CHAPTER 3

An Overview of Global Legislation, Regulation, and Policies

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INTRODUCTION

With the steady increase in international collaborations in animal research, testing, and teaching, there is a concomitant increase in a need to be familiar with the standards of oversight in different countries. This task has been made difficult by the lack of a single, concise compilation of the laws, rules, regulations, policies, and guidelines in use around the world, and by their constant evolution toward a more restrictive stance. The goal of this chapter is to provide an introduction to the governance of animal use in a variety of countries, with more detail provided for certain parts of the world than others principally due to the greater complexity of standards to be met in those countries.

EUROPE

Changing Political Climate

At the time of this writing (fall 2009), considerable change is taking place within the legislative climate in Europe. The number of European member states has increased from 15 in 1995 to 27, including several that formerly had close social and economic ties with the USSR; concerns for animal well-being and the regulation of the scientific uses of animals were previously a low priority for many of these countries. Technological developments have resulted in the availability of new animal models—particularly genetically altered animals, which are now increasingly used as models of human disease—and in preparation of gene knockouts and gene knock-ins as a means of better understanding biological processes, particularly as they relate to humans. Developments in scientific equipment make it possible to conduct long-term studies on unrestrained animals, continuously administer substances using implanted minipumps, and obtain information about important biological mechanisms using noninvasive imaging or telemetry equipment, thereby avoiding the need always to kill animals and process tissues postmortem.

Changes are similarly taking place in the way in which animals are cared for; generally, laboratory animals are free of the principal clinical and subclinical infections common in the 1990s and are caged in ventilated racks or similar housing under conditions of much improved hygiene. It is debatable how much our knowledge has increased concerning the biological needs of the animals we care for, but most people are now more aware of perceived good practice. Against this backdrop, existing Europe-wide regulation is being reexamined with a view to bringing it up to date and ensuring wider compliance.

National Legislation

Historically, European nations had implemented laws that prohibited the ill treatment of animals. Among the earlist of these were Martin’s laws (1822) in the United Kingdom, which prohibited cruelty to sheep, cattle, and horses, and were expanded in 1835 to protect dogs and bulls and...
to outlaw cruel sports. More wide ranging legislation was later introduced into Britain, under the Protection of Animals Act of 1911. In France, the Grammont law of 1850 prohibited the ill treatment of animals, but only when this took place in public; it was repealed in 1959 by Decree No. 59-1051, which removed the requirement for witnesses to be present and hence greatly expanded its scope. The Norwegian Animal Welfare Act of 1935, revised in 1974 (and several times subsequently), required that animals (mammals, birds, toads, frogs, salamanders [newts], reptiles, fish, and crustaceans) must be treated well and account taken of their instinctive behavior and natural needs, to prevent causing them unnecessary suffering.

In Switzerland, which is not a member of the European Union, the Federal Act on Animal Protection (1978) set out measures to ensure animal protection and welfare. The measures outlined the responsibilities of animal owners in order to help prevent cruelty to animals and provided guidelines to ensure animal welfare. Both this act and the Animal Protection Ordinance (1981) included measures to regulate the use of animals in experiments, including specifying the need to train staff involved in the conduct of such experiments, authorization of procedures, arrangements for inspection of facilities, etc. Switzerland ratified the European Convention ETS 123 (Council of Europe 1986) in November 1993 and implemented it in the following year. Switzerland also tends to implement the requirements of Directive 86/609 (European Commission 1986), although it is under no obligation to do so.

Much of the earlier animal protection legislation remains in place today. In order to create a legislative framework that permits the conduct of animal experimentation, enabling legislation must be implemented that sets aside laws that safeguard animal welfare. This immediately raises substantial ethical issues for people who place a high regard on existing animal-welfare legislation. Some believe that it is wrong to set aside that legislation under any circumstances, although the majority recognizes that some exemptions may be necessary. In particular, governments attempt to create an economic climate that favors advances in understanding human and animal biology and medical applications of this knowledge—for example, by developing new treatments for diseases, such as effective medicines, new surgical approaches, and new therapeutic programs.

In the UK, such enabling legislation was included in the Cruelty to Animals Act (1876), introduced in response to concerns among the public and the scientific community about the conduct of animal experiments in physiology, which at the time were often conducted with little or no anesthesia. Anesthetic techniques of the time were crude, and there was little understanding of the impact of procedures that we recognize today as painful would have on sentient animals. Indeed, for many, the sentience of animals was still questioned. The Cruelty to Animals Act for the first time specifically authorized carrying out experiments on living animals, but placed conditions on the way in which they were done, the reasons for which they were done, and the qualifications of persons responsible for performing them; however, there was little uniformity in the provisions introduced.

Europe-wide Regulation

In 1986, two pan-national regulatory developments within Europe attempted to introduce a level of uniformity to the ways in which experimental animals are kept and used. These were the convention for the protection of vertebrate animals used for experimental and other scientific purposes (ETS 123) (Council of Europe 1986) and the directive on the approximation of laws, regulations, and administrative provisions of the member states regarding the protection of animals used for experimental and other scientific purposes (86/609/EEC) (European Council 1986a).

The Council of Europe is an intergovernmental body of 47 member states, established in 1949, whose objective is to promote human rights and democracy in Europe; one of the ways it does this is by issuing conventions. European conventions must be approved by the Committee of Ministers (its decision-making body) and constitute an open treaty that can be “signed” by member states of the council. They have no statutory force, but subject to sufficient support, parties who sign (express an interest) and then ratify the treaty are legally bound to implement its provisions.
In the same year (1986), the European Commission introduced a directive (86/609) that further regulated the way in which animals could be kept and used (European Council 1986a). The European Commission is a politically independent institution that oversees the interests of the European Union as a whole and has powers to make proposals for legislation, policies, and programs of action and for implementing the decisions of Parliament and the council. A complex legislative process is involved, but it has powers (through the European Parliament) to introduce directives and regulations.

A directive requires all members of the European Union to introduce, into their national law, measures that either match or exceed the conditions specified, whereas regulations become effective without further action at a national level. Nations that fail to implement legislation to enforce directives satisfactorily may be subject to European Court proceedings and subjected to fines. The directive of 1986, for “the protection of vertebrate animals used for experimental and other scientific purposes (86/609/EEC)” was adopted by the European Council. The intention of this directive was to ensure that when animals are used for scientific purposes, all member states would introduce similar measures, thereby ensuring uniform application of the principles of the three Rs (reduce, refine, replace) of Russell and Burch (1959). This was seen as a means of maintaining a free and open market and avoiding distorting competition or introduction of unfair trade barriers.

The directive regulated the use of vertebrate animals from specified stages of development for any experimental or other scientific purpose that may cause them pain, suffering, distress, or lasting harm. It set out a series of minimum regulatory controls for the acquisition and care of the animals and for staff. It defined requirements for registration and control of establishments where animals are bred, kept, and used, and it required that some species, such as nonhuman primates, dogs, and cats, must be individually identified and their life-long records maintained. Statistical data were to be collected for EU-wide compilation and publication by the European Commission. The controls specifically excluded certain actions, such as humane killing or using the least painful method to allow an animal to be identified. The powers of the European Economic Community under the Treaty of Rome allowed it only to regulate animal experimentation conducted for commercial purposes; consequently, when the directive was approved, a resolution was also approved in which member states agreed to apply similar controls to all types of animal experimentation (European Council 1986b).

Although one intention of Directive 86/609/EEC had been to harmonize the regulation of animal experimentation in the EU, some member states chose to enact further reaching legislation whereas others applied only minimum rules. Additionally, the legal provisions made for enforcement differed in different countries. For example, procedures for granting of project authorization, authorization of reuse of animals, and arrangements for national inspections vary widely in different member states. Similarly, requirements for the collection and publication of annual statistics are implemented in different ways by different states; for example, some reporting requirements include numbers of animals killed for use of tissues whereas others exclude these. In part, these differences arise from the different agencies that states have identified as enforcement bodies (competent authorities). In the UK, this is the Home Office; in France, the Ministry of Agriculture; in the Netherlands, the Ministry of Health, Welfare and Sport; and, in Italy, the Ministry of Health.

