

Introduction to Laboratory Animal Medicine

The health and welfare of animals used in biomedical research must be supported to be consistent with contemporary ethical standards and to help ensure the scientific validity of research results. Providing this support requires individuals with expertise in many fields including basic and applied sciences, bioethics, regulatory oversight, experimental design, and laboratory animal science. Laboratory animal science is defined by the US National Library of Medicine as “[t]he science and technology dealing with the procurement, breeding, care, health, and selection of animals used in biomedical research and testing” (Box 1.1). It includes husbandry, nutrition, behavior, health care, production, and management of laboratory animals.

Laboratory animal medicine is a specialized field within laboratory animal science and a recognized specialty within veterinary medicine. At its core, laboratory animal medicine encompasses the diagnosis, treatment, and prevention of diseases in animals used in research, teaching, and testing. It emphasizes methods to prevent and minimize pain, discomfort, and distress in research animals; facilitates acquisition of biologically meaningful results; and minimizes experimental variability. The field has progressively grown and evolved in response to scientific and medical advances, shifts in the regulatory environment, and the ever-changing focus of scientific inquiry.

Diverse groups of individuals play important roles within laboratory animal medicine. Veterinarians have a variety of responsibilities within an animal care and use program that may include provision of veterinary care, management of animal care

Clinical Laboratory Animal Medicine: An Introduction, Fifth Edition.

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Box 1.1

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and use facilities, education of individuals who care for and use laboratory animals, assisting biomedical scientists in the selection of and humane use of animals, obtaining and interpreting biologically relevant data, and assuring compliance with regulations and policies that affect research animals. Veterinary technicians work under the supervision of a veterinarian, assisting them in carrying out these responsibilities. They often provide technical support in disease detection, including oversight of colony health monitoring programs, treatment of ill animals, blood sampling, and necropsy and tissue collection. When engaged in research or drug study positions at a pharmaceutical firm or university, they administer test products and collect data. This type of employment often requires the veterinary technician to be credentialed and have a bachelor's degree. Credentialed veterinary technicians, with sufficient education, training, and experience, and who have completed testing requirements can apply to join the Academy of Laboratory Animal Veterinary Technicians and Nurses, a specialty organization within the National Association of Veterinary Technicians in America (NAVTA). Veterinary technicians may also work in research compliance or supervise other animal facility staff such as assistant laboratory animal technicians, animal caretakers, and cagewash personnel. It should also be noted that individuals without formal veterinary training make significant contributions in support of laboratory animal medicine. For example, animal caretakers who closely observe and handle animals on a daily basis can be instrumental in detecting behavioral changes and identifying early signs of illness so that animals can be promptly assessed by veterinary personnel.

ANIMALS USED IN RESEARCH, TEACHING, AND TESTING**Biomedical Research**

Remarkable advances have been made in medicine and science over the past century, such as the characterization of complex host–pathogen interactions and immune system functions, development of vaccines for polio and hepatitis B, creation of antibiotics and antivirals for infectious diseases, procedures for organ transplantation and open heart surgery, and development of drugs for chronic disorders such as diabetes and high blood pressure. Animals played a major role in each of these advances (Table 1.1). New treatment modalities for cancer, less invasive surgical approaches, and the development of equipment such as the laser and endoscopic instruments would not have been possible without the use of animals. Often, advances made in human health are also applied to the benefit of companion animals (Figure 1.1). For instance, most cancer treatments and many advanced surgical techniques and imaging modalities developed for use in humans are now routinely available to veterinary practices.

Table 1.1. Animal roles in medical discoveries and advancements

Year*	Scientist(s)	Animal(s) Used	Contribution
1901	von Behring	Guinea pig	Development of diphtheria antiserum
1904	Pavlov	Dog	Animal responses to various stimuli
1923	Banting, Macleod	Dog, rabbit, fish	Discovery of insulin and mechanism of diabetes
1924	Einthoven	Dog	Mechanism of the electrocardiogram
1945	Fleming, Chain, Florey	Mouse	Discovery of penicillin and its curative effect in various infectious diseases
1954	Enders, Weller, Robbins	Monkey, mouse	Culture of poliovirus that led to development of vaccine
1964	Block, Lynen	Rat	Regulation of cholesterol and fatty acid metabolism
1966	Rous	Rat, rabbit, hen	Discoveries concerning hormonal treatment of prostatic cancer
1970	Katz, von Euler, Axelrod	Cat, rat	Mechanism of storage and release of nerve transmitters
1979	Cormack, Hounsfield	Pig	Development of computer-assisted tomography (CAT scan)
1984	Milstein, Koehler, Jerne	Mouse	Techniques of monoclonal antibody formation
1990	Murray, Thomas	Dog	Organ transplant techniques
1997	Prusiner	Mouse, hamster	Discovery of prions, a new biological principle of infection
2003	Lauterbur, Mansfield	Clam, mouse, dog, rat, chimpanzee, pig, rabbit, frog	Discoveries concerning magnetic resonance imaging
2008	Barre-Sinoussi, Montagnier	Monkey, chimpanzee, mouse	Discovery of human immunodeficiency virus
2008	zur Hausen	Hamster, mouse, cow	Discovery of papilloma viruses causing cervical cancer
2011	Hoffman, Beutler	Fruit fly, mouse	Discoveries concerning the activation of innate immunity
2011	Steinman	Mouse	Discovery of the dendritic cell and its role in adaptive immunity
2012	Gurdon, Yamanaka	Frog, mice	Discovery that mature cells can be reprogrammed to become pluripotent
2013	Rothman, Schekman, Sudhop	Mouse, hamster	Discovery of how cells organize movement of materials into and out of cells
2014	O’Keefe, Britt, Moser	Rat	Discovery of cells that constitute the brain’s “inner GPS” positioning system

