Guide for the Care and Use of Laboratory Animals

Introduction

This edition of the *Guide for the Care and Use of Laboratory Animals* (the *Guide*) strongly affirms the conviction that all who care for or use animals in research, teaching, or testing must assume responsibility for their well-being. The *Guide* is applicable only after the decision is made to use animals in research, teaching, or testing. Decisions associated with the need to use animals are not within the purview of the *Guide*, but responsibility for animal well-being begins for the investigator with that decision. Additional responsibilities of the investigator, and other personnel, are elaborated in Chapter 1.

The goal of this *Guide* is to promote the humane care of animals used in biomedical and behavioral research, teaching, and testing; the basic objective is to provide information that will enhance animal well-being, the quality of biomedical research, and the advancement of biologic knowledge that is relevant to humans or animals. The use of animals as experimental subjects in the 20th century has contributed to many important advances in scientific and medical knowledge (Leader and Stark 1987). Although scientists have also developed nonanimal models for research, teaching, and testing (NRC 1977; see Appendix A, "Alternatives"), these models often cannot completely mimic the complex human or animal body, and continued progress in human and animal health and well-being requires the use of living animals. Nevertheless, efforts to develop and use scientifically valid alternatives, adjuncts, and refinements to animal research should continue.

In this *Guide*, laboratory animals include any vertebrate animal (e.g., traditional laboratory animals, farm animals, wildlife, and aquatic animals) used in research, teaching, or testing. When appropriate, exceptions or specific emphases for farm animals are provided. The *Guide* does not specifically address farm animals used in agricultural research or teaching, wildlife and aquatic animals studied in natural settings, or invertebrate animals used in research; however, many of the general principles in this *Guide* apply to these species and situations.

REGULATIONS, POLICIES, AND PRINCIPLES

This *Guide* endorses the responsibilities of investigators as stated in the U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (IRAC 1985; see Appendix D). Interpretation and application of those principles and this *Guide* require professional knowledge. In summary, the principles encourage

- Design and performance of procedures on the basis of relevance to human or animal health, advancement of knowledge, or the good of society.
- Use of appropriate species, quality, and number of animals.
- Avoidance or minimization of discomfort, distress, and pain in concert with sound science.
- Use of appropriate sedation, analgesia, or anesthesia.
- Establishment of experimental end points.
- Provision of appropriate animal husbandry directed and performed by qualified persons.
- Conduct of experimentation on living animals only by or under the close supervision of qualified and experienced persons.

In general, the principles stipulate responsibilities of investigators, whose activities regarding use of animals are subject to oversight by an institutional animal care and use committee (IACUC).

Animal facilities and programs should be operated in accord with this *Guide*, the Animal Welfare Regulations, or AWRs (CFR 1985); the Public Health Service Policy on Humane Care and Use of Laboratory Animals, or PHS Policy (PHS 1996); and other applicable federal (Appendixes C and D) state, and local laws, regulations, and policies.[1] Supplemental information on breeding, care, management, and use of selected laboratory animal species is available in other publications prepared by the Institute of Laboratory Animal Resources (ILAR) and other organizations (Appendix A). References in this *Guide* provide the reader with additional information that supports statements made in the *Guide* or presents divergent opinions.

EVALUATION CRITERIA

The *Guide* charges users of research animals with the responsibility of achieving specified outcomes but leaves it up to them how to accomplish these goals. This "performance" approach is desirable because many variables (such as the species and previous history of the animals, facilities, expertise of the people, and research goals) often make prescriptive ("engineering") approaches impractical and unwarranted. Engineering standards are sometimes useful to establish a baseline, but they do not specify the goal or outcome (such as well-being, sanitation, or personnel safety) in terms of measurable criteria as do performance standards.