Current Developments

Appendix A of the Council of Europe Convention ETS 123 lays down details of the ways in which experimental animals may be kept: husbandry provisions, cage sizes, environmental conditions, etc. The convention incorporates a requirement for the parties to review and, where necessary, update the requirements of Appendix A. Over a 5-year period from the turn of the century, a substantial review of recommendations was carried out; as a result, a number of changes were introduced in 2006. Specifically, the changes related to the way in which laboratory animals are required to be housed (Council of Europe 2006).
Previously, in 1998, the European Commission had ratified the Council of Europe Convention ETS 123 (subject to exclusion of the requirement to communicate certain statistical data) and incorporated the provisions into Directive 86/609 (European Council 2003). Because of this, the terms of the convention are now binding on all member states, rather than only those who chose to sign the convention in their own right.

In November 2008, the European Commission published a draft proposal for a new directive to replace that enacted in 1986. The text of the proposal had been many years in preparation and involved widespread discussion among interested parties, including the scientific community and animal protection organizations. As part of the process of revising the directive, an Internet consultation was carried out between June and August 2006 to determine public opinion in EU countries about the scientific uses of animals. Three quarters of respondents believed that the level of welfare and protection of experimental animals within the EU was either poor or very poor and only 40% agreed with the use of animals to develop medical treatments for disease. This was a self-selected survey susceptible to influences by campaigning organizations, but it suggested the considerable public concern that undoubtedly influenced the European Commission in the measures it has recommended.

At the time of this writing, the proposal has been presented to both the European Parliament (composed of members elected by each nation) and the European Council (which consists of representatives from the member states). Considerable negotiation is under way to achieve final agreement of all three bodies—the commission, council, and parliament—and a number of amendments have already been proposed.

The New Directive

Although the final text of the new directive has yet to be finalized, a number of common themes have emerged that are very likely to be included.

Like the previous directive, the new one will specify circumstances under which animals may be used for experimental purposes. It will require that animals be used for experimental purposes only if there is no suitable alternative and then only under circumstances that ensure that the minimum number is used. The species and methodology chosen should be the ones least likely to result in pain, suffering, distress, or lasting harm, and the experiment should be likely to yield a satisfactory scientific result. Restrictions will be placed on the reuse of animals. Breeders, suppliers, and users of laboratory animals must all be authorized by the authority responsible for implementing the national legislation (the “competent authority”) and such authorization shall be renewable after a fixed period. Member states will be expected to establish inspection procedures to ensure that the terms the directive are adhered to, and the commission itself is likely to retain power to carry out its own inspections when it deems this necessary.

One impact of the new directive will be a focus on scientific projects as the principal point of control. Each project will need to be submitted for authorization to the competent authority. The application must include not only an explanation of the way in which the experiment has been designed, the reason for selection of the model, and a description of the procedures to be carried out, but also a nontechnical summary (this may not be mandatory in all cases). The applicant must also provide evidence that the three Rs have been implemented fully, including the use of humane end points where appropriate. Some tests still occasionally used in toxicity testing, such as the LD50, in which death is used as a final end point, will be prohibited unless there really is no alternative.

Applications will be evaluated from a point of view of their scientific justification and evidence for implementation of the three Rs. It is likely that the severity of procedures will need to be classified according to a scheme established by the European Commission; this will comprise four categories: nonrecovery, mild, moderate, and severe. Procedures likely to cause severe and persistent pain, suffering, or distress that cannot be alleviated are likely to be prohibited.
In deciding whether or not to approve project applications, the competent authority must consider the expertise of those involved in designing the experiments and ensuring the three Rs are implemented and require reassurance that animal husbandry standards are satisfactory and that there is adequate veterinary care. The competent authority will be required to decide whether or not to authorize the project within a fixed time period (currently 40 working days). In some circumstances, member states may be allowed to introduce simplified administrative procedures for projects that do not involve the use of nonhuman primates and are classified as moderate, mild, or nonrecovery.

A system of retrospective project assessment may be required to establish whether or not the objectives of the project were achieved, whether the harms inflicted on animals accorded with those anticipated beforehand, and whether all aspects of the three Rs were adequately implemented. All projects involving the use of nonhuman primates or procedures judged to be severe are likely to be subject to retrospective assessment.

Another major change from the 1986 directive is a move toward more uniform and formal application of the three Rs. One aspect of this is likely to be a requirement for facilities at which animal experimentation takes place to establish a committee responsible for ensuring implementation of the three Rs at a local level. These have been called “animal welfare bodies” or “ethical review bodies,” but their remit will be to ensure that animal welfare receives a high priority at all stages of an animal’s life, from the time it is born or arrives at the establishment until the time it is killed. It is also anticipated that each member state will be required to set up a national committee to advise the relevant competent authority and other interested parties about matters relating to the acquisition, breeding, accommodation, care, and use of animals so as to ensure best practices.

In line with the requirements of the revised European convention, standards of care and accommodation of animals will be expected to ensure that any restrictions on the extent to which animals can satisfy their physiological and ethological needs are minimized and that the environment and condition of animals be checked each day. There may also be a requirement for staff involved in the care and use of animals to be trained adequately. Animals experiencing avoidable pain, suffering, distress, or lasting harm must be identified promptly and palliative measures introduced as far as possible.

Reflecting public concerns, restrictions are likely to be placed on the breeding and use of nonhuman primates. There will probably be a move to prohibit the capture of wild primates for experimental purposes and also to end their use for breeding so that, after an appropriate transition period, only the offspring of nonhuman primates that have been bred in captivity will be used in procedures. Almost certainly, the use of nonhuman primates will be subject to additional constraints, including stronger scientific justification, and there is likely to be a complete ban on the use of great apes except in very special circumstances.

At the time of writing (September 2010) the new Directive has just completed its second reading by the European Parliament and awaits minor revisions of a technical nature, translation, and publication. A period of time will be allowed for member states to implement requirements of the Directive into their national legislation, and it is unlikely that this will be achieved before early 2013. Probably, all member states will find it necessary to make changes to their national legislation; in many cases, these changes may be substantial. Many European countries have decided to avoid making adjustments to their legislation until the requirements the new directive have been published. Despite this, as a condition of entry, new entrants to the European Union are required to comply with the existing directive (86/609) and are therefore obliged to implement provisional legislation, which presumably will have to be changed when the new directive is introduced.

Consequences

Provisions of the European directive must be implemented in national law and, consequently, it is argued that a detailed and finely structured directive will result in broadly similar legislative arrangements within individual countries. Creation of a level economic playing field also provides
opportunities for the more uniform application of general principles, including application of the three Rs, identifying which types of experiments may be permitted or are excluded, ensuring that studies are carried out by competent persons, and ensuring that animals are appropriately sourced, transported, cared for, and used. Establishment of a relatively uniform legislative framework makes it easier for those engaged in commercial or academic investigations that involve laboratory animal science to plan and implement transnational activities, thus facilitating the free movement of people. Individuals should find it easy to adapt to the legislative requirements of different countries. It remains to be seen whether these outcomes will be achieved.

Because of the broad level of consensus necessary for introduction of a directive, there is wide public consultation, which provides an opportunity for the views of all stakeholders to be considered. The bigger the pool of ideas is, the more likely it is that best practice will be identified. Collection of a broad, shared experience from a wide range of experts and the general public ensures that European citizens feel that they can contribute to law making. This can have drawbacks, however, because it provides considerable opportunity for organized lobby groups to exert focused pressure on the legislative program within Europe. Thus, resulting legislation may be distorted by attempts to accommodate extreme viewpoints rather than creating law that is broadly satisfactory to the majority of the European population.

