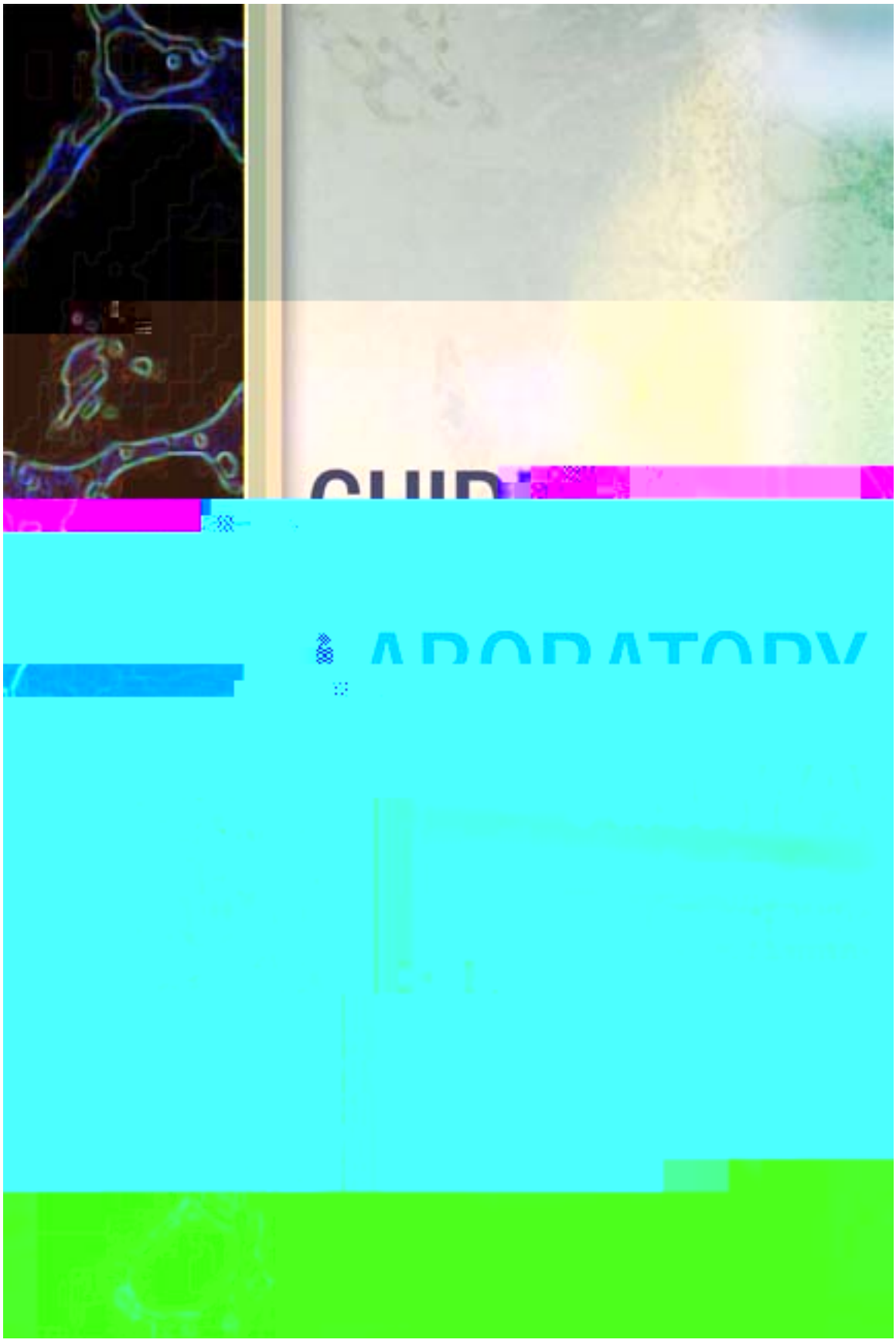

Guide for the Care and Use of Laboratory Animals

PREPUBLICATION DRAFT

Committee for the Update of the
Guide for the Care and Use of Laboratory Animals

Institute for Laboratory Animal Research

Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS 500 Fi fth Street, NW Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from thecouncils of the National Academy of Sciences, the National Academy of Engineering, and the Inst itute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This study was supported by the Office of Extramural Research,Office of the Director, National Institutes of Health/Department of Health and Human Services under Contract Number N01-OD-4-2139 Task Order# 188; the Office of Research Integrity, Department of Health and Human Services; the Animal and Plant Health Inspection Service, U.S. Department of Agriculture; A ssociation for Assessment and Accreditation of Laboratory Animal Care International; American Association fo r Laboratory Animal Scienc e; Abbott Fund; Pfizer; American College of Laboratory Animal Medicine; American Society of Laboratory Animal Practitioners; Association of Prim ate Veternarians.

Any opinions, findings, conclusions, or recommendatio ns expressed in this publication are those of the authors and do not necessarily reflect the views of the organizations or agencies that provided support for the project. The content of this publication does not necessarily reflect the views or policies of the National Institutes of Health, nor does mention of trade na mes, commercial products, or organizations imply endorsement by the US government.

International Standard Book Number

Library of Congress Control Number

Additional copies of this report are available from

The National Academies Press
500 Fifth Street, NW
Box 285
Washington, DC 20055

800-624-6242
202-334-3313 (in the Washington metropolitan area)
http://www.nap.edu

Printed in the United

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REVIEWERS

This eighth edition of the Guide for the Care and Use of Laboratory Animals has been reviewed in draft form by individuals chosen for their diverse perspectives and expertise, in accordance with procedures approved by the Report Review Committee of the National Research Council. The purpose of this independent review is to provide candid and critical comments that will assist the Committee in making its published report as sound as possible, and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberation process. The Committee thanks the following individuals for their review of the draft report:

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Allen W. Singer, Battelle Memorial Institute
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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by John Dowling, Harvard University, and John Vandenbergh, North Carolina State University. Appointed by the National Research Council, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered.

Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

PREFACE

The Guide for the Care and Use of Laboratory Animals (the Guide) was first published in 1963 under the title Guide for Laboratory Animal Facilities and Care and was revised in 1965, 1968, 1972, 1978, 1985, and 1996. More than 550,000 copies have been printed since its first publication. The Guide is an internationally accepted primary reference on animal care and use. Use of the Guide is required by the Public Health Service Policy.

The purpose of the Guide, as expressed in the charge to the Committee to Update the Guide for the Care and Use of Laboratory Animals, is to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. The Guide is also intended to assist investigators in fulfilling their obligation to plan and conduct animal experiments in accord with the highest scientific, humane, and ethical principles. The recommendations are based on published data, scientific principles, expert opinion, and experience with methods and practices that have proved to be consistent with high-quality humane animal care and use. These recommendations should be used as a foundation for the development of a comprehensive animal care and use program, recognizing that the concept and application of performance standards, in accordance with goals, outcomes and considerations defined in the Guide, is essential to this process.

This Committee has carried forward the balance between ethical and science-bassed practice that has always been the basis of the Guide. In doing so, the Committee has fulfilled its role to provide the research community with an updated tool that allows it to responsibly carry on in a self-tregulatory manner with animal experimentation. Consequently, as professional judgment is exercised, the central notion of performance standards is upheld while the need for more stringent regulations is obviated.