The engineering approach does not provide for interpretation or modification in the event that acceptable alternative methods are available or unusual circumstances arise. Performance standards define an outcome in detail and provide criteria for assessing that outcome, but do not limit the methods by which to achieve that outcome. This performance approach requires professional input and judgment to achieve outcome goals. Optimally, engineering and performance standards are balanced, thereby providing standards while allowing flexibility and judgment based on individual situations. Scientists, veterinarians, technicians, and others have extensive experience and information covering many of the topics discussed in this *Guide*. Research on laboratory animal management continues to generate scientific information that should be used in evaluating performance and engineering standards. For some issues, insufficient information is available, and continued research into improved methods of animal care and use is needed.

The *Guide* is deliberately written in general terms so that its recommendations can be applied in the diverse institutions and settings that produce or use animals for research, teaching, and testing; generalizations and broad recommendations are imperative in such a document. This approach requires that users, IACUCs, veterinarians, and producers use professional judgment in making specific decisions regarding animal care and use. Because this *Guide* is written in general terms, IACUCs have a key role in interpretation, oversight, and evaluation of institutional animal care and use programs. The question frequently arises as to how the words *must* and *should* are used in the *Guide* and how IACUCs should interpret their relative priority. In general, the verb *must* is used for broad programmatic or basic aspects that the Committee to Revise the *Guide* considers are imperative. The verb *should* is used as a strong recommendation for achieving a goal. However, the committee recognizes that individual circumstances might justify an alternative strategy.

FARM ANIMALS

Uses of farm animals in research, teaching, and testing are often separated into biomedical uses and agricultural uses because of government regulations (AWRs), institutional policies, administrative structure, funding sources, or user goals. That separation has led to a dual system with different criteria for evaluating protocols and standards of housing and care for animals of the same species on the basis of perceived biomedical or agricultural research objectives (Stricklin and Mench 1994). For some studies, this separation is clear. For example, animal models of human diseases, organ transplantation, and major

surgery are considered biomedical uses; and studies on food and fiber production, such as feeding trials, are usually considered agricultural uses. However, the separation often is not clear, as in the case of some nutrition and disease studies. Administrators, regulators, and IACUCs often face a dilemma in deciding how to handle such studies (Stricklin and others 1990).

The use of farm animals in research should be subject to the same ethical considerations as the use of other animals in research, regardless of an investigator's research objectives or funding source (Stricklin and others 1990). However, differences in research goals lead to fundamental differences between biomedical and agricultural research. Agricultural research often necessitates that animals be managed according to contemporary farm-production practices for research goals to be reached (Stricklin and Mench 1994). For example, natural environmental conditions might be desirable for agricultural research, whereas control of environmental conditions to minimize variation might be desirable in biomedical research (Tillman 1994).

Housing systems for farm animals used in biomedical research might or might not differ from those in agricultural research. Animals used in either biomedical or agricultural research can be housed in cages or stalls or in paddocks or pastures (Tillman 1994). Some agricultural studies need uniform conditions to minimize environmental variability, and some biomedical studies are conducted in farm settings. Thus, the protocol, rather than the category of research, should determine the setting (farm or laboratory). Decisions on categorizing research uses of farm animals and defining standards for their care and use should be based on user goals, protocols, and concern for animal well-being and should be made by the IACUC. Regardless of the category of research, institutions are expected to provide oversight of all research animals and ensure that their pain and distress is minimized.

This *Guide* applies to farm animals used in biomedical research, including those maintained in typical farm settings. For such animals in a farm setting, the *Guide for the Care and Use of Agricultural Animals* in Agricultural Research and Teaching (1988), or revisions thereof, is a useful resource. Additional information regarding facilities and management of farm animals in an agricultural setting can be obtained from the Midwest Plan Service's *Structures and Environment Handbook* (1987) and from agricultural engineers or animal-science experts at state agricultural extension services and land-grant colleges and universities.

NONTRADITIONAL SPECIES

A species not commonly used in biomedical research is sometimes the animal model of choice because of its unique characteristics. For example, hibernation can be studied only in species that hibernate. An appropriate environment should be provided for nontraditional species, and for some species it might be necessary to approximate the natural habitat. Expert advice on the natural history and behavior of nontraditional species should be sought when such animals are to be introduced into a research environment. Because of the large number of nontraditional species and their varied requirements, this *Guide* cannot provide husbandry details appropriate to all such species. However, several scientific organizations have developed guides for particular species of nontraditional animals (e.g., ILAR and the Scientists Center for Animal Welfare, SCAW). A partial list of sources is available in Appendix A.