In consequence, the legislation eventually drafted may prove to be less flexible than originally intended. It can be difficult to take account of differing national cultures and interests—for example, the preponderance of studies involving fish, which have great economic importance in Norway, rather than more conventional warm-blooded vertebrates. Proposals for reporting numbers of animals used and strictures on how they are used may not always be drafted in a way that makes implementation straightforward. One further disadvantage of centralized legislative procedures is that some citizens may feel that the decision-making process is so remote that they cannot contribute effectively to the development of law. It is interesting that in the survey conducted by the European Union preparatory to developing the replacement for Directive 86/609, most citizens polled felt that standards of care and use of laboratory animals within their own country were higher than the average for the European Union.

NORTH AMERICA

United States of America

In the United States, oversight of animal care and use for research, testing, and teaching is achieved by numerous laws, regulations, policies, and guidelines from two principal government organizations: the U.S. Department of Agriculture (USDA) and the U.S. Public Health Service (PHS). Other guidance may be derived from scientific panels (e.g., through the Institute for Laboratory Animal Research [ILAR]) and be endorsed by the government as required standards. Institutions that meet certain standards may participate in the voluntary accreditation program offered by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International), which provides external peer review of an institution’s program and further quality assurance.

Cornerstones of an Animal Care and Use Program

An institution that uses animals for research, education, or testing purposes must determine which of the many federal and state regulations, policies, and guidelines to follow. Although an institution may be obligated to follow a variety of standards, some consistent elements distinguish successful animal care and use programs. These are discussed next.
Institutional Animal Care and Use Committee

The group of individuals comprising the institutional animal care and use committee (IACUC) represents institutional and public interests and has the responsibility for oversight and evaluation of the entire animal care and use program and facilities. Because committee members act on behalf of the institution, their role is pivotal to engendering a humane and progressive animal care and use program. The successful program is overseen by a committee that is engaged and knowledgeable and receives strong administrative support. Because the committee is responsible for investigating reports of concern regarding animal welfare, its functions must be well known throughout the institution and there must be ready (and confidential) access to the committee membership.

Training

The importance of adequate training for all those involved in the animal care and use program is underscored by the emphasis it receives in the USDA’s Animal Welfare Regulations (USDA 1991), PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy, OLAW 2002), and the Guide for the Care and Use of Laboratory Animals (National Research Council 1996). The Animal Welfare Regulations and the PHS Policy require institutions to ensure that people caring for or using animals are qualified to do so. The Animal Welfare Regulations stipulate several key topics be included in the institution’s training program:

- Humane methods of animal maintenance and experimentation, including the basic needs of each species of animal, proper handling and care for the various species of animals used by the institution, proper preprocedural and postprocedural care of animals, and aseptic surgical methods and procedures
- The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress
- Proper use of anesthetics, analgesics, and tranquilizers for any species of animal at the institution
- Methods to report any deficiencies in animal care and treatment
- Use of the services at the National Agricultural Library, such as appropriate methods of animal care and use, alternatives to the use of live animals in research, prevention of unintended and unnecessary duplication of research involving animals, and information regarding the intent and requirements of the Animal Welfare Act

The Guide urges adequate training be provided to members serving on the IACUC so that they can appropriately discharge their responsibilities. In addition to the IACUC members, the Guide recommends that the professional and technical personnel caring for animals be trained, as well as investigators, research technicians, trainees (including students), and visiting scientists. The Guide also endorses training in occupational health and safety, in procedures specific to an employee’s job, and in procedures specific to research (e.g., anesthesia, surgery, euthanasia, recognition of the signs of pain and/or distress, etc.).

Occupational Health and Safety

Although not mandated by the Animal Welfare Regulations, the Guide and thus the PHS Policy require that an occupational health and safety program be in place that is specific to the animal care and use program. The details of the occupational health and safety program will vary among institutions but will be predicated on the experimental and nonexperimental hazards identified at each institution and an assessment of the risks posed to personnel (by either job classification or the health of the individual) by these hazards. The Guide emphasizes that health professionals (doctors or nurses, as appropriate) should be involved in the design and implementation of the program. Participation by individuals involved in the animal care and use program should be based on “the
hazards posed by the animals and materials used; on the exposure intensity, duration, and frequency; on the susceptibility of the personnel; and on the history of occupational illness and injury in the particular workplace.”

Several federal standards and regulations have been published that must be incorporated into the occupational health and safety program, depending on the species and hazardous agents in use: for example, Biosafety in Microbiological and Biomedical Laboratories (Centers for Disease Control and Prevention/National Institutes of Health 2007), Occupational Safety and Health Administration’s Blood-borne Pathogen Standards (Occupational Safety and Health Administration 2001), and Recombinant DNA Guidelines (National Institutes of Health 2009).

Adequate Veterinary Care

The Animal Welfare Regulations and the PHS Policy stipulate that the veterinarian must have the authority to oversee several key components of the animal care and use program, including animal procurement and transportation; quarantine, stabilization, and separation of animals; surveillance, diagnosis, treatment, and control of disease; surgery; the selection of analgesic and anesthetic agents; method of euthanasia; animal husbandry and nutrition; sanitation practices; zoonosis control; and hazard containment. The veterinarian must be qualified through either experience or training in laboratory animal medicine or in the species being used. The veterinarian brings a specific perspective to the deliberations of the IACUC and is a voting member. The Animal Welfare Regulations describe the program of adequate veterinary care as including the following:

- Availability of appropriate facilities, personnel, equipment, and services
- Use of appropriate methods to prevent, control, diagnose, and treat diseases and injuries, inclusive of the availability of emergency, weekend, and holiday care
- Daily observation of all animals to assess their health and well-being
- Guidance to researchers regarding handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia
- Nutrition
- Pest and parasite control
- Adequate preprocedural and postprocedural care in accordance with current professional standards (see also APHIS Tech Note March 1999, Animal Care Policy #3, and APHIS Form 7002) (Animal Plant Health Inspection Service 1992, 1999)

The Report of the American College of Laboratory Animal Medicine on Adequate Veterinary Care in Research, Testing and Teaching (American College of Laboratory Animal Medicine 1996) describes a program of adequate veterinary care as including (1) disease detection and surveillance, prevention, diagnosis, treatment and resolution; (2) guidance on anesthetics, analgesics, tranquilizer drugs, and methods of euthanasia; (3) review and approval of all preoperative, surgical, and postoperative procedures; (4) promotion and monitoring of an animal’s well-being before, during, and after its use; and (5) involvement in the review and approval of all animal care and use at the institution. This report is used by AAALAC International as a reference standard in its assessments of animal care and use programs.

Resources

The infrastructure of the animal care and use program, including facilities, equipment, number and qualifications of personnel, and genetic and health status of the animals used, has a significant influence on the quality of the program. The Animal Welfare Regulations specify the size of the primary enclosures in which animals are to be kept. The Guide describes several environmental variables—such as temperature, ventilation, illumination, sanitation standard, and cage size, as
well as the components of the physical plant—that can facilitate the research, testing, or teaching goals of the institution and states that “a well-planned, well-designed, well-constructed, and properly maintained facility is an important element of good animal care and use” (National Research Council 1996).

AAALAC International has identified that physical plant deficiencies (specifically, the operation of the heating, ventilation, and air conditioning systems) rank as the third most common concern (following the scope of the occupational health and safety program and the functioning of the IACUC) requiring correction before a full accreditation status can be granted. In this manner, the impact of the facility on the safety and well-being of the animals is underscored.