(Continued)

Table 1.1. (Continued)

Year*	Scientist(s)	Animal(s) Used	Contribution
2015	Campbell, Omura, Tu	Mouse, dog, sheep, cattle, chicken, monkey	Discoveries contributing to development of novel therapies for roundworm and for malarial infections
2016	Ohsumi	Mouse	Discovery of mechanisms for cellular autophagy
2017	Rosbash, Hall, Young	Fruit flies	Discovery of molecular mechanisms controlling the circadian rhythm

Sources: National Association of Biomedical Research (<https://www.nabr.org/biomedical-research/medical-progress>), Foundation for Biomedical Research (<https://fbresearch.org/medical-advances/nobel-prizes>), and Nobel Prize (www.nobelprize.org).

* Year of occurrence or award recognition.

Box 1.2

Ex vivo experimental methods should be used in place of in vivo experimental methods whenever possible.

Significant advances have been made in the development and use of *ex vivo* (“out of the living”) experimental methods which do not require the use of animals or animal-derived products. These experimental methods should be used in place of *in vivo* (“in life”) experimental methods whenever possible, but only when resultant experimental findings are truly representative and predictive of the system(s) they are intended to model (Box 1.2). Unfortunately, most *ex vivo* testing systems cannot generate sufficiently comprehensive and accurate data representative of an intricate, living being. As a result, use of *in vivo* experimental methods is still required until more refined alternatives are developed and validated. In the interim, use of *ex vivo* experimental methods can be effective and valuable in refining and reducing animal use for some areas of study such as early identification of toxic or ineffective experimental compounds and modeling compound–receptor interactions.

Teaching

Animals play a valuable role in education, starting from preschool and continuing to the college and graduate levels. Although computer modeling and videos can replace select learning experiences, some personal learning styles and educational objectives are best suited to hands-on learning. Through interactions with animals, children can learn how to care for another living being. They also learn lessons in responsibility and respect. At the middle and high school levels, animal tissues may be used for hands-on experience with dissection and now-common laboratory methods such as immunoassays and molecular diagnostics. These experiences often reveal the amazing world of biology and science to young people as they learn about the complex and specialized processes that form the basis of biological functions. In college, animals

are used in a variety of professional and graduate-level courses in medical and health-related fields. Surgery courses provide young veterinary surgeons a chance to hone their skills before performing them on client-owned animals. Physicians use animals to practice robotic, endoscopic, and laser surgery prior to performing them in people. Animals are used in training courses for medical personnel so they may acquire and advance their skills in emergency and critical care environments. Clinical technique courses provide veterinary students and veterinary technician students opportunities to develop the diverse range of skills necessary for the safe and humane care of their future animal patients, such as animal handling and performance of physical exams, injections, and catheterizations. It is now common for animals used for educational purposes to either be temporarily housed in a research/teaching environment and then adopted into loving homes or be pets brought in by their owners to assist with training.

Product Safety Testing

Several decades ago, consumers were subjected to publicly marketed drugs and cosmetics that were not adequately tested to assess human safety. Examples included early treatments for syphilis containing mercury and arsenic, an eyelash dye that caused blindness in numerous individuals, and an elixir marketed for use by children and that caused the death of over 100 people. These and other similar events led to the passage of the Food, Drug, and Cosmetic Act (FD&C) in 1938. Broadly speaking, the FD&C was created to safeguard and protect consumer health and safety from the sale of dangerous products. The Act is enforced primarily by the Food and Drug Administration (FDA) which requires animal testing of products when a scientifically valid, alternative testing method is not available. When animal testing is required to obtain FDA approval, the FDA requires product manufacturers and sponsors to conduct the studies in accordance with the Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR Part 58). Recently, many manufacturers have marketed cosmetic products as “cruelty-free.” This unregulated labeling or advertising practice can be deceiving to consumers who may incorrectly assume that neither the product nor any product components were tested in animals. However, it is more likely that animal safety testing had been performed on individual product components (but not necessarily the final product) or that testing had been contracted by the manufacturer to be performed by an external testing group. As a consequence, consumers must be savvy in their interpretation of unregulated product labeling.

Animal Usage Statistics

According to the US Department of Agriculture (USDA) *Animal Report Animal Usage by Fiscal Year*, 792,168 animals whose use is regulated by the Animal Welfare Act were used for research, teaching, and product safety testing in the United States in 2017. It should be noted that this figure does not include the annual usage of mice, rats, birds, or fish as the USDA is not charged with regulatory oversight of these species as required by Animal Welfare Act. Rather, use of these species is regulated by other entities and the precise numbers of their use is unknown. However, it is estimated that up to 26 million animals of these species are used annually. Mice and rats

