ISSUE

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REGULATION OF BIOMEDICAL RESEARCH USING ANIMALS

Public polls reveal most people are unaware of the laws and regulations that govern the use of laboratory animals in biomedical research. Lacking this awareness, the average person is more likely to believe erroneous charges of abuse made by those who completely oppose animal research. In fact, scientists who use animals in their work must comply with a comprehensive system of federal, state and local laws and regulations.

Even if such legal requirements did not exist, researchers know that laboratory animals must be cared for humanely for both ethical and scientific reasons. In order to understand the needs of these animals, the veterinary specialty of laboratory animal medicine was established. A host of organizations and programs exist within the scientific community dedicated solely to promoting excellence in laboratory animal care. In addition, academic and professional societies have longstanding policies, procedures and standards defining the ethical treatment of animals. To understand more about the scientific community's dedication to the highest-quality animal care, policies and procedures, please refer to the NABR *Issue* entitled *Humane Care and Treatment of Laboratory Animals*.

The purpose of this *Issue* is to outline the major laws, regulations and guidelines that must be followed when laboratory animals are used. They include:

- *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*
- Animal Welfare Act and the U.S. Department of Agriculture Animal Welfare Regulations and Standards
- Public Health Service Act and the *U.S. Public Health Service Policy on Humane Care and Use of Laboratory Animals*
- *Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences Institute for Laboratory Animal Resources*
- Good Laboratory Practice Standards of the Food & Drug and Environmental Protection Administrations
- Endangered Species Act
- Freedom of Information Act

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Public Accountability is Essential to the Future of Biomedical Research

A 1995 Associated Press poll showed that 70% of Americans support biomedical research using laboratory animals.[1] As a result of the general public's interest in animal welfare, a comprehensive system of federal, state and local laws and regulations governing the use of laboratory animals has evolved. This report outlines the mandatory legal requirements with which scientists must comply when using animals in research, testing and education programs.

U.S. Government Principles

U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training (see insert) express the tenets that underlie our current system of federal regulation. These principles succinctly describe the framework within which all activities involving laboratory animals must be conducted.

Animal Welfare Act

The Animal Welfare Act[2] (AWA) was enacted in 1966 and has been amended by Congress four times. The Act applies to all research facilities — public or private, academic or industry-based, whether or not they receive federal funds — that use animal species designated by the U.S. Secretary of Agriculture. Currently, the species so designated are guinea pigs, hamsters, gerbils, rabbits, dogs, cats, nonhuman primates, marine mammals, farm animal species when used in biomedical research, and warm-blooded wild animals. Rats, mice and birds are not covered.

All covered research facilities must register with the U.S. Department of Agriculture (USDA) and comply with USDA animal welfare regulations and standards. Each facility must report to the USDA annually, verifying compliance and indicating the number and species of animals used by type of procedure (painless, pain relief/anesthesia given or not given because of scientific necessity). The USDA is required to inspect each research facility at least annually. These inspections are unannounced. More frequent unscheduled inspections are made if significant deficiencies are identified.

All registered research facilities are required to have an Institutional Animal Care and Use Committee (IACUC) that reviews and approves procedures involving animals in advance. The IACUC inspects facilities biannually and reviews the overall animal care program annually for compliance with the AWA. At least one member of the Committee must be a veterinarian. At least one member must be a "public" member, not affiliated in any way with the institution, who represents general community interests in the care and treatment of animals.

USDA Animal Welfare Regulations and Standards[3]

As required by the AWA as amended, USDA's Animal and Plant Health Inspection Service (APHIS) administers detailed regulations defining the responsibilities of research facilities, the duties of IACUCs and specific standards for animal care. In experimental procedures, research facilities must ensure that any animal pain and distress are minimized, including adequate veterinary care with the appropriate use of anesthetic, analgesic, tranquilizing drug or euthanasia. Principal investigators must consider alternatives to any procedure using animals, especially those procedures likely to cause pain to a laboratory animal and provide written assur-

ance of this consideration. They must also assure that activities do not unnecessarily duplicate previous experiments. Research facility personnel working with animals must have appropriate qualifications and training.

