CRC

HANDBOOK of LABORATORY ANIMAL SCIENCE

Volume I

E. C. Melby, Jr.
N. H. Altman

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PREFACE

The field of laboratory animal science has literally exploded within the past two decades, coming into its own as a recognized scientific body of knowledge. As with any dynamic situation, the growth has not necessarily been orderly, for the very breadth of the field precludes the opportunity for any single individual to maintain competency in all areas encompassed. By necessity, laboratory animal science embraces numerous disciplines, deriving specific knowledge from each as required to develop concepts, methods, programs, and instrumentation.

The literature appropriate to the field is scattered in a broad array of journals, bulletins, monographs, and books, resulting in confusion and frustration when one attempts to research a specific point of information. Those individuals actively working in the field fully appreciate the problem, especially when called upon to answer questions or provide guidance to others utilizing laboratory animals in biomedical research, testing, or education.

It is intended that this series of handbooks will represent a major attempt to bring order to existing chaos. The literature and knowledge currently available in laboratory animal science have been reviewed in an effort to provide a concise overview of the field, amply supported by references for those workers requiring greater detail on a specific subject. These series are not intended to provide comprehensive information on all subjects, yet the reader will find certain subject areas covered in greater depth than others. By and large this lack of uniformity is intentional on the part of the editors and authors, for some areas were considered amply covered in sources which are readily available, whereas other information may be found only in obscure places or perhaps has never before been published.

It is the intention of the editors, contributors, and publisher to make available through these series a ready resource of information on laboratory animal science to all workers who find need to utilize animals in research, education, or testing. The scientific disciplines intended to be reached are many. Additional handbooks will be published as completed, followed by periodically issuing selected revisions of specific subject areas which, by their dynamic state of change, will require updating with greater frequency than the whole.

As editors of this series, we are indebted to the many contributors who have labored long and diligently to prepare their material for presentation. The charge given to each contributor has necessarily been broad, and even possibly vague, for which we accept full responsibility. We also apologize for the sequence of presentation of material, for it will be readily apparent that certain sections should logically be placed together. Although intentions were excellent, delays in submitting material proved to be so monumental as to necessitate making a decision to group sections as best we can, leaving others to be published at a later date. It is our hope, however, that readers will find the handbooks of great value in their respective fields of endeavor. Criticisms and suggestions for change or improvement will be gratefully accepted, for it is the intention to make this series the useful, living documents required by users of research animals.

Edward C. Melby, Jr.
Norman H. Altman

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Dr. Melby was educated at the University of Pennsylvania, the University of Vermont, and received the D.V.M. degree from Cornell University in 1954. Following an internship, Dr. Melby entered private veterinary medical practice in Vermont. In 1962 he joined the Faculty of the Johns Hopkins University, where he organized an academic program in laboratory animal science and comparative medicine which is today one of the most extensive of its kind in this country.

Dr. Melby is a diplomate or member of numerous professional societies, serves on committees of the National Institutes of Health and the National Academy of Sciences, and has authored some 40 papers in laboratory animal medicine. He has recently been elected Dean of the College of Veterinary Medicine at Cornell University, a post which he will assume during the fall of 1974.

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LEGISLATION REGULATIONS PERTAINING TO LABORATORY ANIMALS – UNITED STATES

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Legislation and regulations relating to laboratory animals generally fall into two categories. One category deals with the importation and shipment of animals and is designed either to protect human beings and other animals from diseases that may be carried by animals or to prevent exploitation of endangered animal species. The second category of laws and regulations is designed to assure that animals used in laboratories are not mistreated and receive appropriate care. Related to this category are regulations pertaining to the methods of acquisition of animals for use in laboratories.

I. ANIMAL IMPORTATION AND SHIPMENT

Laws and regulations governing the importation and shipment of animals are designed to:

1. Protect human and animal populations from dieseases which may be carried by animals.
2. Protect agriculture, wildlife, and wildlife resources from injurious species and pests.
3. Protect endangered animal species from an additional threat to their populations.

A. Public Health

Special requirements must be met if animals known to be carriers of diseases contagious to human beings are to be imported. All dogs, cats, and nonhuman primates brought into the United States from any foreign country are inspected by a Public Health Service quarantine officer at the port of entry. Only animals with no evidence of communicable disease are admitted. In addition, dogs, except for puppies under 3 months of age and dogs originating in areas designated by the Public Health Service as being rabies-free, must be vaccinated against rabies at least 30 days prior to entry into the United States. Nonhuman primates arriving from, or having passed through, a yellow fever area shall be admitted only if inspection of the animal reveals no sign of yellow fever and if there is evidence that (1) at least 9 days have elapsed following their departure from the last such infected area or (2) they arrive in a mosquito-proof structure and have been in such a structure for at least 9 days or (3) they have been vaccinated against yellow fever. Special conditions must be met for the importation of psittacine birds and small turtles. There are no restrictions on laboratory-reared rodents or amphibians except that they be free of all ectoparasites and evidence of diseases communicable to man when examined at the port of entry. If additional information is needed concerning the importation of any of these animals, inquiries should be addressed to the Center for Disease Control, Atlanta, Georgia 30333, Attention: Office of Veterinary Public Health.