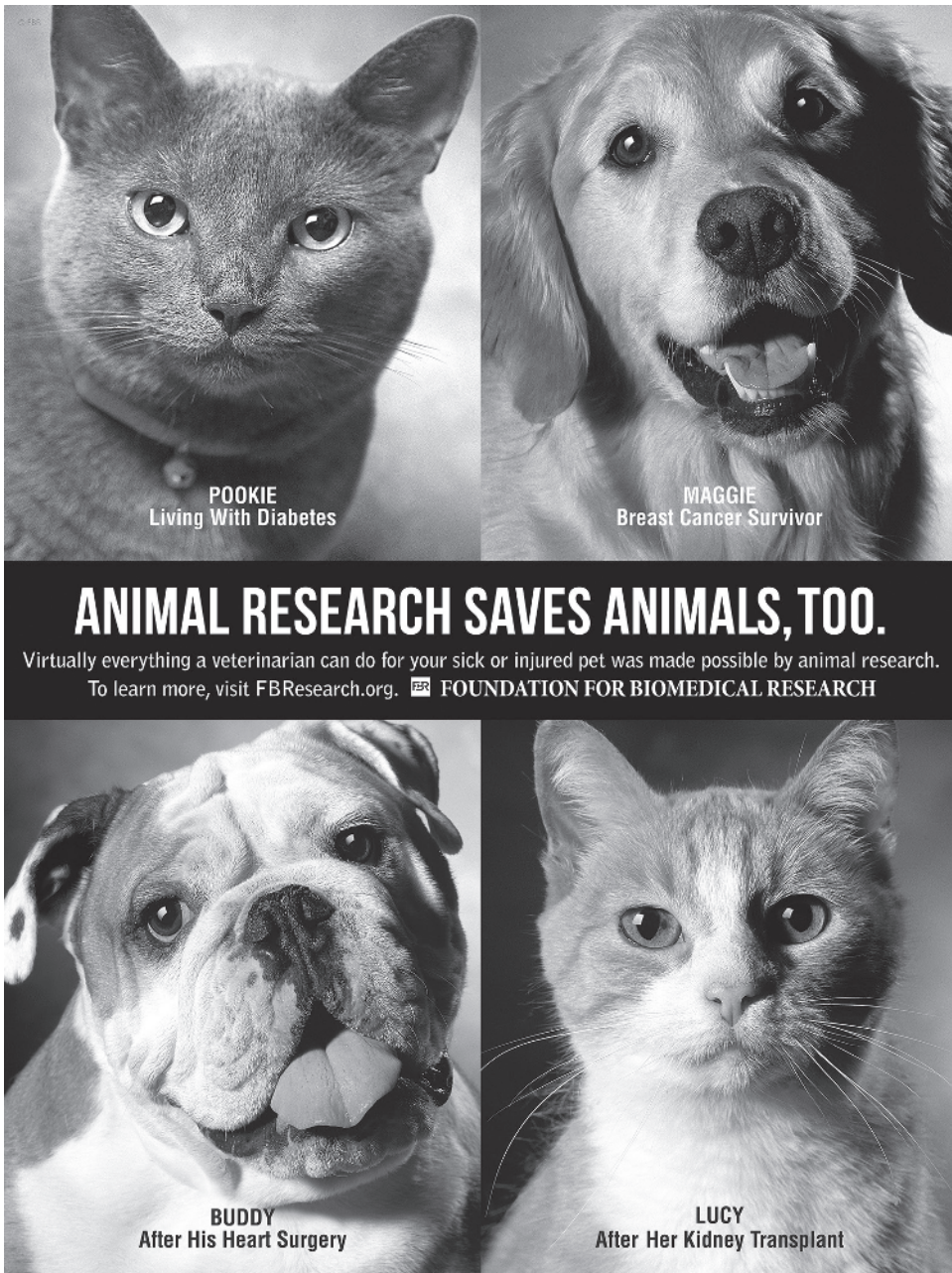


Fig 1.1. Animal research saves animals too. (Source: Foundation for Biomedical Research.)

account for greater than 95% of all animals used while the number of dogs, cats, and nonhuman primates combined account for less than 1% of the animals used.

With the exception of the increased use of zebrafish, the use of nonrodent animals has been declining over the past three decades primarily due to use of more refined experimental systems and an intense effort by the biomedical research community to

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decrease animal use (Box 1.3). The number of dogs used in research currently is less than one-third of its numbers in the late 1970s. The number of nonhuman primates used over the past decade has risen slightly, in part due to increasing emphasis of research into human brain function and neurodegenerative diseases such as Alzheimer's. Across all species, the majority of animals used in biomedical research are bred specifically for that purpose.

To put the numbers in perspective, approximately 12–27 million animals are used in research in the United States. All but approximately 1 million of these are mice, rats, birds, or fish. According to Speaking of Research (www.speakingofresearch.com), “we consume over 1800 times the number of pigs than the number [of pigs] used in research” and we consume over 340 times more chickens than the total number of animals used in biomedical research.

Funding Sources

In the United States, the National Institutes of Health (NIH) and the National Science Foundation (NSF) are the primary public granting agencies for biomedical research. The NIH, a branch of the Public Health Service (PHS), provides competitive federal grants for investigators interested in the health-related advancement of humans and animals. The NSF encourages basic research in behavior, mathematics, physics, medicine, biology, and other sciences. In addition to the NIH and NSF, funding is available from universities and colleges, state governments, industry, and private foundations. Acquiring funds to conduct research is difficult as competition for grant money is high, with only 10%–20% of submitted proposals receiving funding. Typically, a grant provides money for the primary scientist's and research team's salaries, supplies, equipment, and purchase and care of animals for a 3-year period. The primary scientist, or principal investigator (PI), is responsible for planning and coordinating all phases of the research study, including tabulating data, reporting findings to the funding agency, and publication of results. When a study yields valuable results, the funding agency may renew the grant for an additional period of time.

Regulatory Oversight and Accreditation

Multiple levels of regulation (e.g., federal, state, and local) function to provide oversight of animal research including mandating standards for animal care and use. In addition, many institutions choose to participate in voluntary assessment and accreditation programs which recognize institutions that have exceeded the minimum standards required by law and have achieved excellence in animal care and use. Chapter 2 provides additional information regarding the oversight provided by governmental and voluntary organizations.

