Resources for Research Ethics Education

Animal Subjects

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Summary

Critically evaluate the decision to conduct research with animal subjects.
Both the spirit of the regulations and good science require that individuals give thoughtful consideration to what defines an acceptable use of animals.

Comply with regulations.
Once having made a considered decision to use animal subjects, no use of animals for the purposes of research, teaching, or testing should commence that is not explicitly part of an approved protocol.

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, identify relevant regulations, and promote responsibility in studies having animal subjects. If significant violations of animal welfare are observed, those observations should be reported to the appropriate people in the institution.

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 share an 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 general nature of research with animals, as well as an impassioned opposition, by some vocal action groups, to any use of animals.

Such 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 (cf. Singer, 1975; Regan, 1983), despite the fact that such studies might contribute important new knowledge about physiology and the mechanisms of disease in both humans and animals. 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, that animal research has provided no useful data, and that there are negative consequences of animal research for humans (cf. Greek and Greek, 2002).

Most researchers recognize the need to employ animal subjects responsibly. Yet poorly trained or inexperienced investigators may perform studies that deviate from approved protocol, provide inadequate care or feeding for animal subjects, or some leave animals poorly attended during recovery from anesthesia and surgery. Although these lapses may occur rarely, they are never acceptable.

Unfortunately, some instances of animal abuse have been far worse than inadequate care or feeding. 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. In studies with restrained baboons, researchers were testing the effects of rapid, traumatic head injury. Some of those researchers 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.

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).

Despite the potential importance of what might be learned from such a study, 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.

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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 charged with implementing 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 (PHS agencies include the National Institutes of Health (NIH), 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, day-to-day responsibility for complying with federal regulations is largely located within 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.

Discussion

Case Study 1[i]

Your colleague, Dr. Jay Mahata, is an NIH supported investigator who has an established collaboration with a field biologist, Dr. Ellen Yu, in another state. Dr. Yu does not receive any grant support for her research. Dr. Mahata sometimes receives blood and other tissue samples for analysis from the wild rodents that Dr. Yu traps for her research. Dr. Mahata has asked you to read his latest IACUC protocol prior to its formal submission. You know about his collaboration with Dr. Yu but note that it is not mentioned in the protocol. When you ask Dr. Mahata about this he says that he "does not have to report this activity to the IACUC because there are not any animal welfare concerns involved". He points out to you that he does not sacrifice the rodents or collect the blood and tissues. He maintains that the relevant animal welfare concerns are between Dr. Yu and her institution. Lastly, he suggests that because the NIH does not support her work, it does not have to conform to the same guidelines to which his own work is subject.

Case Study 2[ii]

You are beginning a new post-doctoral position at the same time that your mentor is moving her laboratory into a new building. She is obsessive about animal care and wants to ensure that the colony of animals to be established in the new facility is healthy. You are assigned the task of developing a system of "sentinel" animals to monitor the health status of all new incoming shipments of animals as well those in the established animal colony. You establish a system that involves selected animals being sacrificed on a regular basis and screened for the presence of specific pathogens by a contract laboratory. Because these animals are not being used for research do you have to submit a protocol to the IACUC to cover these activities?

Case Study 3[iii]

You are a graduate student working on a project that involves administering nerve toxins directly into the cerebrospinal fluid of rats by using a special infuser connected to tubing that you have surgically implanted into the base of each rat's skull. Administering different nerve toxins to block specific effects of different types of drugs will help determine how the drugs work. After surgery, the nerve toxin is given, then a few days later the investigational drug is given to determine whether it will have an effect. This protocol has been approved by the Institutional Animal Care and Use Committee (IACUC) and is being funded by a grant from the Department of Defense. Over the past few weeks, you have carefully implanted a catheter into the base of each rat's skull, then infused the specified amount of nerve toxin. When you go to the vivarium to bring the rats to the lab to administer the investigational drugs, you find that a number of the rats are paralyzed or dead. You did not expect this. The lab director is currently out of town, so you go to the lab's senior graduate student, Tom, for advice. Tom will be able to complete his dissertation writing when this experiment is done and he has made it clear that he wants this experiment to run without delay. You ask him whether you should stop the experiment to determine why some of the rats are dead or paralyzed. He responds that stopping the experiment now would waste

several weeks of work and delay completion of his dissertation. Stopping now may mean having to start over later and could result in using even more rats. He further explains that the IACUC might even prohibit restarting the experiment, so the rats would have died for nothing because the data would have to be obtained another way. He suggests that the paralysis and death of some of the rats may be due to your inadequate experience performing rat surgery or infusions, so further practice by continuing this experiment may result in better outcomes for the rest of the rats on which you perform surgery. What do you do now? Do you continue performing surgery and infusions on the rats, knowing that more rats may be harmed? Do you stop the experiment and inform the IACUC, which risks earning the disfavor of Tom, with whom you have to work? How would you explain each course of action to the IACUC?

Discussion Questions

1. Discuss the benefits of using animals in biomedical research and list at least three different studies that could be accomplished only with the use of animal subjects.
2. To what extent does your field of work depend on the use of animal subjects? To what extent is your work intended to benefit both humans and other animals?
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.
4. Define the terms replacement, reduction, and refinement in the context of research with animal subjects.
5. What are the responsibilities of an IACUC?
6. In your institution, what minimal changes (e.g., increase in number of animals) to your protocol require review and approval of the IACUC? What changes are of a magnitude to require submission, review, and approval of a new protocol?
7. If you observed another investigator abusing the privilege of animal use, who should be notified?
8. Describe your criteria for the acceptable use of animals. Consider the importance and likelihood of benefits to be obtained, the nature of the species to be used (e.g., invertebrates versus vertebrates, primates versus non-primates, dogs or cats versus rats or mice), the number of animals to be used, and the extent of likely pain or suffering.
9. What forums are available in your institution to examine the ethical and/or legal ramifications of animal use? What, if anything, can you do to promote such discussion?

Additional 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 unconscious or 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.

The strategies of 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 altogether, 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.

Resources

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Endnotes

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[ii] © ASM Press, 2000, Scientific Integrity by F.L. Macrina, used with permission.
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