Federal Oversight of Animal Research, Testing, and Teaching

Federal laws for the humane treatment of animals have been in place since 1873, when Congress passed a law governing the treatment of livestock during shipment for export. The law was called the 28 Hour Law after the maximum length of time animals could be transported before receiving food, water, and rest (Anderson 2002). This law was later repealed and a new 28 Hour Law was passed in 1906 that is still in effect today. However, the first federal law to protect nonfarm animals was not passed until 1966: the Laboratory Animal Welfare Act, administered by the Animal and Plant Health Inspection Service (APHIS) of the USDA. At the time, this law was primarily directed at dog and cat dealers and required that individuals or corporations that bought or sold dogs or cats for laboratory activities be licensed and adhere to certain minimum standards for the care of animals and that users of cats or dogs for research register with the USDA and meet minimum standards for animal care. For animal users, the law applied only to animals held prior to or after the laboratory activity. Interestingly, the New York Anticruelty Bill of 1866 addressed the use of animals in research and predated federal interest in this subject (Rozmiarek 2007).

The Laboratory Animal Welfare Act of 1966 was amended in 1970, 1976, 1985, 1990, 2002, and 2008 to broaden its coverage. Public Law 91-579, the Animal Welfare Act of 1970, increased the species of animals covered under the law to include all warm-blooded animals and increased the scope of applicability of the law to include the time animals were held in the facility. Specifically exempted were horses not used in research and agricultural animals used in food and fiber research, retail pet stores, state and county fairs, rodeos, purebred cat and dog shows, and agricultural exhibitions. Public Law 94-279, the Animal Welfare Act Amendments of 1976, included common commercial carriers, such as airlines, under the law, which subsequently led to standards being developed for shipping containers and conditions of shipment.

Public Law 99-198, the Improved Standards for Laboratory Animals Act, added several new provisions to the law, including minimization of animal pain and distress and consideration of alternatives to painful procedures, consultation with a doctor of veterinary medicine for any practice that could cause pain to animals, limitation on conducting more than one major survival surgery on an animal, establishment of an IACUC to provide oversight of the animal care and use program and facilities, provision of specific training to personnel, provision of exercise to dogs, and a stipulation to promote the psychological well-being of nonhuman primates. The 1990 amendment to the Animal Welfare Act, Public Law 101-624 Food, Agriculture, Conservation, and Trade Act of 1990, Section 2503, Protection of Pets, established a holding period for dogs and cats at shelters and other holding facilities prior to sale to dealers. The law also requires dealers to provide written certification to the recipient regarding the background of each animal.

Of increasing debate has been the exclusion of rats and mice from the Animal Welfare Act. The 1970 amendment to the Animal Welfare Act stated that an animal was defined as “any live or dead dog, cat, monkey (nonhuman primate animal), guinea pig, hamster, rabbit, or other such warm-blooded animal as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes, or as a pet.” In this way, the Secretary
of the Department of Agriculture was provided the authority to determine which animals would be covered by the act. In 1977, the USDA promulgated regulations that specifically excluded rats, mice, and birds used for research from the definition of “animal.”

In 2002, Senator Jesse Helms added an amendment to the AWA in the Farm Bill, signed by President George W. Bush on May 13, 2002, that redefined the term “animal” in the law to match the current definition in the regulations. This change means that the definition of “animal” in the Animal Welfare Act excludes “birds, mice of the genus *Mus,* and rats of the genus *Rattus,* bred for use in research” from the definition of “animal.” By changing this term, the USDA does not have the authority to regulate animals excluded by the new definition. However, the USDA general counsel has determined that the uses of these animals for other purposes are now covered by the law.

Since the 1966 Act, Congress has vested the USDA with both promulgation and enforcement authority. The USDA is required to conduct unannounced annual inspections of research facilities, with follow-up inspections until any cited deficiency has been corrected. Exempt from this provision are federal research facilities. Researchers, intermediate handlers, and common carriers are required to register with the USDA, while animal dealers and exhibitors must be licensed. Research facilities and U.S. government agencies are required to purchase animals only from licensed sources, unless the source is exempted from obtaining a license.

Failure to comply with regulatory requirements, despite formal notification of an item or items of noncompliance and an opportunity to effect a correction, can result in fines levied on the facility, suspension of authority to operate, and even permanent revocation of the facility’s license to operate. Thus, the enforcement arm of the USDA’s oversight responsibility is strong and has been used over the years to improve animal welfare at dealers, exhibits, and research facilities.

The other federal agency charged with oversight of research animal care and use is the PHS. The PHS Policy was implemented in 1973 and was revised in 1979 and 1986. Today, the PHS authority is derived from Public Law 99-158, the Health Research Extension Act of 1985, Section 495, Animals in Research. Under this Act, institutions conducting animal research using PHS funding, such as through the National Institutes of Health, must comply with the PHS Policy. The policy requires submission by the funding recipient (referred to as an “awardee institution”) of an Animal Welfare Assurance Statement, which must be approved by the PHS’s Office of Laboratory Animal Welfare (OLAW), National Institutes of Health, which commits the institution to follow the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (Interagency Research Animal Committee 1985) (see Table 3.1) and the Guide (National Research Council 1996).

Because the PHS Policy’s (OLAW 2002) standards for animal care and use are based on the Guide, the PHS Policy covers all vertebrate animals used in research, testing, or teaching. In addition to stating a commitment to animal welfare, the Assurance Statement must designate clear lines of authority and responsibility for institutional oversight of the work, inclusive of a designated “Institutional Official,” who is ultimately responsible for the animal care and use program; identify a qualified veterinarian involved in the program; provide a description of the occupational health and safety program for relevant personnel in the program; provide a description of mandated training; and provide a description of the facility.

In the Assurance Statement, the institution must indicate whether the animal care and use program is reviewed by a third party, such as the Association for Assessment and Accreditation of Laboratory Animal Care International, or the program and facilities are reviewed solely by internal systems of the institution. Institutions in this latter category must provide a copy of their most recent semiannual report with the assurance. The Assurance is renegotiated with OLAW every 5 years. OLAW can approve, disapprove, restrict, or withdraw approval of the Assurance.

PHS awarding agencies, such as the NIH, may not make an award for an activity involving live vertebrate animals unless the prospective awardee institution and all other institutions participating
The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

I. The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et seq.) and other applicable Federal laws, guidelines, and policies.

II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.

IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally, the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

VIII. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.

IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

<table>
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in the animal activity have an approved Assurance with OLAW and provide verification that the IACUC has reviewed and approved those sections of the grant application that involve the use of animals. Applications from organizations with approved Assurances must address five specific points pertaining to the use of animals:

- A detailed description of the proposed work, including species, strain, sex, age, and number of animals to be used in the proposed work
- A justification of the use of animals, species, and number of animals
- Information on the veterinary care for the animals
- A description of the procedures for ensuring that discomfort, distress, pain, and injury will be minimized
- A description of the method of euthanasia and the reason for the selection of that method, including a justification for any method that does not conform with the American Veterinary Medical Association's (AVMA) euthanasia guidelines

Awardee institutions that do not comply with the standards of the Guide, the USDA Animal Welfare Regulations (USDA 1991), and other standards referenced in the PHS Policy (e.g., the AVMA's Euthanasia Guidelines; AVMA 2007) may have their Assurance Statement restricted,
which in turn can limit access to PHS funding for research. Sustained noncompliance with the PHS Policy can result in withdrawing the approval of the Assurance and cessation of all PHS funding for animal-based activities.

The awardee institution must also submit an annual report. Institutions must report any change in category status from that noted in the Assurance Statement. Institutions indicate the dates of their IACUC semiannual program reviews and facility inspections and provide copies of any “minority views” filed by IACUC members with the annual report. The role of the IACUC in providing local oversight of animal care and use is a key element of the PHS Policy. Although the required composition of the IACUC for the PHS differs slightly from USDA requirements, due to the memorandum of understanding concerning laboratory animal welfare among APHIS/USDA, the Food and Drug Administration (FDA), and the NIH that sets forth procedures for cooperation among the three agencies in their oversight of animal care and use programs, the general functions and responsibilities of the IACUC are similar (see Table 3.2).