FIELD INVESTIGATIONS

Biomedical and behavioral investigations occasionally involve observation or use of vertebrate animals under field conditions. Although some of the recommendations listed in this volume are not applicable to field conditions, the basic principles of humane care and use apply to the use of animals living in natural conditions.

Investigators conducting field studies with animals should assure their IACUC that collection of specimens or invasive procedures will comply with state and federal regulations and this *Guide*. Zoonoses and occupational health and safety issues should be reviewed by the IACUC to ensure that field studies do not compromise the health and safety of other animals or persons working in the field. Guidelines for using animals in field studies prepared by professional societies are useful when they adhere to the humane principles of the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* (Appendix D) and this *Guide* (see Appendix A, "Exotic; Wild, and Zoo Animals" and "Other Animals").

OVERVIEW

In an attempt to facilitate its usefulness and ease in locating specific topics, the organization of this edition of the *Guide* is slightly different from that of the preceding edition. Material from the preceding edition's Chapter 5, "Special Considerations," has been incorporated into Chapters 1-4. Genetics and nomenclature are now discussed in Chapter 2; facilities and procedures for animal research with hazardous agents and occupational health and safety are considered in Chapter 1. Recommendations for farm animals are incorporated throughout the text where appropriate.

This edition of the *Guide* is divided into four chapters and four appendixes. Chapter 1 focuses on institutional policies and responsibilities, including the monitoring of the care and use of animals, considerations for evaluation of some specific research procedures, veterinary care, personnel qualifications and training, and occupational health and safety; the latter section summarizes another National Research Council committee report (NRC In press) and includes information about facilities and procedures for animal research with hazardous agents. Chapter 2 focuses on the animals themselves and provides recommendations for housing and environment, behavioral management, husbandry, and population management, including discussions of identification, records ,genetics, and nomenclature. Chapter 3 discusses veterinary medical care and responsibilities of the attending veterinarian; it includes recommendations relative to animal procurement and transportation, preventive medicine, surgery, pain and analgesia, and euthanasia. Chapter 4 discusses the physical plant, including functional areas and construction guidelines, with expanded discussions of heating, ventilation, and air-conditioning (HVAC) systems and facilities for aseptic surgery.

The appendixes in this edition remain largely the same as in the preceding edition. Appendix A contains an updated bibliography, categorized by topic; Appendix B lists selected organizations related to laboratory animal science; Appendix C presents federal laws relevant to animal care and use; and Appendix D provides the PHS endorsement of the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* (IRAC 1985).

REFERENCES

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Institutional Policies and Responsibilities

Proper care, use, and humane treatment of animals used in research, testing, and education (referred to in this Guide as animal care and use) require scientific and professional judgment based on knowledge of the needs of the animals and the special requirements of the research, testing, and educational programs. The guidelines in this section are intended to aid in developing institutional policies governing the care and use of animals.

Each institution should establish and provide resources for an animal care and use program that is managed in accord with this Guide and in compliance with applicable federal, state, and local laws and regulations, such as the federal Animal Welfare Regulations, or AWRs (CFR 1985), and Public Health Service Policy on Humane Care and Use of Laboratory Animals, or PHS Policy (PHS 1996). To implement the recommendations in this Guide effectively, an institutional animal care and use committee (IACUC) must be established to oversee and evaluate the program.

Responsibility for directing the program is generally given either to a veterinarian with training or experience in laboratory animal science and medicine or to another qualified professional. At least one veterinarian qualified through experience or training in laboratory animal science and medicine or in the species being used must be associated with the program. The institution is responsible for maintaining records of the activities of the IACUC and for conducting an occupational health and safety program.