Beyond annual reporting to USDA, research facilities are required to keep extensive records on IACUC activities (minutes of meetings, reports of biannual inspections, etc.) and documentation of the source of animals. These records are available to USDA staff during inspection.

Animal welfare standards by species include requirements for handling, housing, cage size, feeding, watering, sanitation, ventilation, temperature, humidity and adequate veterinary care. Research facilities also must have individualized, written plans for exercise programs for dogs and for addressing the psychological well-being of nonhuman primates.

Public Health Service Act

In 1985 Congress passed the Health Research Extension Act (P.L. 99-158), which created a federal mandate for longstanding policies governing the use of animals supported by Department of Health and Human Services (DHHS) funds. The DHHS units that typically support animal research include the Centers for Disease Control, the Food and Drug Administration and the National Institutes of Health. These legal requirements are similar to and consistent with the federal Animal Welfare Act, and they apply to all DHHS-conducted or supported research, research training, and biological testing activities involving the use of all vertebrate animals, including rats and mice.

Public Health Service Policy on Humane Care and Use of Laboratory Animals

The *Public Health Service (PHS) Policy*[4] implements and supplements the laboratory animal-related provisions of the Public Health Service Act and the general U.S. Government Principles. Compliance with the *Policy* is required for activities conducted by DHHS units and by awardee institutions as a condition of receiving DHHS funds. DHHS grants or contracts can be suspended or revoked for noncompliance.

A major provision of the *Policy* is the filing and annual updating of an Animal Welfare Assurance. The assurance document must fully describe the institution's animal care and use program. That program must comply with the Animal Welfare Act and other applicable federal laws and must adhere to the *Guide for the Care and Use of Laboratory Animals (Guide)*. Like the AWA, the *Policy* requires each institution to establish an IACUC with at least one outside member representing the public. As described in the *Policy*, the duties and responsibilities of the IACUC are comparable to AWA requirements. Also, each application for a DHHS award includes the number and species of animals to be used, rationale for the use of animals, description of the proposed use, procedures to minimize pain and discomfort and method of euthanasia.

The NIH Office for Protection from Research Risks (OPRR) administers the *Policy* on behalf of the DHHS. OPRR is responsible for reviewing and approving institutional assurances, advising research facilities about compliance, evaluating allegations of noncompliance with the *Policy* and conducting site visits as needed.

Other federal agencies, such as the National Science Foundation, rely upon the *PHS Policy* and assurance system. If a potential awardee is not a DHHS-assured institution, special arrangements must be made.

Guide for the Care and Use of Laboratory Animals

The *Guide*[5] is widely accepted by scientific institutions as a primary reference on animal care and use. First published in 1963, it has been revised six times, most recently in 1996. The purpose of the 118-page *Guide* "is to assist institutions in caring for and using animals in ways judged to be scientifically, technically and humanely appropriate." The *Guide* was compiled by a panel of veterinary and other scientific experts brought together by the Institute of Laboratory Animal Resources (ILAR), Commission on Life Sciences of the National Research Council.

Sections of the *Guide* cover recommended institutional policies (monitoring, veterinary care, and personnel qualifications, training and safety); animal environment, housing and management (cage size, behavioral management, food, water, bedding, sanitation and other issues); veterinary care (preventive medicine, surgery, pain, anesthesia, analgesia and euthanasia); and physical plant. Extensive references and a bibliography are provided.

Good Laboratory Practice Standards

Both the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) enforce "Good Laboratory Practice" (GLP) rules.[6] The FDA regulations apply to all projects yielding data to support new drug and medical device applications. EPA regulations apply to all studies related to new pesticides or toxic substance approvals. The GLPs for both agencies address all areas of laboratory operations. Provisions relating to care and housing of test animals are identical in both GLP rules. Each has a full section on animal care, specifying Standard Operating Procedures for housing, feeding, handling and other standards of care.