Animal vectors of human disease such as insects, other arthropods, snails, bats, wild rodents, etc. are admissible only by a special permit. Application for those permits should be submitted to the Center for Disease Control, Atlanta, Georgia 30333, Attention: Office of Biosafety.

Several states have laws designed to protect human beings from exposure to diseases carried by animals. For example, California has a Wild Animal Importation Law that requires a permit to import all nonhuman primates and South American cats (Felidae). The South American Felidae must be quarantined at least 90 days, chimpanzees 60 days, and other primates 30 days in an approved facility under the supervision of a veterinarian. Primates must receive two negative tuberculin tests 30 days apart before being released from quarantine. California also prohibits the importation of skunks except by permit for research and zoological parks. Colorado has a recently enacted law governing pet shops and kennels which prohibits the importation or sale of skunks and nonhuman primates. Bonafide zoological parks and research institutions are exempt from the prohibition with respect to primates. Georgia has a law which regulates importation, sale, and possession of exotic animals.

B. Animal Health

The United States Department of Agriculture controls the importation of animals which are capable of transmitting diseases of domestic live-

stock. These include all ruminants and swine, members of the equine family, poultry, other birds, hatching eggs, and certain wild animals. Their responsibility includes all transmissible diseases of livestock, but of special concern are diseases exotic to the United States, such as foot-and-mouth disease, rinderpest, and African horsesickness.

Special permits must be obtained prior to importation of these animals. In addition, animals are subject to quarantine at a place designated by the USDA. For additional information and applications for permits, contact Import-Export Animals and Products Staff, Veterinary Services, Animal and Plant Health Inspection Service, USDA, Federal Building, Hyattsville, Maryland 20782.

The importation and interstate movement of organisms and vectors of animal diseases are also regulated. A permit must be obtained prior to the importation of any organism which might infect animals even though the same organism occurs naturally in the United States. Tissues, tissue cultures, blood, serum, and other diagnostic specimens from other countries must be accompanied by a permit. Such materials could unknowingly be infected with agents of exotic diseases and must be handled in a manner which prevents exposure of domestic animals. Issuance of a permit prior to the interstate movement of all animal pathogens occurring in the United States is not practical because of the volume. It has been USDA policy to require a permit for the movement of only those pathogens which are enzootic, such as bluetongue virus, scrapie, and vesicular stomatitis virus, or of extremely high virulence, or for which there is a national disease eradication program (except tuberculosis and brucellosis at this time). Disease agents and vectors indigenous to all states may be moved interstate without a permit. Additional information on the movement of animal disease agents and vectors and permit applications may be obtained from: Organisms and Vectors Staff, Veterinary Services, Animal and Plant Health Inspection Service, USDA, Federal Building, Hyattsville, Maryland 20782.

All states have laws which govern the shipment of animals into the state. In general, these laws have no specific regulations pertaining to shipment of common laboratory animals except dogs, and in some states cats, for which vaccination against rabies may be required. Domestic livestock generally require a veterinarian's certificate of health which includes specific tests to insure freedom from tuberculosis, brucellosis, and certain other specified diseases. While common laboratory rodents do not require health certificates, almost all states prohibit by law the importation of any bird or animal which is infected with or has recently been exposed to any transmissible disease. Several state game departments have regulations prohibiting or controlling importations of wild animals.

C. Endangered Species and Wildlife Protection

The Lacey Act of May 25, 1900 governs the importation of foreign wildlife. Regulations implementing this Act require, among other things, the reporting of incoming live wildlife and dead, fresh salmonid fish. In addition, wildlife must be imported through designated ports and accompanied by documentation showing the wildlife was lawfully exported from the country of origin. These requirements may be met by a valid export permit, a signed statement from the responsible government official in the country of origin, or a certificate from the U. S. counsel in the country of origin. The importation of harmful species such as fruit bats (genus *Pteropus*), mongooses, meerkats, European rabbits (*genus Oryctologus*), Indian wild dogs, multimammate rats (genus *Mystomys*), the pink starling, dioch, quelea quelea, Java sparrow, red-whiskered bulbul, and the catfish (family *Clariidae*) are all restricted. All of these species have been deemed injurious or potentially injurious to the public health and welfare, or to agricultural interests, or to the welfare and survival of wildlife and wildlife resources of the United States. When there has been a proper showing of responsibility and continued protection of the public interest and health, they may be imported for zoological, educational, medical, and research purposes by permit. The permits and additional information may be obtained from the Fish and Wildlife Service, U. S. Department of the Interior, Washington, D. C. 20240. The Department of the Interior is proposing revised regulations for importation of wildlife under the Lacey Act. These regulations would in effect require import permits for all animals except certain named species such as hamsters, gerbils, guinea pigs, and laboratory mice and rats. These regulations are expected to become final during 1974.