MONITORING THE CARE AND USE OF ANIMALS

Institutional Animal Care and Use Committee

The responsible administrative official at each institution must appoint an IACUC, also referred to as "the committee," to oversee and evaluate the institution's animal program, procedures, and facilities to ensure that they are consistent with the recommendations in this Guide, the AWRs, and the PHS Policy. It is the institution's responsibility to provide suitable orientation, background materials, access to appropriate resources, and, if necessary, specific training to assist IACUC members in understanding and evaluating issues brought before the committee.

Committee membership should include the following:

- A doctor of veterinary medicine, who is certified (see American College of Laboratory Animal Medicine, ACLAM, Appendix B) or has training or experience in laboratory animal science and medicine or in the use of the species in question.
- At least one practicing scientist experienced in research involving animals.
- At least one public member to represent general community interests in the proper care and use of animals. Public members should not be laboratoryanimal users, be affiliated with the institution, or be members of the immediate family of a person who is affiliated with the institution.

The size of the institution and the nature and extent of the research, testing, and educational programs will determine the number of members of the committee and their terms of appointment. Additional information about committee composition can be found in the PHS Policy and the AWRs.

The committee is responsible for oversight and evaluation of the animal care and use program and its components described in this Guide. Its functions include inspection of facilities; evaluation of programs and animal-activity areas; submission of reports to responsible institutional officials; review of proposed uses of animals in research, testing, or education (i.e., protocols); and establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution.

The IACUC must meet as often as necessary to fulfill its responsibilities, but it should meet at least once every 6 months. Records of committee meetings and of results of deliberations should be maintained. The committee should review the animal-care program and inspect the animal facilities and activity areas at least once every 6 months. After review and inspection, a written report, signed by a majority of the IACUC, should be made to the responsible administrative officials of the institution on the status of the animal care and use program and other activities as stated herein and as required by federal, state, or local regulations and policies. Protocols should be reviewed in accord with the AWRs, the PHS Policy, U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (IRAC 1985; see Appendix D), and this Guide (see footnote, p.2).

Animal Care and Use Protocols

The following topics should be considered in the preparation and review of animal care and use protocols:

- Rationale and purpose of the proposed use of animals.
- Justification of the species and number of animals requested. Whenever possible, the number of animals requested should be justified statistically.
- Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation (see Appendix A, "Alternatives").
- Adequacy of training and experience of personnel in the procedures used.
- Unusual housing and husbandry requirements.
- Appropriate sedation, analgesia, and anesthesia. (Scales of pain or invasiveness might aid in the preparation and review of protocols; see Appendix A, "Anesthesia, Pain and Surgery.")
- Unnecessary duplication of experiments.
- Conduct of multiple major operative procedures.
- Criteria and process for timely intervention, removal of animals from a study, or euthanasia if painful or stressful outcomes are anticipated.
- Postprocedure care.
- Method of euthanasia or disposition of animal.
- Safety of working environment for personnel.

Occasionally, protocols include procedures that have not been previously encountered or that have the potential to cause pain or distress that cannot be reliably controlled. Such procedures might include physical restraint, multiple major survival surgery, food or fluid restriction, use of adjuvants, use of death as an end point, use of noxious stimuli, skin or corneal irritancy testing, allowance of excessive tumor burden, intracardiac or orbital-sinus blood sampling, or the use of abnormal environmental conditions. Relevant objective information regarding the procedures and the purpose of the study should be sought from the literature, veterinarians, investigators, and others knowledgeable about the effects on animals. If little is known regarding a specific procedure, limited pilot studies designed to assess the effects of the procedure on the animals, conducted under IACUC oversight, might be appropriate. General guidelines for evaluation of some of those methods are provided in this section, but they might not apply in all instances.

Physical Restraint

Physical restraint is the use of manual or mechanical means to limit some or all of an animal' 5 normal movement for the purpose of examination, collection of samples, drug administration, therapy, or experimental manipulation. Animals are restrained for brief periods, usually minutes, in most research applications.