OLAW conducts site visits of awardee institutions “for cause” and “not for cause.” In addition, an ongoing significant mission of OLAW is the educational outreach it performs in collaboration with awardee institutions. Jointly sponsored workshops focus on information of value to Institutional Officials and IACUCs to provide appropriate oversight of animal care and use. OLAW also provides guidance through articles in journals, commentary on other articles, NIH guide notices, and a listserv.

Other Laws, Regulations, and Policies

In 1978, the FDA promulgated regulations for the conduct of animal-based research of new or existing pharmaceutical agents, food additives, or other chemicals. These regulations, known as the good laboratory practice (GLP) regulations (Code of Federal Regulations 1998), specify appropriate diagnosis, treatment, and control of disease in animals used in this work. The Environmental Protection Agency (EPA) has issued companion regulations for conducting research pertaining to health effects, environmental effects, and chemical fate testing in a separate set of GLP regulations (Code of Federal Regulations 1997). GLP regulations of both the FDA and EPA rely heavily on adequate and detailed record keeping. Records must include standard operating procedures,
animal identification, food and water analysis, documentation that any pesticides or chemicals used near the animals do not interfere with the study, and documentation of any disease and treatments that animals experience. On-site inspections are conducted to ensure compliance with the GLP standards.

The Department of Defense (DoD) developed a “Policy on Experimental Animals” in 1961 to ensure that all research at DoD facilities involving animals was conducted in accord with certain principles of animal care (Department of Defense 1995). Later versions of this policy included overseas sites. Subsequently, a joint regulation, entitled “The Use of Animals in DoD Program,” from the Army, Navy, Air Force, Defense Nuclear Agency, and Uniformed Services University required all DoD facilities to “seek accreditation by AAALAC” and to establish local institutional animal care and use committees.

State laws to protect animals have a long history, with the first anticruelty law passed in 1641 in the Massachusetts Bay Colony to prevent riding or driving farm animals beyond established limits (U.S. Congress Office of Technology Assessment 1986). All 50 states and the District of Columbia have enacted anticruelty laws. The overarching goals of these laws are to protect animals from cruel treatment, require that animals have access to suitable food and water and shelter from extreme weather. Some state laws define “animal” and some do not. The state laws encompass a diversity of approaches to providing protection to animals. Some states have additional provisions for animals used in research, and many states prohibit the sale of pound animals into the research stream. In general, criminal penalties are imposed for offenses. On occasion, state anticruelty laws have been used against research facilities. In recent years, state and federal laws have been used by private citizens or citizen groups claiming “standing to sue” on behalf of animals. The issue of “standing” has undergone a long litigation process and a chronology of court decisions on this issue has been compiled by the National Association for Biomedical Research (1999).

Because animal research can involve a variety of different species, several other federal acts, laws, and treaties have bearing on animal use. These include the U.S. Endangered Species Act, which restricts the research conducted on these animals to research that would directly benefit the species under investigation; the Marine Mammal Protection Act, which provides authority for scientific research on marine mammals by special permit; the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), which requires signatory countries to obtain a permit for the import or export of certain species; the Lacey Act, which governs import, export, and interstate commerce of foreign wildlife; and the Migratory Bird Treaty Act, which makes it unlawful to take or possess any protected bird except by permit.

Canada

The Canadian constitution precludes federal legislation pertaining to the use of animals in research, testing, or education because such use is under provincial jurisdiction. Six provinces have established legislation regarding animal research, five of which reference the Canadian Council on Animal Care (CCAC) guidelines and policies. In addition, although there is no federal requirement to participate in the CCAC assessment program, the two principal funding agencies require grantee institutions to have a Certificate of Good Animal Practice® and to comply with CCAC guidelines and policies for continued funding. Contractors performing work for the federal government are required to adhere to CCAC guidelines, as specified in the Public Works and Government Services Canada Standard Acquisition Clauses and Conditions Manual, Section 5, Subsection A, Clause A9015C: Experimental Animals.

The CCAC, founded in 1968, places responsibility for humane animal care and use with the animal care committee (ACC) at each institution. The ACCs are granted specific authority and provided with terms of reference under which they operate (e.g., membership, authority, responsibilities, and functioning). The CCAC’s mission is “to act in the interests of the people of Canada to ensure
through programs of education, assessment and persuasion that the use of animals, where necessary, for research, teaching and testing employs optimal physical and psychological care according to acceptable scientific standards, and to promote an increased level of knowledge, awareness and sensitivity to relevant ethical principles.” Thus, the CCAC has two principal functions: (1) developing guidelines and policies to govern experimental animal care and use, and (2) monitoring compliance with those guidelines and policies. The CCAC is an independent organization and receives funding from the Medical Research Council (MRC) and the Natural Sciences and Engineering Research Council (NSERC).

The CCAC establishes guidelines for its certified institutions to follow; these are currently contained in the two-volume Guide to the Care and Use of Experimental Animals (Canadian Council on Animal Care 1984, 2000). Adjunct guidelines address topics such as animal use protocol review, transgenic animals, selecting appropriate endpoints, and developing an animal user training program. The CCAC also has established several policies, including the ethics of animal research, review of scientific merit, social and behavioral requirements of experimental animals, acceptable immunological procedures, and categories of invasiveness.

On-site assessments using panels of experts from the animal care and use community and a representative nominated by the Canadian Federation of Humane Societies are conducted triennially. An institution is deemed to be in compliance if the CCAC report prepared by the assessment panel and approved by the assessment committee (a standing committee composed of at least four council members) contains only regular, minor, and/or commendatory recommendations, and the institution submits an implementation report for any regular recommendations that is judged to be satisfactory. Institutions found to be in compliance or conditional compliance will receive a CCAC Certificate of Good Animal Practice.

If the CCAC report contains major and/or serious recommendations whose correction does not require verification by an on-site reassessment, but rather can be verified through documentation, and the institution provides to the CCAC an implementation report that is judged to be satisfactory, then compliance is maintained. An assessment report containing major or serious recommendations may place the institution in a status of conditional compliance, probation, or noncompliance. All relevant funding agencies and government ministries and departments are notified of an institution’s noncompliance with CCAC guidelines (Canadian Council on Animal Care 2000). Sustained noncompliance with CCAC guidelines and policies can ultimately result in withdrawal of all animal-based research funding to the institution.

LATIN AMERICA (LA)

As is true in the rest of the world, LA has a wide range of public and private institutes, centers, and institutions that carry out experimental procedures that involve the use of animals. With the purpose of meeting international requirements and to ensure appropriate treatment of these animals, most of LA countries have included in their legislation some reference regarding animal care, use, and welfare. In some cases, this has entailed taking legislation applied in other countries, such as the United States and Canada, as a model; in other instances, the country has or has created its own legislation in which aspects from other countries’ legislation are included.

In many countries, standards regarding laboratory animal care and use are, at present, considered under more general laws for the protection and care of animals, which also describe guidelines for the treatment of domestic, companion, decoration, and exotic species. Some countries, such as Argentina, Chile, and Brazil, have bills specifically designed for laboratory animals that are under review for approval by the local authorities.

Relative to this, it is important to mention that, since 1999, Mexico has had a federal regulation (NOM-062-ZOO-1999, Technical Specifications for the Production, Care and Use of Laboratory
Animals) and was the first country in LA to legislate specifically on the subject. Argentina has three laws or regulations issued by independent organizations (one by the National Drug and Food Administration and the other two by the National Service of Agrifood Health and Quality of the Argentina Republic (Servicio Nacional de Sanidad y Calidad Agroalimentaria [SENASA]) that complement one another and regulate the use of laboratory animals in quality control procedures, teaching, and investigation, as well as animal facility operations.