Institutional Animal Care and Use Committee

Prior to the use of animals in research, teaching, or testing, a protocol must be submitted to and approved by the institution's Institutional Animal Care and Use Committee (IACUC) (Box 1.4). The protocol is a detailed, written description of the proposed animal care and use. It justifies the use of vertebrate animals to accomplish the study's aims, details the procedures that will be performed on the animals, and describes how the animals will be housed and cared for throughout the project. Additionally, the PI must give several assurances, including that the study does not unnecessarily duplicate previous studies, that the staff working with the animals have adequate training to accomplish the study tasks in a humane manner, that alternatives to animal use have been carefully considered, and that any activities that may induce animal pain or distress are scientifically necessary. Animal use protocols are usually approved for 3 years, may undergo an annual review by the IACUC, and must be resubmitted for full, *de novo* (anew) review every 3 years. IACUCs must formally review and approve all changes to approved protocols prior to their implementation. Moreover, IACUCs are required, at a minimum frequency (usually twice yearly), to review their institution's established program of animal care and use and physically inspect facilities where animals are housed or manipulated. Additional information about IACUCs can be found at www.iacuc.org.

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ETHICAL CONSIDERATIONS

The 3Rs: Replacement, Refinement, and Reduction

Two English scientists, Russell and Burch, coined the term “the 3Rs.” In 1959, they examined the ethical aspects and “the development and progress of humane techniques in the laboratory” (Russell and Burch, 1959). The 3Rs represent three ethical tenets of responsible animal use: replacement, refinement, and reduction (Box 1.5). Research institutions and regulatory authorities continually strive to apply the principles of the 3Rs to ensure animals are used in an ethical manner. There is an ethical imperative that scientists use animals only when they have provided assurance to the

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IACUC that no nonanimal methods will allow them to achieve their scientific aim. This search for alternatives is mandated for species covered by the Animal Welfare Act (AWA; see APHIS, 2017). For species not covered by the AWA, both the Public Health Service Policy and the *Guide for the Care and Use of Research Animals* (ILAR, 2011; the *Guide*) refer to the “US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training” (OLAW, 1985), which includes language about alternatives to animal use (see Chapter 2, Table 2.1). The US Government Principles also mandate using the minimum number of animals necessary to obtain valid results. This is synonymous with reduction, one of the 3Rs.

Replacement refers to replacing animals with a nonanimal alternative, such as *in vitro* (“in glass,” outside of the body) screens with cell culture or computer (*in silico*) modeling, or by using the least sentient animal (e.g., rat in place of dog; fish in place of mouse) that will enable collection of meaningful and valid data. Continued advances in the sciences and testing methods have helped to spur development of animal testing alternatives. Any alternative test, however, must be validated before it can be used to replace a test currently using animals. The development and use of genetically specialized animals, such as nude and transgenic mice, has made it possible to reduce the number of other species such as dogs and cats. Environmental toxicity studies often use zebrafish rather than mice or other mammals. Alternate tests for ophthalmic safety testing have been developed using tissues obtained from slaughterhouses as well as specially designed cell and tissue culture systems. In addition, the limulus amoebocyte lysate (LAL) assay has largely replaced the rabbit pyrogen test for detecting pyrogens, such as endotoxin, in injectable substances.

Refinement refers to methods that incorporate modification of a procedure to lessen animal pain and distress or enhance animal well-being. Use of less invasive procedures, provision of pain relief, provision of environmental enrichment, and decreased restraint time are examples of refinements. For example, through advanced imaging techniques, such as magnetic resonance imaging (MRI), researchers can now view structures and observe anatomic functions that once could only be accomplished during surgery or at necropsy. Investigators must constantly review the way animal studies are conducted to ensure that the methods used are the most humane and refined to minimize pain and distress. In addition, investigators work closely with laboratory animal veterinarians and the IACUC to assure that humane experimental endpoints are in place to minimize pain and distress to the greatest degree possible. The IACUC often collaborates with investigators and veterinary personnel to develop humane endpoint guidelines that help determine when an animal should be euthanized or removed from a study. Examples of humane experimental endpoints include a defined percentage of weight loss, tumor size, presence of labored breathing, or an inability to ambulate. There is a delicate balance between collecting the necessary scientific data from a study and ensuring that animal welfare is preserved. For example, it can be difficult to identify the point at which an animal should be removed from study or euthanized before it becomes significantly ill. When appropriate, the least invasive experimental methods should be used, and anesthesia or analgesia be administered to eliminate unnecessary pain and distress.

Reduction refers to using the minimal number of animals in a study while remaining consistent with sound scientific and statistical standards. Investigators must

constantly strive to find ways to reduce animal numbers. Using a combination of computer-based simulators in conjunction with animal subjects, employing better statistical methods, or using one control group with multiple study groups are examples of methods used to reduce animal numbers. The number of animals used in product safety testing has been significantly reduced through validation of alternative testing methods. Experiments can be designed using multiple sections with the results derived from earlier sections used to refine the number of animals or experimental groups used in later sections. For example, a “staircase design” is often used in acute toxicology testing. This method involves administration of a limited number of drug dosages (high and low) to then determine a more precise dose range for further testing. Used with sophisticated computer-assisted computational methods, the staircase design can determine a point estimate of the lethal dose, approximate confidence intervals, and determine toxic signs for the substance tested, yet use fewer animals.

Overall, the research community must continually challenge itself to consider whether the animal research being performed is ethical and justifiable. The principles underlying the “3Rs” should be observed so that animal use in biomedical research is minimized while at the same time, data obtained from animal research is optimized. Only in that way will we be assured of continued public support for the animal research that benefits so much of society, including the health and welfare of nonhuman animals!

