Since the ultimate responsibility for compliance with regulations that affect the care and use of animals lies with the investigator, it is important that he/she have a working knowledge of the basic regulatory requirements. In this SOP, the types of regulations will be discussed under two broad general headings: Involuntary and Voluntary.

Involuntary regulations can be defined as those required by law or set forth as a condition of funding. There are four types of regulatory controls, which can be considered as involuntary:

- The Animal Welfare Act (AWA) – administered by the USDA
- The Public Health Service Policy
- The Good Laboratory Practices Act
- The Requirements of Private Funding Agencies

Voluntary regulations can be defined as those that an individual or institution adheres to as part of their overall commitment to research and academic excellence. There are several types of regulatory controls which can be considered as voluntary:

- Requirements of Individual Institutions and IACUCs
- Requirements of Individual Users

A. INVOLUNTARY REGULATIONS

1. Animal Welfare Act

   a. Summary of the Act:

   The Animal Welfare Act of 1966 and its amendments regulate the transportation, purchase, sale, housing, care, handling, and treatment of animals used in research and teaching, for exhibition, and sold by commercial enterprises as pets. The Act specifically includes dogs, cats, nonhuman primates, guinea pigs, hamsters, rabbits, wild animals (excluding birds and cold-blooded), farm animals used in biomedical research, and any other warm-blooded animals that the Secretary of Agriculture determines are being used or are intended for use for research, experimentation, testing, teaching, exhibition purposes, or as pets. Historically, the Secretary has not regulated rats and mice bred for research and birds, however repeated lawsuits are being heard in Federal Court which attempt to change this policy.
The Act addresses such issues as exercise for dogs, obtaining dogs and cats from sources which have complied with holding periods, care of nonhuman primates to ensure their psychological well-being, the composition and duties of an institutional animal care and use committee (IACUC), adequate veterinary care and responsibilities of the attending veterinarian, record keeping, and training of all personnel using animals in humane methods of animal maintenance and experimentation.

The United States Department of Agriculture (USDA) administers the Animal Welfare Act. Research facilities are subject to unannounced inspections by USDA personnel and required to furnish annual reports that include, besides other information and assurances, the common names and numbers of animals used listed by procedures involving (a) no pain or distress (routine procedures which produce only momentary pain, such as injections are included in this category), (b) pain or distress for which appropriate anesthetic, analgesic or tranquilizing drugs were used, and (c) pain or distress for which the use of appropriate drugs would adversely affect the procedures, results, or interpretation of the research. The report must certify that anesthetic, analgesic, and tranquilizing drugs were used appropriately during research and testing and that the principal investigator has considered alternatives to painful procedures.

Noncompliance with USDA standards for the humane handling, treatment, and transportation of animals may lead to substantial fines and/or suspension of animal research activities.

**b. The IACUC and the ACT**

The 1985 amendment requires the Chief Executive Officer of each research facility appoint a committee consisting of at least three members including a doctor of veterinary medicine and one member who is not affiliated with the institution. The regulations promulgated to implement the amendment designate this committee as the “Institutional Animal Care and Use Committee (IACUC)” and charge it to act as an agent of the research facility in assuring compliance with the Act. Every six months, the committee is required to inspect all animal facilities and study areas and to review the research facility’s program to assure that the care and use of the animals conform to the regulations and standards. The Committee must file a report of its inspection with the Institutional Official of the research facility. If significant deficiencies or deviations are not corrected in accordance with the specific plan approved by the Committee, the USDA and any Federal funding agencies must be notified in writing.

The Committee must also review and approve all proposed activities involving the care and use of animals in research, testing, or teaching procedures and all subsequent significant changes of ongoing activities. As part of this review, the
Committee must evaluate procedures which reduce discomfort, distress and pain, ensure that when an activity is likely to cause pain that a veterinarian has been consulted in planning for the administration of anesthetics, analgesics and tranquilizers, and ensure that paralytic agents are not employed except in the anesthetized animal. The IACUC must also determine that animals which experience severe or chronic pain are euthanized in a manner consistent with the design of the study, that living conditions meet the species needs, that necessary medical care will be provided, that all procedures will be performed by qualified individuals, that survival surgery will be performed aseptically and that no animal will undergo more than one operative procedure which has not been justified and approved. Methods of euthanasia must be consistent with the definition contained in the regulations.

The IACUC must also assure on behalf of the research facility that the principal investigator has considered alternatives to painful procedures and that the work being proposed does not unnecessarily duplicate previous experiments. To provide this assurance, the Committee must review the written narrative description provided by the investigator. This description must include the methods and sources used in determining that alternatives were not available.

In reviewing proposed activities and modifications, the IACUC can grant exceptions to some of the regulations and standards, if they have been adequately and scientifically justified in writing by the principal investigator.

In addition to the above requirements, the research facility is required to provide training in the following areas to scientists, animal technicians and other personnel involved with animal care and use:

1. Humane practice of animal maintenance and experimentation
2. Research or testing methods that reduce or eliminate the use of animals or limit pain or distress.
3. Utilization of the information service of the National Agricultural Library.
4. Methods whereby deficiencies in animal care and treatment should be reported.

The regulations require that each research facility establish a program of adequate veterinary care that includes: appropriate facilities, personnel and equipment; methods to control, diagnose and treat diseases; daily observation and provision of care; guidance to personnel on the use of anesthetic, analgesic and euthanasia procedures and pre- and post-procedural care.