In a similar way, Costa Rica has an animal welfare law (republic law) in which a whole chapter is dedicated to experimental animals. This law has a special appendix (Science and Technology Ministry Decree 26668) that goes into detail of some aspects regarding laboratory animal production, care, and use.

The laws, regulations, and guidelines that regulate the use of experimental animals in LA countries, as well as the date on which and purpose for which they were created, are summarized in the following sections.

Colombia

In 1989, the 84 Law of December 27, 1989, adopted the National By-Law of Animal Protection, which includes a special chapter dedicated to the use of experimental animals with investigation purposes (sixth chapter). This law requires or recommends the creation of an ethics committee (Art. 26) and the application of the three Rs. The law established economic sanctions that may include disqualification of the offender for a maximum of 5 years if a federal employee is involved. This is a national law and not only refers to the use of animals with experimental purposes, but also covers all animal species that are directly or indirectly related to men and those that are part of the local fauna.

Costa Rica

Since December 1994, Costa Rica has had an animal welfare law. In 1992, this country presented a bill intended to regulate the animal rights proclaimed in the Universal Animal Rights Declaration that is now filed. In 1993, the Gazette 242, December 20 1993, published a bill, Animal Welfare and Ethology Law that has practically no relation to laboratory animal use. The animal welfare law of 1992 includes some chapters regarding experimental animals and establishes some considerations related to animal experimentation. It has some general ethical principles related to the Three Rs of Russell and Burch (1959). As in Colombia, this is a general law, though it has an attached decree issued by the Science and Technology Ministry, which includes specific points that address the production, care, and use of experimental animals; these are considered mandatory standards in this country.

Argentina

On December 20, 1996, the National Administration of Drugs, Food and Medical Technology approved the Animal Facility Regulation for laboratories that manufacture medical products and/or conduct tests for third parties (ANMAT disposition no. 6344; published in the official bulletin 20-01-97). This regulation is a requirement for companies that manufacture medical products, carry out control tests, and/or work as third-party contractors; it includes standards related to facilities, environmental conditions, animal welfare, hygiene, reinvestments, and waste management in these activities. However, even if it is considered mandatory, the regulation does not include other establishments that produce and maintain animals for experimental purposes. This regulation does not mention the type of sanction that would be applied to an institution in a noncompliance situation.

In a similar way, in 2002 SENASA issued the 617/02 resolution, Requirements, Conditions and Procedures for the Technical Equipment of Laboratories with Production and Maintenance
Animal Facilities, and Experimental Areas, and in 2003 the 76/03 resolution, Creation, within the Management of Laboratories and Technical Service Control of the National Health and Food Processing Areas, of the Permanent Assessment Council in Animal Facility Management.

Argentina also has a bill formulated by its local laboratory animal association (AACyTAL), which was published in its 15/16 bulletin and is now waiting to be revised and approved by the local authorities. The aim of this bill is to guarantee the protection of animals used in experimental procedures and other scientific purposes, taking into consideration the three Rs and, as in the Mexican federal regulation, the control and maintenance of records of the facilities dedicated to these types of activities, regardless of their purpose (animal production; research, testing, or teaching; and/or the combination of any of these). Recently, this bill was sent to the senate and parliament to be analyzed and approved. There is still no resolution regarding this request.

Uruguay

Before September 15, 2009, the production, care, and use of animals for experimental purposes were regulated to some extent by an Animal Experimentation Honorary Commission that had, since 1996, organized and given training courses in laboratory animal science to technicians, researchers, teachers, and students. After September 15, 2009, Uruguay implemented specific federal regulation for the production, care, and use of laboratory animals (Use of Animals in Experimental, Teaching and Scientific Investigation Activities) that, as with the federal Brazilian law, refers only to species from phylum Chordata, subphylum Vertebrata. This law required the creation of a National Experimentation Commission (Comisión Nacional de Experimentación, CNEA), and ethical committees for the use of animals for experimental purposes, establishing administrative and economic penalties for those institutions that fail to comply with it.

Uruguay also has a general decree (Decree 82000-200) that establishes responsibilities toward animal welfare. This decree has important similarities to the anticruelty laws of other countries in this region. The only public university of the country, the University of the Republic, has an ordinance regarding the use of animals for experimental and/or teaching purposes.

Mexico

To standardize and regulate the production, care, and use of laboratory animals within its territory, in 1999 Mexico published a federal regulation, Norma Oficial Mexicana NOM-062-ZOO-1999, Technical Specifications for the Production, Care and Use of Laboratory Animals, which is current, but undergoing a second revision that will include some animal species not considered when the law was created, as well as some ethical principles related to the care and use of these animals. This law is based mainly on the Guide for the Care and Use of Laboratory Animals (National Research Council 1996). The current version applies to animal facilities and/or other establishments that produce and/or maintain rodents (rats, mice, guinea pigs, hamsters, and gerbils), rabbits, carnivores (dogs and cats), nonhuman primates, and swine.

Besides addressing issues related to the production, care, and use of the previously mentioned species, installation design, and environmental considerations, it states that each facility must have a veterinarian, an IACUC, and an occupational health program. Moreover, it requires each facility that produces and/or maintains animals for experimental purposes to register with the corresponding authorities and to send an annual activity report that addresses specific information requested. Oversight of this law is the responsibility of the Agriculture, Livestock and Rural Development, Fisheries and Food Secretariat and state governments. Compliance is the responsibility of the General Directorate of Animal Health and the delegations of the secretary of Agriculture, Livestock and Rural Development, Fisheries and Food Secretariat. The law does not mention the type of
sanction that would be applied to facilities that fail to comply with its content, leaving these aspects to the application of other laws, which are also mentioned in the document as references.

Besides this federal law, Mexico has local and/or institutional laws and regulations such as the Animal Protection Law, which includes general standards regarding laboratory animal care and use. In a similar way, in Chapter 3, Title 7, of the General Heath Law, Articles 121–126 refer to general aspects regarding the use of animals for research and experimentation purposes related to human health, stating clearly that all experimental protocols should be designed to minimize or prevent animal suffering, that animals must be euthanized using appropriate means, that all animal facilities should have facilities and spaces according to the requirements of each of the animal species housed, and that the production areas must be under the management of qualified personnel. Under this law, the manager or director of the institution is responsible for the security measures pertaining to the care and use of laboratory animals and for establishing an effective occupational health program.

**Cuba**

The National Center for Production of Laboratory Animals (CENPALAB) published the Practical Code for the Use of Laboratory Animals in 1992. In this same year, the Academy of Sciences of Cuba created and approved the Cuban Professional Workers Ethical Code, which is mandatory for all researchers in the country. This code considers legal sanctions defined and determined by different Cuban organizations. Resolution 110, which establishes the creation of ethics committees in institutions of the Cuban national health system, was developed in 1997 and approved in 2000 by the Vadi Resolution No. 4/00. Chapters V and VII of this resolution refer specifically to the use of animals in research. In 2001, a group of Cuban scientists presented a bill of animal welfare, which was later incorporated into the animal welfare law as a result of an agreement taken under the National Veterinary Sciences Plenum. In 2004, in Regulation 39/04 (BPS 2004), the creation of the IACUC was approved and, during April 2007, the Guide for Determination of Humane Final End Point in Animals Used in Biomedical Research was submitted for approval to the plenum in the International Veterinary Sciences Meeting at La Habana.

**Venezuela**

On June 21, 1999, the Sciences and Technology Ministry of Venezuela published the Code of Bioethics and Biosecurity, which established guidelines for the use of live animals in research based on bioethical principles such as responsibility, justice, autonomy, and caution. The first and second chapters of this code mention the requirements that must be fulfilled for the use of animals for experimental purposes. These include the application of the three Rs and issues related to animal welfare, personnel training, reduction of pain, veterinary supervision, and humane euthanasia; it refers to ICLAS international guidelines for aspects regarding animal facility design.