Animal Rights and Animal Welfare

The terms “animal rights” and “animal welfare” are not synonymous. Animal rights represents a philosophical belief that gives animals the same equality and protection as humans (Box 1.6). According to this philosophy, a field mouse has the same right to life as a human. Animal rights purports that animals should not be regarded as property. No matter how humane, animal use is viewed as exploitation and should be banned. This includes keeping dogs and cats as pets; displaying animals in zoos and aquariums; using chickens, cattle, or swine for food; and using animals in research, teaching, and testing. Furthermore, adherence to this philosophy prohibits one’s use of medications including vaccines and medical treatments that were developed through animal research.

Animal welfare represents a philosophical belief that it is morally acceptable for humans to use animals provided they are treated humanely and their physical and psychological well-being is met (Box 1.7). This philosophy is based on a belief that animals can contribute to human welfare. Animals provide companionship, entertainment, labor, food, fiber, and advancement of knowledge when used in research and teaching. When animals are used, it is paramount that responsible practices of animal

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welfare are adhered to, including provision of appropriate housing, handling, management, disease prevention and treatment, and, when necessary, euthanasia.

Sources of Animals Used in Biomedical Research

Animals used in research may be obtained from a variety of sources. The sale of AWA-covered species (e.g., dogs and cats) to research facilities is regulated by the USDA who licenses Class A and Class B animal dealers. USDA-licensed Class A dealers supply “purpose bred” animals, animals bred and raised specifically for use in research. Purpose-bred animals are of genetically similar backgrounds, often with defined pedigrees, and have well-documented health histories. To help ensure that these animals are accustomed to the research environment and are easy to handle, many vendors have instituted robust animal handling and socialization programs as components of their animal care programs.

A small number of animals used in research are obtained from USDA Class B dealers, who acquire animals from “random sources” such as individual owners, hobby breeders, and pounds and shelters. Although Class B dealers are subject to federal legislation under the Animal Welfare Act and are licensed by the USDA, public concern regarding acquisition of dogs and cats from Class B dealers led to the decision by NIH to discontinue funding of experiments using random source dogs and cats. Institutions do occasionally elect to obtain animals directly from random sources when purpose-bred animals do not possess the characteristics necessary for study, such as advanced age or preexisting health conditions. Acquisition of these animals is tightly regulated.

Nonhuman Primate Use

Nonhuman primates are human’s closest genetic relatives. Due to this and their associated high level of sentience, their use in research should be reserved only for when another animal model cannot be used. Nonhuman primates account for less than 1% of the USDA-regulated animals used in the United States. The vast majority of nonhuman primates used are rhesus and cynomolgus macaques. Although the use of chimpanzees was invaluable in advancing human health, including for the development of vaccines for polio and hepatitis B, the NIH no longer supports the use of chimps in research and all use of chimps in research has been significantly restricted and effectively eliminated. Chimps previously used in research have been retired to designated sanctuaries or have been retired “in place” when it was reasonably expected that they would experience harm if relocated.

ORGANIZATIONS

The need for more systematic and specialized information on laboratory animal husbandry, medical care, and management of animal facilities and the desire to foster collaborative environments led to the development of several organizations that support the laboratory animal science community. The following is an introduction to some of the most important organizations and a brief description of their purpose.

American Association for Laboratory Animal Science

In 1950, the Animal Care Panel (ACP), a national professional organization dedicated to the care, production, and study of laboratory animals, was established. In 1967, the ACP became the American Association for Laboratory Animal Science (AALAS) whose mission is to advance “responsible laboratory animal care and use to benefit people and animals.” AALAS is a nonprofit, professional association that serves as the principal means of communication between individuals and organizations within the field of laboratory animal science. AALAS currently has over 14,500 individual and institutional members and more than 43 local branches. AALAS produces two scientific journals, *Comparative Medicine* and *Journal of the American Association for Laboratory Animal Science*, and several technician-targeted publications including the quarterly magazine, *Laboratory Animal Science Professional*. AALAS also certifies trained technicians; promotes education through publications; supports the AALAS Learning Library, an extensive Web-based continuing education site; and hosts an annual national meeting. Scientists, veterinarians, technicians, managers, and suppliers share information through presentations, discussions, and exhibits at the annual meeting. Recently, AALAS has increased its role in public outreach and promoting the benefits of biomedical research. For further information, visit www.aalas.org.

AALAS administers the AALAS Technician Certification Program through which technicians receive certification at one of three levels: Assistant Laboratory Animal Technician (ALAT), Laboratory Animal Technician (LAT), and Laboratory Animal Technologist (LATG) (Figure 1.2). The minimum qualifications required to take each certification exam are listed in Figure 1.3. The duties of assistant laboratory animal technicians are primarily related to animal care and facility sanitation. Laboratory animal technicians are expected to have increased diagnostic and technical skills and research responsibilities. Laboratory animal technologists are frequently involved in



Fig 1.2. AALAS technician certification level logos. (Source: AALAS.)

► Eligibility requirements

Below are the minimum eligibility requirements for each exam. To be eligible for the exam you wish to take, you must meet one of the combinations of education and work experience.

		Education level				Lab animal work experience (years)
		Current cert. level	HS/ GED or higher	AA/AS or higher	BA/BS or higher	
ALAT Exam	<input type="checkbox"/>					2
	<input type="checkbox"/>		•			1
	<input type="checkbox"/>			•	•	0.5
LAT Exam	<input type="checkbox"/>		•			3
	<input type="checkbox"/>			•		2
	<input type="checkbox"/>				•	1
	<input type="checkbox"/>	ALAT	•			0.5*
	<input type="checkbox"/>	ALAT				2**
LATG Exam	<input type="checkbox"/>		•			5
	<input type="checkbox"/>			•		4
	<input type="checkbox"/>				•	3
	<input type="checkbox"/>	LAT	•			0.5*

* Work experience must be acquired after attaining the specified certification.
** Option for those without documentation of education level.