Animals can be physically restrained briefly either manually or with restraint devices. Restraint devices should be suitable in size, design, and operation to minimize discomfort or injury to the animal. Many dogs, nonhuman primates (e.g., Reinhardt 1991, 1995), and other animals can be trained, through use of positive reinforcement, to present limbs or remain immobile for brief procedures.

Prolonged restraint, including chairing of nonhuman primates, should be avoided unless it is essential for achieving research objectives and is approved by the IACUC. Less-restrictive systems that do not limit an animal's ability to make normal postural adjustments, such as the tether system for nonhuman primates and stanchions for farm animals, should be used when compatible with protocol objectives (Bryant 1980; Byrd 1979; Grandin 1991; McNamee and others 1984; Morton and others 1987; Wakeley and others 1974). When restraint devices are used, they should be specifically designed to accomplish research goals

that are impossible or impractical to accomplish by other means or to prevent injury to animals or personnel.

The following are important guidelines for restraint:

- Restraint devices are not to be considered normal methods of housing.
- Restraint devices should not be used simply as a convenience in handling or managing animals.
- The period of restraint should be the minimum required to accomplish the research objectives.
- Animals to be placed in restraint devices should be given training to adapt to the equipment and personnel.
- Provision should be made for observation of the animal at appropriate intervals, as determined by the IACUC.
- Veterinary care should be provided if lesions or illnesses associated with restraint are observed. The presence of lesions, illness, or severe behavioral change often necessitates temporary or permanent removal of the animal from restraint.

Multiple Major Surgical Procedures

Major surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic function. Multiple major survival surgical procedures on a single animal are discouraged but may be permitted if scientifically justified by the user and approved by the IACUC. For example, multiple major survival surgical procedures can be justified if they are related components of a research project, if they will conserve scarce animal resources (NRC 1990; see also footnote, p.2), or if they are needed for clinical reasons. If multiple major survival surgery is approved, the IACUC should pay particular attention to animal well-being through continuing evaluation of outcomes. Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures (AWRs).

Food or Fluid Restriction

When experimental situations require food or fluid restriction, at least minimal quantities of food and fluid should be available to provide for development of young animals and to maintain long-term well-being of all animals. Restriction for research purposes should be scientifically justified, and a program should be established to monitor physiologic or behavioral indexes, including criteria (such as weight loss or state of hydration) for temporary or permanent removal of an animal from the experimental protocol (Van Sluyters and Oberdorfer 1991). Restriction is typically measured as a percentage of the ad libitum or normal daily intake or as percentage change in an animal's body weight.

Precautions that should be used in cases of fluid restriction to avoid acute or chronic dehydration include daily recording of fluid intake and recording of body weight at least once a week (NIH 1990)-or more often, as might be needed for small animals, such as rodents. Special attention should be given to ensuring that animals consume a suitably balanced diet (NYAS 1988) because food consumption might decrease with fluid restriction. The least restriction that will achieve the scientific objective should be used. In the case of conditioned-response research protocols, use of a highly preferred food or fluid as positive reinforcement, instead of restriction, is recommended. Dietary control for husbandry or clinical purposes is addressed in Chapter 2.

VETERINARY CARE

Adequate veterinary care must be provided, including access to all animals for evaluation of their health and well-being. Institutional mission, programmatic goals, and size of the animal program will determine

the need for full-time, part-time, or consultative veterinary services. Visits by a consulting or part-time veterinarian should be at intervals appropriate to programmatic needs. For specific responsibilities of the veterinarian, see Chapter 3.

Ethical, humane, and scientific considerations sometimes require the use of sedatives, analgesics, or anesthetics in animals (see Appendix A). An attending veterinarian (i.e., a veterinarian who has direct or delegated authority) should give research personnel advice that ensures that humane needs are met and are compatible with scientific requirements. The AWRs and PHS Policy require that the attending veterinarian have the authority to. oversee the adequacy of other aspects of animal care and use. These can include animal husbandry and nutrition, sanitation practices, zoonosis control, and hazard containment.