The need for continual updating of the Guide is implicit in its objective "…to provide information that will enhance animal well-being, the quality of research, and the advancement of scientific knowledge that is relevant to both humans and animals" (Chapter 1). The irregular and increasing intervals between updates, reaching a 14-year gap between the seventh edition and this eighth edition, means that important new research findings might wait more

than a decade before being reflected

The Committee acknowledges the contributions of William I. Gay and Bennett J. Cohen in the development of the original Guide. In 1959, Animal Care Panel (ACP) President Cohen appointed the Committee on Ethical Considerations in the Care of Laboratory Animals to evaluate animal care and use. That Committee was chaired by Dr. Gay, who soon recognized that the Committee could not evaluate animal-care programs objectively without appropriate criteria on which to base its evaluations; that is, standards were needed. The ACP executive committee agreed, and the Professional Standards Committee was appointed. NIH later awarded the ACP a contract to "determine and establish a professional standard for laboratory animal care and facilities." Dr. Cohen chaired the ACP Animal Facilities Standards Committee, which prepared the first Guide

OVERVIEW

This eighth edition of the Guide is divided into five chapters and four appendices.

Chapter 1 incorporates some of the material from the Introduction to the last edition and presents key concepts and terminology essential to the premise and utilization of the Guide. The Chapter highlights a commitment to the concepts of the Three Rs (Replacement, Reduction and Refinement) and presents an enhanced discussion of the ethics of animal use and investigator/institutional obligations. The goals and intended audiences of the Guide are also discussed.

Chapter 2 focuses on the overall institutional Animal Care and Use Program (Program), in addition to many of the topics previously covered in Chapter 1. It defines the evolved concept of Program and provides a framework for its intra-institutional integration, including a focus on institutional policies and responsibilities; regulatory considerations; Program and personnel management (including training and occupational health and safety); and Program oversight. The latter includes institutional animal care and use committee (IACUC) functions; protocol and Program review, a new section on post-approval monitoring, and discussion of special considerations, such as humane endpoints and multiple survival surgical procedures. The American College of Laboratory Animal Medicine's "Guidelines for Adequate Veterinary Care" are endorsed.

Chapter 3 focuses on the animals themselves and unlike prior editions, addresses terrestrial and aquatic animals in separate sections reflecting the growing role of aquatic animals in biomedical research. In this chapter, recommendations for housing and environment and enhanced sections on environmental enrichment, animal well-being and scientific validity are presented. The importance of social housing is also emphasized.

In this chapter, space recommendations were minimally expanded based on the Committee's professional and expert opinion and currently applied housing methods. The cage sizes have historically been interpreted as minimum space needs by the users of the Guide, and were labeled as such ("recommended minimum space") in this edition. The use of the word "minimum" does not further restrict users of the Guide because although the space requirements are numbers (i.e., engineering standards), they are utilized within a performance standards framework. In light of many comments submitted to the Committee requesting more information on performance goals and how to achieve them,

rodent breeding recommendations are accompanied by substantial guidance on important considerations, and recommended minimum space for female rodents with litter has been added. Further, the cage height recommendation for rabbits increased to 16".

With respect to NHPs the Committee endorses social housing as the default and has provided some species-specific guidance. Additional NHP groups have been added to include baboons, while the chimpanzees were separated in a new category. These changes were motivated by the Committee's recognition (affirmed by the solicited comments from NHP experts) that these animals need more vertical space, at least in some groups, to exercise their natural habits.

Chapter 4 discusses veterinary care and the responsibilities of the attending veterinarian. It introduces the concept of animal biosecurity to affirm its central role in assuring the health of laboratory animals. It includes recommendations relative to animal procurement, transportation and preventive medicine, and expands the sections on clinical care and management; surgery (introduces intraoperative monitoring); pain and distress; and euthanasia.

Chapter 5 discusses physical plant-related topics and includes updated and new material on such topics as vibration control; physical security and access control; hazardous agent containment; and special facilities for imaging and whole body irradiation, barrier housing, behavioral studies, and aquatic species housing. Detailed discussion of centralized vs. decentralized animal facilities is provided and the concept of variable-volume HVAC systems is introduced with a nod toward energy conservation and efficiency.

Appendix A is the updated bibliography; Appendix B contains the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used

CONTENTS

CHAPTER 1. Key Concepts

This edition of the Guide for the Care and Use of Laboratory Animals (the Guide) strongly affirms the principle that all who care for, use or produce animals for research, testing or teaching must assume responsibility for their well-being. The Guide plays an important role in decision-making regarding the use of vertebrate

Applicability and Goals

Laboratory animals or animals- Any vertebrate animal (e.g., traditional laboratory animals, agricultural animals, wildlife and aquatic species) produced for or used in research, testing or teaching.