Fig 1.3. Minimum eligibility requirements for AALAS technician certification. (Source: AALAS.)

supervisory capacities and conducting portions of the research study. The achievement of certification at any level denotes an individual dedicated to the pursuit of a higher standard of technical skill and knowledge. Many institutions now require or prefer AALAS certification as a prerequisite for obtaining jobs in their animal facility. Alternatively, many institutions encourage employees to pursue certification as a means of advancing their careers and offer classes as part of their training programs. AALAS offers training manuals for each of the three levels and suggests other materials appropriate for examination preparation. Employers often provide employees with financial support for the examinations and frequently reward the achievement of certification with a specific increase in salary.

AALAS also sponsors the Certified Manager of Animal Resources (CMAR) program. The CMAR designation is a sign of professionalism in the field of animal resources management. Certification requires successful completion of a series of general business management exams offered through the Institute for Certified Professional Managers (ICPM) or through AALAS as well as completion of the more specialized Animal Resources Exam offered by AALAS. Educational materials for the exams are available from ICPM and from AALAS, including AALAS’ *Management Training Manual*. The minimum eligibility requirements for CMAR designation are

Table 1.2. Eligibility requirements for CMAR designation

Education Level	Total Work Experience	Total Management Experience
BA/BS	5 years	3 years
AA/AS	8 years	3 years
HS/GED	10 years	3 years

Source: AALAS.

Note: Candidates meeting these requirements who pass the Animal Resources Exam and the Certified Manager (CM) exams will achieve the status of a Certified Manager of Animal Resources and will be able to use the CMAR acronym after their names.

listed in Table 1.2. CMAR recipients must fulfill continuing education requirements to maintain their designation.

Laboratory Animal Management Association

The Laboratory Animal Management Association (LAMA) was established in 1984 with the mission of “enhancing the quality of management and care of laboratory animals throughout the world” by “promot[ing] education, knowledge exchange and professional development” of facility managers and supervisors (www.lama-online.org). The organization publishes a quarterly journal, *LAMA Review*, sponsors training sessions, and hosts an annual educational meeting. For further information, visit www.lama-online.org.

American Society of Laboratory Animal Practitioners

In August 1966, the Laboratory Animal Welfare Act became law and mandated that “adequate veterinary care” be provided to select laboratory animals. The American Society of Laboratory Animal Practitioners (ASLAP) was founded later that same year, partially in response to the Act’s passage. ASLAP is a professional organization through which veterinarians engaged or interested in the practice of laboratory animal medicine can freely exchange ideas, experiences, and knowledge. In 1967, ASLAP was officially recognized as an ancillary organization of the American Veterinary Medical Association (AVMA) and in 1986, ASLAP became an affiliate of AALAS. Both veterinarians and veterinary students make up the membership of ASLAP. According to its website, the objectives of ASLAP are to (1) “provide a mechanism for the exchange of scientific and technical information among veterinarians engaged in laboratory animal practice,” (2) “actively encourage its members to provide training for veterinarians in the field of laboratory animal practice at both the pre and postdoctoral levels and lend their expertise to institutions conducting laboratory animal medicine programs,” (3) “encourage the development and dissemination of knowledge in areas related to laboratory animal practice,” and (4) “act as a spokesperson for laboratory animal practitioners within the AVMA House of Delegates and to work with other organizations involved in the care and use of laboratory animals in representing our common interests and concerns to the scientific community and the public at large.” For further information, visit www.aslap.org.

American College of Laboratory Animal Medicine

As stated in their website, the College was originally established as the American Board of Laboratory Animal Medicine in 1957 to “encourage education, training, and research in laboratory animal medicine”; to “establish standards of training and experience for veterinarians professionally involved with the care and health of laboratory animals”; and to “recognize qualified persons in laboratory animal medicine, through certification examination and other means.” The name of the organization was changed to the American College of Laboratory Animal Medicine (ACLAM) in 1961. ACLAM is a specialty board recognized by the AVMA. Veterinarians who have successfully completed the comprehensive certification examination and fulfilled other stated requirements earn the right to be board certified and to be called Diplomates of the American College of Laboratory Animal Medicine. ACLAM sponsors an annual educational meeting, the ACLAM Forum, to highlight different topics of importance to the laboratory animal medicine community. In addition, ACLAM has developed a series of textbooks and programs to promote education about laboratory animal medicine. For further information, visit www.aclam.org.

National Association for Biomedical Research

The National Association for Biomedical Research (NABR) was founded in 1979. It is a national, nonprofit organization that advocates for sound public policy in support of ethical and essential animal use in biomedical research. NABR serves as a unified voice in Washington, DC, for the scientific community on legislative and regulatory matters affecting laboratory animal research.

NABR supports the responsible and humane care and use of laboratory animals and believes that only as many animals as necessary should be used; that the pain or distress animals may experience should be minimized; and that alternatives to the use of live animals should be developed and employed whenever feasible. NABR, however, recognizes “that now, and for the foreseeable future, it is not possible to completely replace the use of animals in biomedical research, and that the study of whole, living organisms is an indispensable element of biomedicine that is beneficial to both veterinary and human health.” For more information, visit www.nabr.org.