PERSONNEL QUALIFICATIONS AND TRAINING

AWRs and PHS Policy require institutions to ensure that people caring for or using animals are qualified to do so. The number and qualifications of personnel required to conduct and support an animal care and use program depend on several factors, including the type and size of institution, the administrative structure for providing adequate animal care, the characteristics of the physical plant, the number and species of animals maintained, and the nature of the research, testing, and educational activities.

Personnel caring for animals should be appropriately trained (see Appendix A, "Technical and Professional Education"), and the institution should provide for formal or on-the-job training to facilitate effective implementation of the program and humane care and use of animals. According to the programmatic scope, personnel will be required with expertise in other disciplines, such as animal husbandry, administration, laboratory animal medicine and pathology, occupational health and safety, behavioral management, genetic management, and various other aspects of research support.

There are a number of options for the training of technicians. Many states have colleges with accredited programs in veterinary technology (AVMA 1995); most are 2-year programs that result in associate of science degrees, and some are 4-year programs that result in bachelor of science degrees. Nondegree training, with certification programs for laboratory animal technicians and technologists, can be obtained from the American Association for Laboratory Animal Science (AALAS). There are commercially available training materials that are appropriate for self-study (Appendix B). Personnel using or caring for animals should also participate regularly in continuing-education activities relevant to their responsibilities. They are encouraged to be involved in local and national meetings of AALAS and other relevant professional organizations. On-the-job training should be part of every technician's job and should be supplemented with institution-sponsored discussion and training programs and with reference materials applicable to their jobs and the species with which they work (Kreger 1995). Coordinators of institutional training programs can seek assistance from the Animal Welfare Information Center (AWIC) and ILAR (NRC 1991). The Guide to the Care and Use of Experimental Animals by the Canadian Council on Animal Care (CCAC 1993) and guidelines of some other countries are valuable additions to the libraries of laboratory animal scientists (Appendix B). Investigators, technical personnel, trainees, and visiting investigators who perform animal anesthesia, surgery, or other experimental manipulations must be qualified through training or experience to accomplish these tasks in a humane and scientifically acceptable manner.

OCCUPATIONAL HEALTH AND SAFETY OF PERSONNEL

An occupational health and safety program must be part of the overall animal care and use program (CDC and NIH 1993; CFR 1984a,b,c; PHS Policy). The program must be consistent with federal, state, and

local regulations and should focus on maintaining a safe and healthy workplace. The program will depend on the facility, research activities, hazards, and animal species involved. The National Research Council publication *Occupational Health and Safety in the Care and Use of Research Animals* (NRC In press) contains guidelines and references for establishing and maintaining an effective, comprehensive program (also see Appendix A). An effective program relies on strong administrative support and interactions among several institutional functions or activities, including the research program (as represented by the investigator), the animal care and use program (as represented by the veterinarian and the IACUC), the environmental health and safety program, occupational-health services, and administration (e.g., human resources, finance, and facility-maintenance personnel). Operational and day-to-day responsibility for safety in the workplace, however, resides with the laboratory or facility supervisor (e.g., principal investigator, facility director, or veterinarian) and depends on performance of safe work practices by all employees.

Hazard Identification and Risk Assessment

Professional staff who conduct and support research programs that involve hazardous biologic, chemical, or physical agents (including ionizing and nonionizing radiation) should be qualified to assess dangers associated with the programs and to select safeguards appropriate to the risks. An effective occupational health and safety program ensures that the risks associated with the experimental use of animals are reduced to acceptable levels. Potential hazards-such as animal bites, chemical cleaning agents, allergens, and zoonoses-that are inherent in or intrinsic to animal use should also be identified and evaluated. Health and safety specialists with knowledge in appropriate disciplines should be involved in the assessment of risks associated with hazardous activities and in the development of procedures to manage such risks. The extent and level of participation of personnel in the occupational health and safety 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 (Clark 1993).

