
University of Arizona Program in Research Integrity Education Monthly Newsletter

A Federally Mandated Compliance Education Program

September 1, 2006

Volume 6, No. 9

This month the Program in Research Integrity Education (P.R.I.E.) newsletter focuses on the topic of “*Animal Subjects*.” We are continuing to highlight each month one of the nine core instructional areas in the Responsible Conduct of Research (RCR). Last month the topic of “*Human Subjects*” was discussed. The information presented below is authored by Michael Kalichman and P. D. Magnus and may be viewed at the *RCR Education Resources* web site, which is: <http://rcrec.org/r/index.php>.

Responsible Conduct of Research (RCR)

P.D. Magnus and Michael Kalichman,
September 2002

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 furor and virtually no oversight until the 1960's. 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 non-sterile 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.

Rules and regulations

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 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.

Principles

Living creatures deserve respect.

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:** Where it is without a loss of significance or precision, fewer animals should be used.
- ✚ **Refinement:** Procedures should be designed so as to minimize the incidence and severity of harm to the animal subjects.

Reduction, Replacement, and Refinement are ethical principles, 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.

Guidelines

The PHS, USDA, and IACUCs are the key components of a regulatory environment that promotes the principles described above. However, the ultimate responsibility for the ethical and legal use of animals in research rests with those who conduct the research. The following are guidelines for responsible conduct of such research:

Comply with regulations

Any use of animals for the purposes of research, teaching, or testing is subject to regulation. Before such use, knowledgeable individuals should be asked about any obligations to be met by users of animals. This begins with the assumption that no procedure or study should be performed that is not explicitly part of an approved protocol.

Critically evaluate the use of animals

The responsible use of animals requires much more than complying with regulations. The spirit of the regulations and good science both require that individuals give thoughtful consideration to what defines an acceptable use of animals. This consideration is necessarily an ongoing and evolving process. Factors to be considered include new understandings of the science involved, potential benefits of the use of animals, possible alternative methods of study, etc. Such issues should be considered by individuals as well as in discussions that involve co-workers, other researchers, and/or the public.

A prerequisite for the responsible use of animals is a realistic examination of the intended and likely benefits of that use. Does the benefit warrant the cost to animal subjects?

Protect animal welfare

The decision to use animals in research and teaching carries a responsibility for the welfare of those animals. That responsibility includes, but is not limited to: ensuring the use of appropriate and adequate anesthesia and analgesia; providing of appropriate feeding, care, and protection from infection, pain, or suffering; selecting humane methods for euthanasia; and obtaining adequate training to fulfill responsibilities for animal welfare.

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. This obligation is certainly for the sake of the animals, but it also helps to protect the integrity of the research, the status of the institution, and the institution's privilege for self-regulation

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

Animal Welfare Principles and Guidelines

- American College of Laboratory Animal Medicine (ACLAM) (1996): *Adequate Veterinary Care*.
<http://www.aclam.org/adequate.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://omni.ucsb.edu/connect/acc/ess_index.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://grants.nih.gov/grants/olaw/references/phspol.htm#principle>
- 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

As of 2000, the Office of Laboratory Animal Welfare (OLAW) has responsibility for implementing and interpreting the PHS policy. The PHS policy requires an Animal Welfare Assurance from institutions. This Assurance covers the IACUC, review of PHS projects, information to be included in PHS applications and proposals, recordkeeping, and reporting. In addition, compliance with applicable Animal Welfare Regulations is required by PHS policy

- 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.nal.usda.gov/awic/pubs/noawicpubs/vmaeuth.htm>
- Health Research Extension Act of 1985: *Animals in Research*
<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/oa/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, ed.) *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 (2000): *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
- Singer P (1990): *Animal Liberation: A New Ethic for Our Treatment of Animals*. Random House, New York.