Inspections are conducted by federal agency investigators, who visit each facility and are given access to all parts of the premises, all pertinent personnel and documentation. A final report and more detailed facility inspection reports are prepared after an audit is concluded. Noncompliance with GLPs can result in the federal agency's refusal to consider a study in support of an application; disqualification of the testing facility; or, in cases of alleged fraud, recommendation for criminal prosecution.

Endangered Species Act

A variety of federal and international laws and agreements exist to protect animals. Statutes such as the Endangered Species Act[7] prohibit or control acquisition of wild or captive-bred, domestic and non-domestic animals classified as "endangered" or "threatened." At a minimum, a permit or authorization from one or more federal agencies is required, if the animal can be obtained at all. Wild-caught chimpanzees, for example, are classified as "endangered" and have not been imported into the U.S. since 1976. Only chimpanzees bred in this country are available for research purposes, and their use is strictly controlled by a national committee that reserves the captive-bred chimps for high-priority research for which there is no alternative, such as AIDS vaccine studies.

Freedom of Information Act

The Freedom of Information Act (FOIA)[8] provides for public access to government information. A wide range of information about animal research and testing as well as its federal oversight is therefore available to the public through written requests and/or electronically. Requesters can and do obtain details about federally conducted or supported research projects, copies of PHS animal welfare assurance documents from awardee institutions, USDA annual reports filed by research facilities, and USDA, EPA and/or FDA inspection reports.

Public accountability is essential to the future of biomedical research.

State or Local Laws and Regulations

Many states have statutes and regulations in place relevant to laboratory animals. Typical state requirements fall into these broad categories:

Regulation of Research Facilities — Nineteen states and the District of Columbia have laws concerning licensing of research facilities. For licensing purposes, state officials may set rules, regulations and standards of animal care and treatment. A number of states also have facility inspection programs.

Availability of Pound Animals for Research — Currently, 13 states prohibit the use of animals obtained from in-state pounds; in one of these states the use of pound animals from inside and outside the state is prohibited. Three states require the release of pound animals for research purposes. In 10 states and the District of Columbia, law permits research use of pound animals. The disposition of abandoned pound animals is not specifically prohibited, required or permitted in 24 states. In these 24 states, as well as the 10 states and the District of Columbia that permit release, county and local governments often exercise jurisdiction over the question of whether unclaimed pound animals may be obtained for research.

Animal Cruelty Prevention — Longstanding laws against cruelty to animals exist in every state. In 36 states and the District of Columbia, research use of animals is exempted or protected.

For full details and specific citations for these laws, please refer to the NABR publication, *State Laws Concerning the Use of Animals in Research*.

[1] ICR Survey Research Group, Associated Press , "How AP Poll on Animal Rights Was Conducted," December 3, 1995.
[2] Animal Welfare Act, 7 U.S.C. 2131 et seq.
[3] U.S. Department of Agriculture, Animal Welfare Regulations and Standards, 9 C.F.R., Ch. 1, Parts 1, 2 and 3.
[4] U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, *Office of Protection from Research Risks, Public Health Service Policy on Humane Care and Use of Laboratory Animals*, revised September 1986, pursuant to Health Research Extension Act of 1985 (P.L. 99-158, Sect. 495, Nov. 20, 1985).
[5] Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, *Guide for the Care and Use of Laboratory Animals*, (Washington, DC, National Academy Press, 1996).
[6] Food and Drug Administration, Good Laboratory Practices, 21 C.F.R. 58 and Environmental Protection Agency, Good Laboratory Practices for Pesticide Program, 40 C.F.R. 160, and for Toxic Substances, 40 C.F.R. 792.
[7] Endangered Species Act, 16 U.S.C. 1531.
[8] Freedom of Information Act, 5 U.S.C. 552.

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