The U. S. Department of the Interior, Fish and Wildlife Service, also administers the Endangered

Species Act of 1973 and the Marine Mammal Protection Act of 1972. Among other things, the Endangered Species Act of 1973 implements U. S. participation in an international convention on trade in wildlife. This convention establishes a system to regulate trade of endangered and potentially endangered species of wildlife through a system of import and export controls. The 1973 Act prohibits the following activities with regard to endangered species:

1. Importation.
2. Exportation.
3. Taking, and, if an animal is illegally taken, possessing, selling, delivering, carrying, transporting, or shipping.
4. Commercial activities in interstate or foreign commerce.

These activities may be engaged in only by obtaining a permit from the Department of the Interior. Permits may be issued for scientific purposes or to enhance the propagation or survival of the affected species. By law, such permit applications must be published in the *Federal Register,* and public comment invited for 30 days. Taking and importing marine mammals also require a permit. The list of endangered species is published in the *Federal Register,* Volume 39, Number 3, January 4, 1974, pages 1171 to 1175, as Title 50, Chapter I, Subchapter B, Part 17 of the *Code of Federal Regulations*. It includes a number of primate species of potential research interest, including the gorilla, oranguatan, all species of lemurs, and some subspecies of spider monkeys (*Ateles geoffroyi frontatus* and *Ateles geoffroyi panamensis*). Other listed primate species are indris, sifakas, and avahis (all members of genera *Indri, Avahi,* and *Propithecus*), aye-aye (*Daubentonia madagascariensis*), red-backed squirrel monkey (*Saimiri oerstedii*), woolly spider monkey (*Brachyteles arachnoides*), white-nosed saki (*Chiropotes albinasus*), uakari – all species (*Cacajao spp.*), Goeldi's marmoset (*Callimico goeldii*), golden-rumped tamarin, golden-headed tamarin, golden lion marmoset (*Leontideus spp.*), lion-tailed macaque (*Macaca silenus*), Tana River manabey (*Cerocebus galeritus galeritus,* douc langur (*Pygathrix nemaeus*), red colobus (*Colobus badius rufomitratus*), Pagi Island langur (*Simias concolor*), Zanzibar red colobus (*Colobus badius kirkii*), pileated gibbon (*Hylobates pileatus*), and the kloss gibbon (*Hylobates klossi*).

For additional information on federal laws and regulations relating to wildlife, write to the Director, (FSF/LE), Fish and Wildlife Service, Washington, D. C. 20240.

II. ANIMAL WELFARE

The ethics of use of animals in laboratory experiments is a hotly debated issue. A small, but vocal, group of antivivisectionists believes that animals absolutely should not be used in laboratory research. They take the position that man has no right to inflict any pain on a "defenseless" animal no matter what the potential benefit to man or other animals. A much larger segment of the animal humane movement believes it is appropriate to use animals in experiments, but sometimes they advocate regulations that according to researchers would severely restrict their ability to do meaningful research with animals. Most investigators and, apparently, the vast majority of the American public believe it is fully justified to use animals in research and testing because of the benefits to human and animal health and well-being resulting from such endeavors. At the same time, they believe that every reasonable effort should be made to provide proper care for these animals and to minimize pain and painful procedures. The laws and regulations in effect reflect this point of view. Those engaged professionally in the care of laboratory animals have a responsibility to provide humane care and to guard against cruel treatment of animals, as well as to facilitate the use of animals in biomedical activities.

A. State Laws and Regulations

All 50 states and the District of Columbia have animal anticruelty laws. Most of these laws have provisions to (1) protect animals from cruel treatment, (2) require that animals have access to wholesome food and water, and (3) require that animals have shelter from extreme weather. Fifteen of the state anticruelty laws (Alaska, California, Florida, Hawaii, Idaho, Missouri, Nebraska, Nevada, New Jersey, New York, Pennsylvania, South Dakota, Texas, Washington, and Wisconsin) make special provisions for the use of animals in bonafide medical research. Generally, these provisions are a statement to the effect that "No part of this act shall be construed as interfering with properly conducted scientific

experiments or investigations performed under the authority of a regularly incorporated medical college, university, or scientific institution."[1]

At least three states (Michigan, California, and New York) have laws which empower the state health department to inspect all institutions using research animals. The authority of the institutions to conduct animal experiments may be suspended or revoked by the state if they do not meet certain standards for the care and treatment of laboratory animals.

