thoughtful consideration not only to compliance with regulations, but to what defines an acceptable use of animals.
- Protect animal welfare
  The decision to use animals in research and teaching carries a responsibility to protect animals from all unnecessary suffering or pain.

- Promote responsible use of animal subjects
  If you are responsible for training others or if you observe indifference to considerations for animal welfare, you should make attempts to initiate discussion, to identify relevant regulations, and to promote responsibility in studies involving animal subjects. If significant violations of animal welfare regulations are observed, then those observations should be reported to the appropriate people in the institution.

Discussion questions

Answer all questions in your own words and submit your responses to Andrekia Branch (aebranch@vcu.edu) in the Office of Postdoctoral Services:

1. Define the terms replacement, reduction, and refinement in the context of research with animal subjects.

2. What are the responsibilities of an IACUC?

3. Describe at least one instance in which abuse of animals in research resulted in public concern about the use of animals in research. Identify federal regulations that were apparently direct responses to such abuses.

Suggested reading(s)

North Carolina State University

University of Montana (posted by the Office of Research Integrity)

Resources

Works cited

- Regan T (1983): The Case for Animal Rights. University of California Press, Berkeley, CA.

- Russell WMS, Burch RL (1959): Principles of Humane Animal Experimentation. Charles C. Thomas, Springfield, IL, 238 pp.
  Also available in parts at http://altweb.jhsph.edu/publications/humane_exp/hettoc.htm

- Singer P (1975): Animal Liberation. Distributed by Random House, New York.

Further Resources

Animal Welfare Principles and Guidelines

- American College of Laboratory Animal Medicine (ACLAM) (1996): Adequate Veterinary Care.
  http://www.aclam.org/pub_adquate_care.html

- Bennett BT, Brown MJ, Schofield JC (1994): Essentials for Animal Research: A Primer for Research Personnel. United States Department of Agriculture, National Agricultural Library, Beltsville, MD.
  http://research.ucsb.edu/connect/acc/ess_idex.html

- Interagency Research Animal Committee (1985): U.S. Government principles for the utilization and care of vertebrate animals used in testing, research, and training. In: U.S. Public Health Service Policy on Humane Care and Use of Laboratory Animals.
  http://history.nih.gov/laws/pdf/US_Principles.pdf

- NASA (1997): Principles for the Ethical Care and Use of Animals. NASA has proposed three principles for the use of animal subjects: respect for life, societal benefit, and non-maleficence.
  http://grants.nih.gov/grants/olaw/references/dc97-2.htm

- National Research Council (1996): Guide for the Care and Use of Laboratory Animals. National Academy Press, Washington, D.C.

- Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals
  http://grants.nih.gov/grants/olaw/references/phspol.htm

Animal Welfare Regulations and Oversight

- Animal Welfare Act and Regulations
  http://www.nal.usda.gov/awic/legislat/usdaleg1.htm

- Animal and Plant Health Inspection Service (APHIS)
  http://www.aphis.usda.gov

- Beaver BV, Reed W, Leary S, McKiernan B, Bain F, Schultz R, Bennett BT, Pascoe P, Shull E, Cork LC, Francis-Floyd R, Amass KD, Johnson R, Schmidt RH, Underwood W, Thornton GW, Kohn B (2001): 2000 Report of the AVMA Panel on Euthanasia. Journal of the American Veterinary Medical Association 218(5):669-696
  http://www.avma.org/resources/euthanasia.pdf

- Health Research Extension Act of 1985: *Animals in Research*
  http://grants.nih.gov/grants/olaw/references/hrea1985.htm

- National Research Council (1996): Guide for the Care and Use of Laboratory Animals. Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, Washington, D.C. http://www.nap.edu/readingroom/books/labrats
- Office of Laboratory Animal Welfare (OLAW) http://grants.nih.gov/grants/olaw
- United States Department of Agriculture (USDA) http://www.usda.gov
- License requirements http://www.aphis.usda.gov/lpa/pubs/awact.pdf
- Consequences of noncompliance http://www.aphis.usda.gov/ac/info.html

Animal Welfare vs. Animal Rights

- Cohen C (1986): The case for the use of animals in biomedical research. New Engl J Med 315: 865-870.
- Fox MA (1986): The Case for Animal Experimentation: An Evolutionary and Ethical Perspective. University of California Press, Berkeley.
- Fuchs BA (2000): Use of animals in biomedical experimentation. In: (Macrina FL) Scientific Integrity. American Society for Microbiology, Washington, DC.
- Rowan AN (1984): Of Mice, Models, and Men: A Critical Evaluation of Animal Research. State University of New York Press, Albany, NY, 323 pp.
- Rudacille D (2001): The Scalpel and the Butterfly: The War between Animal Research and Animal Protection. Farrar, Straus and Giroux, New York.
- Russell SM, Nicoll CS (1996): A dissection of the chapter 'Tools for Research' in Peter Singer's Animal Liberation'. Proceedings of the Society for Experimental Biology and Medicine. 211(2): 109-138.

Animal Welfare and Animal Rights Organizations

- American Association for Laboratory Animal Science http://www.aalas.org
- Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC)

http://www.aaalac.org

- Foundation for Biomedical Research
  http://www.fbresearch.org
- National Association for Biomedical Research
  http://www.nabr.org
- Humane Society of the United States
  http://hsus.org