**Chile**

A bill intended to regulate the use of animals for experimental purposes has been introduced in Chile. This document has been in the congress for several years, waiting to be analyzed and approved. The only law in the country regarding animal treatment is quite general and includes only welfare issues. Nevertheless, most universities and research institutes have ethics committees that regulate the use of animals for experimental purposes, ensuring compliance with international specifications. The National Council of Research, Science and Technology, which is responsible for funding research projects in the country, requires that all projects that use animals be approved by the ethics committee of the institution and then reviewed by its own bioethics commission. Moreover, in some universities, research protocols must be evaluated by a bioethics and biosecurity commission. Due
to the lack of specific legislation, Chile bases its requirements on the FELASA recommendations, the CCAC guidelines, and the *Guide for the Care and Use of Laboratory Animals.*

**Brazil**

PL 1.153, 1995, was approved by the congress in October 2008 as no. 11794 and enforced by Decree No. 6899 in July 2009 (i.e., Law 11794/2008, Decree 6899/2009). This bill considers species of the phylum Chordata, subphylum Vertebrata, except man. The decree obliges the Ministry of Science and Technology to create CONCEA, the National Council on the Control of Animal Experiments. CONCEA will develop the guidelines and potentially act as an appellate body if the local institutional committee cannot solve a particular question or problem. Each institution conducting animal research must register with CONCEA and must have an ethics committee (Comisiones de Ética en el Uso des Animales, Ceua).

**Peru and Guatemala**

These two countries have no legislation. The institutes and universities of Peru base their internal guidelines on the *Guide for the Care and Use of Laboratory Animals.* Guatemala has only the internal guideline of the Central Animal Facility of the University of San Carlos.

**Ecuador**

Although Ecuador has no specific laboratory animal legislation, there is an animal protection foundation with legal attributes that oversees issues related to laboratory animal use.

**Panama**

Panama has a bill, PL 20, which, under its fifth chapter, mentions some general aspects related to the use of animals in research.

**Paraguay**

In Paraguay, there is only a general anticruelty guideline that refers to farm animals and regulates aspects related to compliance with international requirements for exportation of animals for food purposes.

**Puerto Rico**

An animal protection law was created in Puerto Rico in 2004. Chapter V of this law refers to general aspects of animal welfare related to animals used for experimental purposes.

**Nicaragua**

Nicaragua has a special law for animal protection and a bill, 121/000123, which establishes guidelines for the production, transport, experimentation, and euthanasia of all animal species.

**ASIA**

The importance of laboratory animal science is becoming more recognized in Asian countries. Several national laboratory animal science associations have been established in the region. One of the oldest national associations in Asia is the Japanese Association of Laboratory Animal Science.
(JALAS), founded in 1951. Biomedical scientists have worked to establish a national legislation system in their respective countries to reflect the public’s concern for research-animal welfare. One progressive legislative system in Asia is the amendment of Law for the Humane Treatment and Management of Animals (Law No. 105, 1973) in Japan. In other Asian countries, as in Japan, laws, regulations, and guidelines pertaining to laboratory animals follow with scientists’ advice. The most recent improvement of the legislative system pertaining to laboratory animals is based on the advancement of biomedical science, the internationalization of Asian countries, and public interest in animal welfare in Asia.

In 2003, the Asian Federation of Laboratory Animal Science Associations (AFLAS) was established. The exchange of information this forum presents, including legislation in laboratory animal science, increased among the member countries of AFLAS. The initial establishment of a legislative system for laboratory animals was influenced by Western countries, but more recent amendments of the legislation have been influenced by neighboring Asian countries as well as Western countries.

In a recent revision of laws, regulations, and guidelines in Asia, the three Rs have been emphasized (e.g., in the Japanese Law for the Humane Treatment and Management of Animals, revised in 2005, and the Korean Animal Protection Law, revised in 2007) (Korea Animal Protection Law 2007).

The standard of laboratory animal welfare in Asia is influenced by AAALAC International. Revisions of laws, regulations, or guidelines in some Asian countries, such as the Korean Animal Protection Law (enforced in 2008) and guidelines noticed in 2006 by various ministries in Japan, encourage assessment by an independent body.

Japan

The Law for the Protection and Management of Animals was amended in 1973. The most recent revision was made in 2005 and the name was changed to the Law for the Humane Treatment and Management of Animals (Japan 2009). Before the revision, “refinement” was the only “R” of the three Rs that was directly included. The principles of “reduction” and “replacement” were subsequently added to the law. More specifically for laboratory animals, the document, “Standards Relating to the Care and Management of Experimental Animals” (Notice No. 6 of the Prime Minister’s Office 1980), was revised in 2006 by the Ministry of Environment. At this time, the name changed to “Standards Relating to the Care and Management of Laboratory Animals and Relief of Pain” (Notice No. 88 of the Ministry of Environment, April 28, 2006, Science Council of Japan 2009).

The Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labor and Welfare developed “Fundamental Guidelines for Proper Conduct of Animal Experiments and Related Activities in Academic Research Institutions under the Jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology” and “Basic Policies for the Conduct of Animal Experimentation in the Ministry of Health, Labor and Welfare.” The ministry of Agriculture and Fisheries published the “Guideline for the Proper Conduct of Animal Experimentation.” These guidelines require the establishment of institutional regulation for animal experiments. The president of a research institution is the responsible person for the proper conduct of animal experimentation. The president is required to designate institutional laboratory animal care committee members to review animal use protocols and to oversee management of the laboratory animal care program. The guidelines also require disclosure pertaining to information about animal experiments.

The Science Council of Japan prepared the “Guidelines for Proper Conduct of Animal Experiments” to serve as a reference material or a model when research institutions compile their own regulations for animal experimentation in accordance with the preceding fundamental guidelines and basic policies in 2006. The guidelines resemble the ILAR Guide (National Research Council 1996).
It was thought that laboratory animal housing and holding should be regulated by law in Japan. However, there was strong opinion that animal experiments conducted as a component of academic activities should not be over-regulated by law. In this way, Japan favors the establishment of a system based on Japanese customs.

The “Guidelines on Methods of Sacrificing Animals” (Notice No. 40 of the Prime Minister's Office, July 4, 1995) were revised in 2007. The methods of euthanasia of laboratory animals should follow the recommendations in this guideline, with emphasis on minimizing pain and distress during the procedure.

There are many other laws, regulations, and guidelines related to animal experimentation in Japan. For example, the guidelines require safety management for animal experimentation. Genetic engineering experiments; animal experiments using radioactive materials or radiation; experiments using poisons, deleterious substances, or psychotropic drugs; and animal experiments using pathogenic agents or hazardous chemicals must be conducted in strict compliance with related laws and ordinances. Animal carcasses and laboratory waste must be disposed of appropriately, using the methods stipulated in in-house regulations. Laws and ordinances related to waste material regulated by law must be followed. In particular, violations of the Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms are reported. The usage of most transgenic and knockout mice must comply with this law.

Recently, bioterrorism has gained public interest. In response, the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases has been revised several times to restrict the importation of animals and the usage of infectious agents. To prevent the potential spread of infectious diseases in humans when importing living mammals and birds and the carcasses of rodents and lagomorphs, the import of animals is controlled by this law, the Enforcement Regulations of the Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infectious Diseases, and other regulations.

The system of notification of import also applies to rodents to be used as laboratory animals. The importation and exportation of laboratory animals including gene-modified rodents to and from Japan must comply with this law. The importation of primates is restricted by the Invasive Alien Species Law and Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases. The importation of farm animals is regulated by the Domestic Animal Infectious Disease Control Law. The importation of dogs and cats and some other species of animals, including laboratory animals, is regulated by the Rabies Prevention Law. A stringent quarantine program, vaccinations, and individual identification with microchips are applied to these species of animals.