A number of states have laws regulating the release of impounded animals for medical research. There are three states (Maine, Pennsylvania, and Hawaii) in which state laws absolutely prohibit the release of impounded animals to scientific institutions. There are 10 states (Connecticut, Illinois, Iowa, Massachusetts, Minnesota, New York, Oklahoma, South Dakota, Utah, and Wisconsin) which provide for such release under conditions specified by the legislature. In these states, institutions which receive impounded animals must be inspected and licensed by the board of health or some other appropriate state agency or by the U.S. Department of Agriculture under the Animal Welfare Act of 1970. Other states either have no laws governing the release of impounded animals or laws which provide for local option.[2]

B. Federal Laws and Policies

Federal laws for the humane treatment of animals have been on the books since 1873, when a law was passed governing the treatment of farm animals during shipment for export. This law was called the "28-hour law" after the maximum length of time animals could be transported before receiving food and water. The first law protecting nonfarm animals, however, was not passed until 1966. It was commonly referred to as the Laboratory Animal Welfare Act or Public Law 89-544. The 1966 Act was amended in 1970 (P.L. 91-579) and is officially named "The Animal Welfare Act." It is administered by the Department of Agriculture. Purposes of the legislation are to protect owners from the theft of their animals, to prevent the sale or use of animals which have been stolen, and to insure that animals used or intended for use in research, exhibition, or the wholesale pet trade are provided humane care and treatment. Transportation, purchase, sale, housing, care, handling, and treatment of animals are governed by the Act.

Animals covered under this law include any live or dead dog, cat, monkey (nonhuman primate), guinea pig, hamster, rabbit, or other warm-blooded animal designated by the Secretary of Agriculture and used or intended for use in research, exhibition, or the wholesale pet trade. Specific standards have been issued for the care of dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits. General standards have been issued for other animals covered by the Act. These standards include minimum requirements with respect to handling, housing, feeding, watering, sanitation, ventilation, shelter from extremes of weather and temperature, adequate veterinary care including the appropriate use of anesthetic, analgesic, or tranquilizing drugs, and separation of species.

The Animal Welfare Act requires that animal dealers be licensed and that exhibitors and research facilities be licensed or registered. Research facilities are required to submit annual reports showing that professionally acceptable standards governing the care, treatment, and use of laboratory animals, including the appropriate use of anesthetic, analgesic, and tranquilizing drugs, are being followed. The Act prohibits the regulation of design and performance of actual research or experimentation.

Detailed implementing rules and regulations for the Animal Welfare Act are published in the *Code of Federal Regulations* (CFR), Title 9 – Animals and Animal Products, Subchapter A – Laboratory Animal Welfare, Parts 1, 2, and 3. Any and all amendments to the rules and regulations are periodically published in the *Federal Register* under the heading Department of Agriculture, Animal and Plant Health Inspection Service. The first amendments to the Animal Welfare Act of 1970 were published in the *Federal Register,* Volume 36, No. 248, pages 24917 to 24928, December 24, 1971. Copies of the rules and regulations can be obtained from the Animal and Plant Health Inspection Service, Veterinary Services, Room 700, U.S. Department of Agriculture, Hyattsville, Maryland 20782.

The U.S. Department of Health, Education, and Welfare (DHEW) has adopted policies regarding the use of animals in research and other biomedical activities supported by grants, contracts, and awards from the Department. These include all National Institutes of Health awards. The policy requires that institutions using animals in DHEW-supported activities assure the Department in writing that they will evaluate on a continuing

basis their animal facilities in regard to the care, use, and treatment of such animals. The animal facilities are to be evaluated using the *Guide for the Care and Use of Laboratory Animals* (DHEW Publication No. (NIH)73-23, revised 1972) as a primary reference. This Guide was prepared by the Institute of Laboratory Animal Resources (ILAR) of the National Academy of Sciences, National Research Council. It is a comprehensive guide for the optimal care of laboratory animals. Single copies of the Guide are available from the Animal Resources Branch, Division of Research Resources, National Institutes of Health, Bethesda, Maryland 20014.

The evaluation required by the DHEW policy may be satisfied either by accreditation by the American Association for the Accreditation of Laboratory Animal Care (AAALAC), 2317 West Jefferson Street, Room 135, Joliet, Illinois 60435, or by evaluation by an institutional committee. The institutional committee must consist of at least three members, one of whom must be a veterinarian if significant numbers of animals are used.

The DHEW policy on animal welfare is administered by the Institutional Relations Branch, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014. Copies of the full policy statement and sample assurance forms may be obtained from them.

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