Animal Welfare and Animal Rights Organizations

- 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>

Next month the featured RCR topic will be:
"Conflict of Interest and Commitment"

UNIVERSITY OF ARIZONA RESEARCH SUPPORT SERVICES GROUP (RSSG)

HUMAN SUBJECTS PROTECTION PROGRAM

≧Highlights≦

Certificates of Confidentiality*

During the 1970s, Congress recognized that some individuals might elect to not participate in research studies involving certain sensitive topics such as illegal activities unless measures were put into place to protect their privacy. A law was enacted allowing researchers to obtain Certificates of Confidentiality. The Certificate enabled the researcher to refuse to disclose names or other identifying characteristics even if asked to do so by a court or government agency. In essence, individuals who gave sensitive information to a researcher were protected and would not be identified or prosecuted as a result of participation in research.

Investigators who collect sensitive information should consider whether a Certificate of Confidentiality is appropriate in order to protect subject privacy. Applications for a Certificate of Confidentiality should be made to the agency responsible for the funding of the projects. However, Certificates of Confidentiality are not limited to federally funded project. Researchers who conduct unfunded projects may apply for a Certificate of Confidentiality if the research is sensitive and protection is necessary to reach research objectives.

The Office for Human Research Protections (OHRP) defines research as "sensitive" if the collected information could have adverse consequences to participants such as damage to their financial status, employability, insurability, or reputation. The National Institutes of Health uses a non-exhaustive list of sensitive research activities that include:

- Genetic information
- Psychological well-being
- Sexual attitudes, preferences, or practices
- Substance abuse
- Other illegal behaviors

Certificates of Confidentiality do not apply to voluntary disclosure of identifying information by either a participant or investigator. In other words, if the study is covered by a Certificate of Confidentiality, the participant may voluntarily disclose information about himself or herself. The investigator may also voluntarily disclose information about abusive behaviors or a participant's threat of violence to self or others. Information about the Certificate of Confidentiality is put into the **Consent Form** and should clearly outline any exceptions to the protection it offers.

Applications for a Certificate of Confidentiality must be made for a particular research project and are not transferable from one study to another. Additionally, if there are major changes in the protocol during the study, the issuing agency must be notified of the protocol amendment.

Certificates of Confidentiality can promote recruitment of participants into studies that collect sensitive information. The Certificates serve as protection for required disclosure of private, identifiable information against a valid subpoena from a court or administrative agency.

*Kaltman, S. P. and Isidor, J. M. (2006). Certificates of Confidentiality. In E. A. Bankert and R. J. Amdur (Eds.), Institutional Review Board Management and Function (pp. 311-312). Sudbury, MA: Jones and Bartlett.

Office for Human Research Protections (February, 2003). Guidance on Certificates of Confidentiality: <http://www.hhs.gov/ohrp/humansubjects/guidance/certconf.htm>.



News from HIPAA.....

Don't Abuse Your System Access

HIPAA regulations specify that a Covered Entity must identify who needs access to Protected Health Information (PHI) in order to perform his/her job. The PHI that needs to be used to carry out the person's job responsibilities should be included in the job description.

The central aspect of the Privacy Rule is "minimum necessary" use and disclosure of protected health information. The Security Rule requires access control of what a user can do and what a user can access electronically.

Privacy breaches occur when employees misuse their system access to look up medical information on family, friends or even themselves when it isn't job related.

Example: My eight year old daughter is tested for Valley Fever. My job responsibilities include

using my computer access to review laboratory results related to a research study. I access my daughter's lab results because my computer access will allow me to view all laboratory tests. **This is a Privacy Breach.**

Attempting to obtain or use, actually obtaining or using, or assisting others to obtain or use protected health information, when unauthorized or improper will result in a warning and/or disciplinary action up to and including termination.

DON'T PUT YOUR JOB IN JEOPARDY!!

Jeniece Poole, Privacy Officer
Office of the Vice President for Research
jpoole@email.arizona.edu



Good Laboratory Practices (GLP)

As new students and research technicians start the fall semester, this is a good time to initiate or reinforce that good record keeping is the key to successful research.

- ✓ Sign and date all data entries
- ✓ Take forms to work bench to record data as generated
- ✓ Record all data in pen
- ✓ Reference protocol or SOP used to produce data

As Quality Assurance Officer, I am available to laboratories to help with SOP management or data and record keeping suggestions. Excellence in research can be accomplished by all of us working together to this goal.