Personnel Training

Personnel at risk should be provided with dearly defined procedures for conducting their duties, should understand the hazards involved, and should be proficient in implementing the required safeguards.

Personnel should be trained regarding zoonoses, chemical safety, microbiologic and physical hazards (including those related to radiation and allergies), unusual conditions or agents that might be part of experimental procedures (including the use of genetically engineered animals and the use of human tissue in immunocompromised animals), handling of waste materials, personal hygiene, and other considerations (e.g., precautions to be taken during personnel pregnancy, illness, or decreased immunocompetence) as appropriate to the risk imposed by their workplace.

Personal Hygiene

It is essential that all personnel maintain a high standard of personal cleanliness. Clothing suitable for use in the animal facility and laboratories in which animals are used should be supplied and laundered by the institution. A commercial laundering service is acceptable in many situations; however, appropriate arrangements should be made to decontaminate clothing exposed to potential hazards. Disposable gloves, masks, head covers, coats, coveralls, and shoe covers might be desirable in some circumstances. Personnel should wash their hands and change clothing as often as necessary to maintain personal hygiene. Outer garments worn in the animal rooms should not be worn outside the animal facility.

Personnel should not be permitted to eat, drink, use tobacco products, or apply cosmetics in animal rooms.

Facilities, Procedures, and Monitoring

Facilities required to support occupational health and safety concerns associated with animal care and use programs will vary. Because a high standard of personal cleanliness is essential, facilities and supplies for meeting this obligation should be provided. Washing and showering facilities appropriate to the program should be available. Facilities, equipment, and procedures should also be designed, selected, and developed to provide for ergonomically sound operations that reduce the potential of physical injury to personnel (such as might be caused by the lifting of heavy equipment or animals and the use of repetitive movements). Safety equipment should be properly maintained and routinely calibrated.

The selection of appropriate animal-housing systems requires professional knowledge and judgment and depends on the nature of the hazards in question, the types of animals used, and the design of the experiments. Experimental animals should be housed so that potentially contaminated food and bedding, feces and urine can be handled in a controlled manner. Facilities, equipment, and procedures should be provided for appropriate bedding disposal.

Appropriate methods should be used for assessing exposure to potentially hazardous biologic, chemical, and physical agents where the possibility of exceeding permissible exposure limits (PELs) exists (CFR 1984b).

Animal Experimentation Involving Hazards

In selecting specific safeguards for animal experimentation with hazardous agents, careful attention should be given to procedures for animal care and housing, storage and disbursement of the agents, dose preparation and administration, body-fluid and tissue handling, waste and carcass disposal, and personal protection. Special safety equipment should be used in combination with appropriate management and safe practices. As a general rule, safety depends on trained personnel who rigorously follow safe practices.

Institutions should have written policies governing experimentation with hazardous biologic, chemical, and physical agents. An oversight process (such as use of a safety committee) should be developed to involve persons who are knowledgeable in the evaluation of hazards and safety issues. Because the use of animals in such studies requires special considerations, the procedures and facilities to be used should undergo review for specific safety concerns. Formal safety programs should be established to assess the hazards, determine the safeguards needed for their control, ensure that the staff has the necessary training and skills, and ensure that the facilities are adequate for the safe conduct of the research. Technical support should be provided to monitor and ensure compliance with institutional safety policies.

The Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) publication Biosafety in Microbiological and Biomedical Laboratories (1993) and the National Research Council (In press) recommend practices and procedures, safety equipment, and facility requirements for working with hazardous biologic agents and materials. Facilities that handle agents of unknown risk should consult with appropriate CDC personnel about hazard control and medical surveillance.

Special facilities and safety equipment are needed to protect the animal-care and investigative staff, other occupants of the facility, the public, animals, and the environment from exposure to hazardous biologic, chemical, and physical agents used in animal experimentation. Facilities used for animal experimentation

with hazardous agents should be separated from other animal housing and support areas, research and clinical laboratories, and patient-care facilities and should be appropriately identified; and access to them should be limited to authorized personnel. Such facilities should be designed and constructed to facilitate cleaning and maintenance of mechanical systems. A properly managed and used double corridor facility or barrier entry system is an effective means of reducing cross-contamination. Floor drains should always contain liquid or be sealed effectively by other means. Automatic trap priming can be provided to ensure that traps remain filled.