Foundation for Biomedical Research

The Foundation for Biomedical Research (FBR), partner organization to NABR, was established in 1981. It is a nonprofit organization dedicated to improving the quality of human and animal health by promoting public understanding and support for the humane and responsible use of animals in biomedical research. FBR provides information to teachers, students, the media, and the general public on the essential need for animals in medical research and for scientific advancement. A wide variety of educational materials, including brochures, posters, reference papers, discussion papers, and videos to support their effort are available from the FBR (Figure 1.4). For further information, visit www.FBRResearch.org.



Fig 1.4. Educational brochure cover. Full brochure available on the book's accompanying website. (Source: Foundation for Biomedical Research.)

Institute for Laboratory Animal Research

The Institute for Laboratory Animal Research (ILAR) was founded in 1952 under the guidance of the National Research Council (NRC) of the National Academy of Sciences. ILAR functions as an advisor to the federal government, the biomedical research community, science educators and students, and the public. Its mission is “to evaluate and to report on scientific, technological, and ethical use of animals and related biological resources, and of non-animal alternatives in non-food settings, such as research, testing, education, and production of pharmaceuticals.” ILAR’s core values are (1) “support [of] the responsible use of animals in research, testing, and education as a key component to advancing the health and quality of life of humans and animals”; (2) promotion of “high-quality science and humane care and use of research animals based upon the principles of refinement, replacement, and reduction (the 3Rs) and high ethical standards”; and (3) fostering of “best practices that enhance human and animal welfare by organizing and disseminating information and by facilitating dialogue among interested parties.” Advice on all activities of the organization is provided by the ILAR Council which is composed of experts in laboratory animal medicine, medicine, bioethics, and other biomedical sciences. ILAR prepares authoritative reports on subjects of importance to the animal care and use community, including the *Guide for the Care and Use of Laboratory Animals*. ILAR also

publishes the *ILAR Journal*, a quarterly peer-reviewed publication on a variety of topics pertinent to the biomedical research community. For further information, visit www.dels.nas.edu/ilar.

As evident by the diversity of organizations listed above, those who work in laboratory animal medicine continually strive to improve the quality of animal-based biomedical research while at the same time supporting animal welfare. Numerous organizations assist individuals in this pursuit through the educational opportunities, scientific resources, and advocacy activities that they provide.

BIBLIOGRAPHY

- American Association for Laboratory Animal Science (AALAS). <https://www.aalas.org> [accessed September 24, 2018].
- American College of Laboratory Animal Medicine (ACLAM). <https://www.aclam.org> [accessed September 24, 2018].
- American Society of Laboratory Animal Practitioners (ASLAP). <https://www.aslap.org> [accessed September 24, 2018].
- Animal and Plant Health Inspection Service (APHIS). 2017. *The Animal Welfare Act and Animal Welfare Regulations as of January 1, 2017*. Washington, DC: US Department of Agriculture. Available at https://www.aphis.usda.gov/animal_welfare/downloads/AC_BlueBook_AWA_FINAL_2017_508comp.pdf [accessed September 19, 2018].
- Animal and Plant Health Inspection Service (APHIS). 2018a. *AWA Inspection and Annual Reports*. Available at https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_awa/AWA-Inspection-and-Annual-Reports [accessed September 19, 2018].
- Animal and Plant Health Inspection Service (APHIS). 2018b. *Annual Report Animal Usage by Fiscal Year*. Available at https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_awa/AWA-Inspection-and-Annual-Reports [accessed December 28, 2018].
- Foundation for Biomedical Research (FBR). <https://www.FBRResearch.org> [accessed September 24, 2018].
- Institute of Laboratory Animal Resources (ILAR). 2009. *Scientific and Human Issues in the Use of Random Source Dogs and Cats in Research*, National Research Council. Washington, DC: National Academies Press. Available at https://grants.nih.gov/grants/olaw/random_source_dog_and_cat_report.pdf [accessed September 19, 2018].
- Institute of Laboratory Animal Resources (ILAR). 2011. *Guide for the Care and Use of Laboratory Animals*, 8th ed. ILAR, National Research Council. Washington, DC: National Academies Press. Available at <https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf> [accessed September 19, 2018].
- Institute of Laboratory Animal Resources (ILAR). <https://www.dels.nas.edu/ilar> [accessed September 24, 2018].
- Laboratory Animal Management Association (LAMA). <http://www.lama-online.org> [accessed September 24, 2018].

- Levin, J., and F. B. Bang. 1964. The role of endotoxin in the extracellular coagulation of limulus blood. *Bull Johns Hopkins Hosp* 115: 265–274.
- Levin, J., and F. B. Bang. 1968. Clottable protein in limulus: its localization and kinetics of its coagulation by endotoxin. *Thromb Diath Haemorrh* 19(1): 186–197.
- National Association for Biomedical Research (NABR). <https://www.nabr.org/biomedical-research> [accessed September 24, 2018].
- Office of Laboratory Animal Welfare (OLAW). 1985. *US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*. Available at <https://olaw.nih.gov/policies-laws/gov-principles.htm> [accessed September 19, 2018].
- Russell, W. M. S., and R. L. Burch. 1959. *The Principles of Humane Experimental Technique*. London: Methuen.
- Speaking of Research. www.speakingofresearch.com [accessed September 13, 2018].