Marilyn M. Marshall, SpM
Quality Assurance Officer
Office of the Vice President for Research
621-1469 (p), 621-1429 (f)

University of Arizona – Animal Care Quality Care for Research Animals



National Center for Research Resources Animal Facility Improvement Grant Awarded to University Animal Care

University Animal Care has received a \$700,000 grant from the National Center for Research Resources (NCRR), award date July 1, 2006, to be used to purchase Individually Ventilated Racks for mice and the mobile work stations needed to service the IVC's. The equipment will be utilized in the AHSC, CAF, and BIO5 animal facilities.

Another grant will be prepared for the June 1, 2007 deadline and will address other needs of the animal facilities.

If you have questions regarding the awarded grant or suggestions for the new grant submission, please contact Dr. Susan Wilson-Sanders: 626-1066 or email her at: wilson-s@u.arizona.edu.



Radiation Control

Revised Instructions for Ordering Radioactive Materials

Purpose:

There has been a change in the way you order radioactive materials. When ordering radioactive material, including radiopharmaceuticals, a protocol number is required to complete the order. The protocol number for each radionuclide can be found on your most recent radioactive material approval and is also available online as part of the RCO Website's Online Reviews section.

Changes for Ordering Consolidated Purchasing Program (CPP) Radioactive Materials:

- Additional **required** text box titled - **Protocol**. Simply update this text field by entering the protocol identification number, as it appears upon your current online Radioactive Material Approval (e.g. 304-E04), for the material you are ordering.
- Vials ordered for multiple protocol uses merely require one protocol entry during the order process until further notice.

Changes for Ordering Non-CPP Radioactive Materials:

There are two categories of non-consolidated radioactive material customers:

- **1. Radiopharmaceutical imaging agents (Tc-99m, I-123, F-18)**
 - **2. Online requisition (OLR)**
- 1. Tc-99m, I-123 and F-18 orders:**
- Addition of a text field on the Radiotracer Order Form for entry of the **Protocol number**. Simply update this field by entering the protocol identification number, as it appears upon your current online Radioactive Material Approval (e.g. 304-E04), for the material you are ordering.
- 2. Online requisition (OLR) customers:**
- Addition of the **Protocol number in the DPR notepad**. Simply enter the protocol number, as it appears upon your current online Radioactive Material Approval (e.g. 304-E04), for the material you are ordering.

Upcoming Conferences/Workshops

September 14-15, 2006

*Statistics, Images, and Perceptions of Truth:
Detecting Research Bias and Misconduct*
Birmingham, AL

Co-sponsor: University of Alabama School of Medicine

September 25-26, 2006

Crossing the Line: What is Acceptable Risk?
Durham, NC

Co-sponsor: University of North Carolina at Chapel Hill

<http://dukeohrp2006.org/>

September 28-29, 2006

*New Capabilities, Emerging Issues and
Responsible Conduct in Data Management*
Baltimore, MD

Co-sponsor: University of Maryland-Baltimore

October 15-18, 2006

49th Annual Biological Safety Conference
Boston, MA

absa@absa.org

October 16-17, 2006

Fourth Annual RCR Expo
Quebec City, Canada

Contact: LNguyen-Khoa@osophs.dhhs.gov

December 1-3, 2006

Research Conference on Research Integrity
Tampa, FL

Co-sponsors: Association of American Medical Colleges, American Association for the Advancement of Science

Abstracts due: April 28, 2006 (see ORI web site for details on submitting abstracts and to obtain a conference schedule: <http://ORI.hhs.gov>).

Questions should be addressed to Nick Steneck at nsteneck@umich.edu.

University of Arizona Program in Research Integrity Education staff:

Alice C. Langen, Director, Research Compliance
Ruth K. Daniels, Program Coordinator and Editor
of the P.R.I.E. Newsletter rhk@u.arizona.edu

P.R.I.E. – Program phone number: (520) 626-6282

*The P.R.I.E. newsletter is researched
and compiled by Ruth Kurash Daniels.*

Words of Wisdom:

“Laughter is an instant vacation.”

——— *Milton Berle*