Specific requirements for maintaining records and filing annual reports are included in the regulations along with a miscellaneous section containing a variety of requirements to which a research facility must adhere.
2. Public Health Service Policy

The Public Health Service Policy on Humane Care and Use of Laboratory Animals can be found in Chapter 4206 of the NIH Manual and Chapters 1-43 of the PHS Manual. The NIH originally initiated the Policy in 1971. It was extended to all PHS activities January 1, 1979, and was revised in the spring of 1985 with implementation to be effective January 1, 1986. With the passage of the Health Research Extension Act of 1985 (PL-99-158), the policy was further revised and the Director of the NIH was required by law to establish guidelines which heretofore had only been a matter of the PHS policy. An additional revision was released in September 1986 which reflected the changes required by this Act.

Under the PHS policy, each institution using animals in PHS-sponsored projects must provide acceptable written assurance of its compliance with the Policy. In this Letter of Assurance, the institutions must describe:

- The Institutional Program for the Care and Use of Animals
- The Institutional Status
- The Institutional Animal Care and Use Committee (IACUC)

a. The Institutional Program must include a list of every branch and major component, the lines of authority for administering the program; the qualifications, authority and responsibility of the veterinarian(s), the membership of the IACUC and the procedures which they follow must be stated. The Occupational Health and Safety Program must be described for all those who have animal contact. A training or instruction program in the humane practices of animal care and use must be available to scientists, animal technicians and other personnel involved in animal care, treatment and use. The gross square footage, average daily census and annual usage of each animal facility must be listed.

b. The Institutional Status must be stated as either Category one (1) (AAALAC accredited) or Category two (2) (non-accredited). Institutions in Category two (2) must establish a reasonable plan with a specific timetable for correcting any departures from the recommendations in the Guide for the Care and Use of Laboratory Animals (1996).

c. The IACUC must be appointed by the Chief Executive Officer and consist of at least five members; including a veterinarian with program responsibility, a practicing scientist, an individual whose expertise is in a non-scientific area and an individual who is not affiliated with the institution. This Committee must use the Guide to review the animal facilities and the institutional program for humane care and use of animals at least once every six months and prepare
reports of these evaluations for the responsible institutional official. The Committee must review and approve animal-related components of proposals and significant modifications made in ongoing activities involving the care and use of animals. The Committee is responsible for reviewing concerns involving the care and use of animals and making recommendations to the Institutional Official regarding any aspect of the animal program, the facilities, or the personnel training. The Committee is also authorized to suspend activity involving the care and use of animals as set forth in the PHS Policy.

In reviewing the animal care and use component of a proposal, the IACUC must confirm that the project will be conducted in accordance with the AWA and consistent with the recommendations in the Guide. In addition, all procedures are reviewed to assure that pain or distress will be minimized and that (when necessary) appropriate anesthetics, analgesics and tranquilizers will be used. The living conditions and medical care available must be appropriate for the species used, and personnel conducting the procedures must be appropriately trained and qualified. Methods of euthanasia should be consistent with the recommendations of the American Veterinary Medical Association Panel on Euthanasia.

d. The investigator is responsible for completing a proposal in accordance with the recommendations in the PHS Policy and the instructions contained in the PHS 398 application packet. As of October 1988, the instructions for completing 398 can be found in two locations within the application package.

e. The institution is responsible for maintaining all the necessary records to document compliance with the PHS Policy and for filing annual reports which detail any changes in the program and indicate the dates of the semi-annual inspections and programmatic reviews.

f. The PHS Policy described above is intended to implement and supplement the “U.S. Government Principles for the Utilization and Care of Vertebrate Animals in Testing, Research and Training.” The nine principles are published in the PHS Policy and in The Appendix of the Guide. All those responsible for the design, supervision and review of the animal care and use component of a proposal should be familiar with this document.

3. Good Laboratory Practices Act

In 1978, the Food and Drug Administration adopted the Good Laboratory Practices rules which applied to all regulated parties who conduct non-clinical safety assessment studies. The rules require the creation of Standard Operating Procedures for all aspects of the study including animal care and use. A Quality Assurance Unit must be established to conduct internal inspection of practices and records to insure
compliance with established policies and procedures. In general, the recommendations contained in the Guide would suffice in terms of animal care when adherence is properly documented.

4. Private Funding Agencies

In recent years, the requirements of many private funding agencies which fund research projects involving the care and use of laboratory animals have changed. It is important to obtain the requirements from the agency before spending time preparing a proposal. In many instances, the proposals must be reviewed and approved prior to submission.

B. VOLUNTARY REGULATIONS

1. Institutional or Individual IACUC Requirements

Individual institutions or IACUCs may develop policies to assist in implementation of the AWA, PHS Policy, and/or AAALAC standards. Institutional policies may also go beyond the requirements of any federal regulation or AAALAC standard.

2. Individual Users

The instructions for completing PHS 398 clearly define the roles and responsibilities of the investigator assuring proper care and usage of laboratory animals. In addition to this requirement, it should be understood that improper care or use of an animal can result in the creation of non-experimental variables which can potentially compromise the integrity of an entire project. As part of their commitment to scientific excellence, the users should provide the impetus for setting and maintaining high standards for the care and use of laboratory animals within their individual and collective institutions. Failure to do so invites increased internal and external regulatory requirements which can drain limited institutional research resources. Good animal care is good science; the practice of good science should be the primary goal of all who have chosen careers in the scientific community.

C. Summary

In summary, the regulations that affect the use of animals in research, teaching and testing programs are numerous. A working knowledge of the applicable regulations is necessary if the principal investigator is to insure that proposals for funding contain the necessary information and to assure that the conduct of all research proposals is in compliance with the requirements of the regulatory and funding agencies. While the ultimate responsibility for compliance rests with the principal investigator, institutional policies should be designed to provide those responsible for compliance with the necessary resources to do so.

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