Hazardous agents should be contained within the study environment. Control of airflow (such as through the use of biologic-safety cabinets) that minimizes the escape of contaminants is a primary barrier used in the handling and administration of hazardous agents and the performance of necropsies on contaminated animals (CDC 1995; Kruse and others 1991). Special features of the facility-such as airlocks, negative air pressure, air filters, and redundant mechanical equipment with automatic switching-are secondary barriers aimed at preventing accidental release of hazards outside the facility and work environment.

Exposure to anesthetic waste gases should be limited. This is usually accomplished by using various scavenging techniques. If ether is used, personnel safety should be ensured by proper use of signs and by using equipment and practices to minimize risks associated with its explosiveness.

Personal Protection

Personal protective equipment should be provided, and other safety measures should be adopted when needed. Animal-care personnel should wear appropriate institution-issued protective clothing, shoes or shoe covers, and gloves. Clean protective clothing should be provided as often as necessary. If it is appropriate, personnel should shower when they leave the animal-care, procedure, or dose-preparation areas. Protective clothing and equipment should not be worn beyond the boundary of the hazardous-agent work area or the animal facility. Personnel with potential exposure to hazardous agents should be provided with personal protective equipment appropriate to the agents (CFR 1984c). For example, personnel exposed to nonhuman primates should be provided with such protective items as gloves, arm protectors, masks, and face shields. Hearing protection should be provided in high-noise areas. Personnel working in areas where they might be exposed to contaminated airborne particulate material or vapors should be provided with suitable respiratory protection (CFR 1984c).

Medical Evaluation and Preventive Medicine for Personnel

Development and implementation of a program of medical evaluation and preventive medicine should involve input from trained health professionals, such as occupational-health physicians and nurses. Confidentiality and other medical and legal factors must be considered in the context of appropriate federal, state, and local regulations.

A health-history evaluation before work assignment is advisable to assess potential risks for individual employees. Periodic medical evaluations are advisable for people in some risk categories. An appropriate immunization schedule should be adopted. It is important to immunize animal-care personnel against tetanus. In addition, pre-exposure immunization should be offered to people at risk of infection or exposure to such agents as rabies or hepatitis B virus. Vaccination is recommended if research is to be conducted on infectious diseases for which effective vaccines are available. Specific recommendations can be found in the CDC and NIH publication Biosafety in Microbiological and Biomedical Laboratories (1993). Pre-employment or pre-exposure serum collection is advisable only in specific circumstances as determined by an occupational health and safety professional (NRC In press). In such cases, identification, traceability, retention, and storage conditions of samples should be considered and the

purpose for which the serum samples will be used must be consistent with applicable state laws and consistent with the Federal Policy for the Protection of Human Subjects (Federal Register 56(117): 28002-28032, June 18, 1991).

Zoonosis surveillance should be a part of an occupational-health program (CDC and NIH 1993; Fox and others 1984; NRC In press). Personnel should be instructed to notify their supervisors of potential or known exposures and of suspected health hazards and illnesses. Clear procedures should be established for reporting all accidents, bites, scratches. and allergic reactions (NRC In press).

Nonhuman-primate diseases that are transmissible to humans can be serious hazards. Animal technicians, clinicians, investigators, predoctoral and postdoctoral trainees, research technicians, consultants, maintenance workers, security personnel, and others who have contact with nonhuman primates or have duties in nonhuman-primate housing areas should be routinely screened for tuberculosis. Because of the potential for Cercopithecine herpesvirus 1 (formerly Herpesvirus simiae) exposure, personnel who work with macaques should have access to and be instructed in the use of bite and scratch emergency-care stations (Holmes and others 1995). A procedure should be established for ensuring medical care for bites and scratches.

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