Korea

The Korean Animal Protection Law was amended in 1991. This law was not stringently implemented in Korea. However, as a reflection of public concern about animal welfare, the Korean Ministry for Food, Agriculture, Forestry and Fisheries amended the animal protection law in 2007 and the law was enforced in 2008. The law consists of 26 articles, and articles 13 and 14 are directly related to animal experiments.

Article 13, “Experiments with Animals,” states the general requirements for the conduct of animal experimentation, including the consideration of the Three Rs alternatives. As a refinement, animal experiments should be conducted with the least pain and distress, using sound veterinary practices, including analgesics, sedatives, and anesthetics. The law requires euthanasia with the least pain and distress after animal experimentation. Article 14, “Establishment of Animal Experimentation Ethics Committee,” states that the president of the research institution must establish the committee. The committee should comprise one chairman and 3–15 members; at least
one-third of the members must be nonaffiliated members. The four specialists in various areas are defined by the law, such as a registered veterinarian, animal welfare specialist, lawyer, and professor at higher education institutions.

The composition of the Korean Animal Protection Law is very similar to the Japanese Law for the Humane Treatment and Management of Animals, but the Korean law is more stringent for animal experiments. The establishment of the ethics committee is suggested by various guidelines in Japan, but not Japanese law. However, the Korean law clearly states the establishment of an ethics committee and the members of the committee are defined by the law, including a veterinarian and nonaffiliated members. The Korean law is similar to the U.S. Animal Welfare Act, but does not exclude mice, rats, and birds as laboratory animals. The Korean Animal Protection Law may be one of the most stringent laws in terms of animal experimentation. However, another law, the Laboratory Animal Law by the Korean Food and Drug Administration, has been newly enforced. Thus, there are now two laws to regulate laboratory animals in Korea.

People's Republic of China

The Regulation for Administration of Laboratory Animals was amended in 1988. Under this regulation, the National Standards for Laboratory Animals were published in 1997. After the publication of these standards, more practical laws related to laboratory animals were amended—namely, Administration of Laboratory Animal Facility Law in 1998 and Laboratory Animal Permission Law in 2001. For an overview of the framework of regulations pertaining to laboratory animal use in China, see Kong and Qin (2010).

In 2001, following the latest progress of international laboratory animal science, the State Technology Supervision Administration issued a new edition of national standards for laboratory animals. In the revised edition, minimum living space of animals was added to the requirements of environment and housing facilities. The national standard was intended to meet the requirements of animal ecology and welfare.

The guideline for humane treatment of laboratory animals was issued and implemented in 2006 by the Ministry of Science and Technology. The guideline was the first state-policy-related document that specially directed administrators and technicians on how to pay attention to the welfare of laboratory animals. This guideline clearly stipulates the task and responsibility of the administration committee of producing and applying institutions. It also actively initiates the Three Rs principles—reduction, replacement, and refinement. According to the guideline, the institution intending to use laboratory animals has to obtain the administration’s permission.

The national level of laboratory animal issues is the charge of the Ministry of Science and Technology, but the Provincial Bureau of Science and Technology is in charge of this issue locally. The provincial bureau establishes the animal research committee, which approves laboratory animal facilities and laboratory animal specialists and technicians.

The larger cities in China, such as Beijing and Shanghai, have established their own municipal offices for laboratory animal science, including the Beijing Administration Office of Laboratory Animals and the Office of Shanghai Administrative Committee for Laboratory Animals and Regulations. In these cities, biomedical science and industries are advancing very rapidly, and the quality of laboratory animals and laboratory animal welfare are regulated as successfully as in most Western countries.

Taiwan (Chinese Taipei)

The Animal Protection Law was promulgated in 1998 (Taiwan Animal Protection Law 1998). Chapter III of this law specifically addresses scientific application of animal experiments from Article 15 to Article 18. Chapter II, Article 12, of the law precludes the killing of animals. It says
that an animal shall not be allowed to be killed at will with the exception of several instances, including “for the purpose of scientific [experimentation].” Euthanasia of laboratory animals is specifically addressed in Article 17: “After a scientific experiment, the conditions of the experimental animals shall be examined immediately. If parts of their limbs or organs have been lost, or they continue to suffer the pain that affects their living quality, they shall be put to death in a least painful way.” The reuse of laboratory animals is prohibited.

The replacement of animal experimentation is not clearly stated but reduction and refinement are addressed in Article 15. A management system at research institutions to supervise the scientific application of animal experiments is also recommended. The law requires that the competent authority regulate the source, application, and management of experimental animals and set up an ethics committee of animal experimenters to supervise and manage the scientific experiments. The ethics committee is required to have at least a veterinarian and a representative of an animal protection group from the private sector.

The establishment of ethics committees is required by the Regulations for Establishing the Experimental Animal Ethic Committee of the Council of Agriculture. Article 2 of the regulation defines the function of the experimental animal ethics committee, including supervision and management of the scientific application of animal experiments, formulation of the rules, ways and measures for animal protection, and overseeing the management team. The committee is required to meet every 3 months.

The establishment of the management group is more specifically described in the Regulation for Establishing the Management Group of Animal Experiments. In Article 2 of the regulation, the composition of the management group is defined in detail, including a doctor of veterinary medicine and certified trained specialists. Article 3 of the regulation defines five missions for the management group including review of the scientific application of animal experiments, suggestions for the improvement of animal experiments, suggestions for laboratory animal facilities, supervision of animal procurement, and supervision of annual reports of animal experimentation.

The protection of animals is controlled by the Enforcement Rules of Animal Protection. The rules define the institution that performs the scientific application of animal experiments, including:

- Schools above the level of college
- Animal drug manufacturer
- Medicine manufacturer
- Biological drug manufacturer
- Hospital
- Research institution
- Other scientific applications of animal experiments designated by the central competent authority; however, the conduct of animal experiments in educational institutions below the level of junior high school is restricted in Article 17 of the law

The laboratory animal legislation in Chinese Taipei is well defined in various laws, regulations, and rules. These documents are translated into English. In terms of disclosure of laboratory animal welfare legislation, Taiwan is one of the most progressive among the Asian countries.

**Philippines**

Republic Act No. 8485, the Animal Welfare Act, was amended in 1998. Section 6 says that the killing of any animal is unlawful, with exceptions that include authorized research and experiments. The method of killing animals is defined as a humane procedure, which means the use of the most scientific methods available may be determined and proved by the committee. The committee on animal welfare attached to the Department of Agriculture is described in Section 5 of the Act.
However, there are not any specific statements for laboratory animals in the Animal Welfare Act. The Philippine Association for Laboratory Animal Science (PALAS) was established in 1986. PALAS acted as a main scientific body to establish the Animal Welfare Act in 1998 and its corresponding rules in terms of laboratory animals. The PALAS Code of Practice for the Care and Use of Laboratory Animals covers the practical aspects of laboratory animal welfare issues in the Philippines.

**Thailand**

The Ethical Principles and Guidelines for the Use of Animals by the National Research Council of Thailand were published in 1999. This guideline consists of two parts: 1) ethical principles and 2) guidelines for the use of animals and monitoring of the ethical guidelines for the use of animals. The former consists of five chapters:

- Animal users are to be aware of the value of the life of animals.
- Animal users are to be aware of the accuracy of the research outcome using the minimal number of animals.
- The use of wild animals must not violate laws or policies for wildlife conservation.
- Animal users need to be aware that animals are living beings just as humans are living beings.
- Animal users must keep detailed data and records of animal experiments.

These chapters are followed by practical guidelines.

Monitoring of the ethical guidelines for the use of animals consists of two chapters, including an institutional level and a national level. The establishment of at least one committee is advised to manage and be accountable for the use of animals. The committee members should be diversified and comprise upper level administrative members of the institution, researchers, and lay people. The chapter defines the responsibilities of the institutional committee. At the national level, the National Research Council of Thailand is required to appoint a committee to be responsible for and to promote the ethical use of animals in research; the chapter includes language that defines the committee’s authority.

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