FURTHER READING

- American Veterinary Medical Association (AVMA). 2018. *Use of Animals in Research, Testing, and Education*. Available at <https://www.avma.org/KB/Policies/Pages/Use-of-Animals-in-Research-Testing-and-Education.aspx> [accessed December 10, 2018].
- Canadian Council on Animal Care. 2018. *Ethics in Animal Experimentation*. Available at <https://www.ccac.ca/en/training/modules/core-stream/ethics-in-animal-experimentation.html> [accessed December 10, 2018].
- Congressional Research Service (CRS). 2018. *Enforcement of the Food, Drug, and Cosmetic Act: Select Legal Issues*, R43609. Available at <https://fas.org/sgp/crs/misc/R43609.pdf> [accessed September 24, 2018].
- Festing, M. F. W., P. Overend, M. C. Borja, and M. Berdoy. 2002. *The Design of Animal Experiments: Reducing the Use of Animals in Research through Better Experimental Design*. Oxford: Royal Society of Medicine Press.
- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). 2018. *About ICCVAM*. Available at <https://ntp.niehs.nih.gov/pubhealth/evalatm/iccvam/index.html> [accessed December 10, 2018].
- Kilkenny, C., W. J. Browne, I. C. Cuthill, M. Emerson, and D. G. Altman. 2010. Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol* 8(6): e1000412. doi:<https://doi.org/10.1371/journal.pbio.1000412>.
- Office of Laboratory Animal Welfare (OLAW). <https://olaw.nih.gov> [accessed September 24, 2018].
- Online Ethics Center (OEC). 2018. *The Ethics of Using Animals in Research*. Available at <https://www.onlineethics.org/Resources/TeachingTools/Modules/19237/animalres.aspx> [accessed December 10, 2018].

**CHAPTER 1 REVIEW****Matching**

Match the following with their respective descriptions:

- | | |
|----------|----------|
| A. AALAS | H. IACUC |
| B. ACLAM | I. ILAR |
| C. ASLAP | J. LAMA |
| D. CMAR | K. LAT |
| E. FDA | L. NABR |
| F. FBR | M. NIH |
| G. FD&C | |

Fill in the blank

1. ____ Organization that provides educational workshops in support of a certificate program for managers of animal facilities
2. ____ Develops guidelines and disseminates information to the federal government on scientific, technological, and ethical use of animals
3. ____ Prior to use of animals, a protocol must be approved by this committee
4. ____ Certification program for managers of animal facilities that requires applicable experience and successful completion of a series of exams
5. ____ AALAS certification level for technicians who have achieved diagnostic and technical skills
6. ____ Law created to safeguard and protect consumer health and safety from the sale of dangerous products
7. ____ Nonprofit organization that serves as the principal means of communication between individuals and organizations within the field of laboratory animal science
8. ____ Federal agency that requires animal testing of products when a scientifically valid, alternative testing method is not available
9. ____ Nonprofit organization dedicated to promoting public understanding and support for use of animals in research through the creation and distribution of educational materials
10. ____ Specialty board recognized by the AVMA
11. ____ Professional organization for veterinarians engaged or interested in the practice of laboratory animal medicine
12. ____ Nonprofit organization dedicated to advocating sound public policy that recognizes the vital role of animal use in biomedical research
13. ____ Main public granting agency for biomedical research

Below are examples of the application of the 3Rs in animal research. Indicate which of the ethical principles (Replacement, Reduction, or Refinement) is represented by each example:

(Continued)

14. ____ Delivering medications to nonhuman primates in food treats instead of by injection
15. ____ Use of corneas for an ocular irritation assay that are obtained from food animals during the meat processing process and that would otherwise be discarded
16. ____ Use of cell culture in an oncology study
17. ____ Use of the limulus amebocyte lysate assay for pyrogen testing in which blood is taken from horseshoe crabs which are then returned to the ocean
18. ____ Use of a computer model instead of a rat model
19. ____ Corrositex®, an *in vitro* assay used to assess chemicals that are potentially corrosive to skin
20. ____ Use of statistical methods to decrease the number of animals used in a study
21. ____ Use of hollow fiber bioreactors, instead of rabbit models, for monoclonal antibody production
22. ____ Housing female rabbits in groups instead of singly
23. ____ Use of fish animal model instead of a hamster animal model
24. ____ Selection of an appropriate experimental endpoint that occurs earlier in a disease course
25. ____ Use of a dose escalation study design for a drug treatment study
26. ____ Fasting a rat for 8 hours rather than 16 hours before a procedure
27. ____ Utilizing multiple areas on the back of a few pigs instead of using one spot on the back of many pigs for a skin study

Suggested Activities

Watch the video “Love, Care, Progress” produced by Association for Medical Progress at <https://www.amprogress.org/love-care-progress-video>. Discuss your thoughts on the use of dogs in research and the adoption of dogs previously used in research.

Utilize the Foundation for Biomedical Research website: <https://fbresearch.org/biomedical-research/animal-testing-facts> and the Michigan Society for Medical Research website: <http://mismr.org/facts-myths-about-animal-research> to initiate a discussion on common misconceptions about animal testing and research.

Review the AALAS Foundation website: <https://www.aalasfoundation.org/outreach/About-Animal-Research/Animal-Rights-vs-Animal-Welfare> and the AVMA website: <https://www.avma.org/KB/Resources/Reference/AnimalWelfare/Pages/what-is-animal-welfare.aspx> then discuss the difference between the terms Animal Rights and Animal Welfare. How do you define each term and how do these philosophical views differ? What do you believe are our responsibilities to animals? Do you believe that humans are entitled to utilize animals? If so, within what limits?

Utilize the interactive Animal Ethics Dilemma website: <http://www.aedilemma.net> to consider ethical dilemmas about our treatment of animals. The website provides a role-playing game through which multiple case studies can be explored and philosophical views examined.

Seek out information on organizations that you believe make significant contributions to the protection of animals. Explore the organizations' stated philosophies on the use of animals as pets, in food production, in exhibits (e.g., zoos), in research and teaching, and in entertainment. Are the organizations' philosophies and activities consistent with their public image? With your philosophy on the use of animals?