Animal use- The proper care, use and humane treath19v

In the Guide laboratory animals (also referred to as animals) are generally defined as any vertebrate animal (e.g., traditional laboratory animals, agricultural animals, wildlife and aquatic species) produced for or used in research, testing or teaching. Animal use is defined as the proper care, use and humane treatment of laboratory animals produced for, or used in research testing or teaching.

When appropriate, considerations or specific emphases for agricultural animals and non-traditional species are presented. The Guide does not address in detail agricultural animals used in production agri cultural research or teaching, wildlife and aquatic species studied in natural settings, or invertebrate animals (e.g., cephalopods) used in research. Nevertheless, the Guide establishes general principles and ethical considerations that are also applicable to these species and situations. References in the Guide provide the reader with additional information reg arding statements made in the Guide. Supplemental information on breeding, care, management, and use of selected laboratory animal species is available in other publications prepared by the Institute for Laboratory Animal Research (ILAR) and other organizations (Appendix A).

The goal of the Guide is to promote humane care and use for laboratory animals. The Committee recognizes that the use of different species in research is expanding, and that researchers and institutions will face new and unique challenges in determining how to apply the Guide in these situations. In making these determinations, it is important to keep in mind that the Guide is intended to provide information to assist researchers, institutional animal care and use committees (IACUCs), veterinarians, and the other stakeholders in assuring the implementation of effective and appropriate animal care and use programs that are based on humane care. The objective is to provide information that will enhance animal well-being, the quality of research, and the advancement of scientific knowledg e that is relevant to both humans and animals. The Guide encourages scientists and

institutions to give careful and deliberate thought to the decision to use animals, taking into consideration the contribution that such use will make to new knowledge, ethical considerations, and the availability of alternatives to animal use (NRC 1992). A practical strategy for decision-making, described as the Three Rs (Replacement, Reduction and Refinement) approach, is discussed in more detail below. Institutions should use the recommendations in the *Guide* as a foundation for the development of a comprehensive animal care and use program and a process for continually improving this program.

Intended Audiences and Uses of the **Guide**

The *Guide* is intended for a wide and diverse audience, including

- The scientific community
- Administrators
- IACUCs
- Veterinarians
- Educators and trainers
- Producers of laboratory animals
- Accreditation bodies
- Regulators
- The public

It is intended that the *Guide* be read by the user in its entirety, as there are many concepts throughout that may be helpful. Individual sections will be particularly relevant to certain users, and it is expected that the reader will explore in more detail the cited references (including those in Appendix A) on topics of interest.

Members of the scientific community (investigators and other animal users) will find Chapters 1 and 2 (and portions of Chapter 4) of the *Guide* useful for assisting in interactions with the IACUC, attending veterinarian and administrators regarding animal care as well as in preparing animal care and use protocols. Scientific review committees and journal editors may choose to refer to multiple sections of the *Guide* to determine if scientists contributing proposals and manuscripts have met the appropriate standards in their planned use of animals. The *Guide* can assist IACUCs and administrators in protocol review, assessment and oversight of an animal care and use program. Veterinarians should find Chapters 3 through 5 valuable for their oversight and support of animal care and use. Educators and trainers can use the *Guide* as a document to assess both the scope and adequacy of training programs supported by the institution. Accreditation bodies will find the *Guide* useful for evaluating many areas of animal care and use programs not subject to strict engineering standards

(see definition below). Finally, members of the public should feel assured that adherence to the *Guide* will ensure humane care and use of laboratory animals.

Readers are reminded that the *Guide* is used by a diverse group of national and international institutions and organizations, many of which are covered by neither the Animal Welfare Act nor the PHS Policy. The *Guide* uses some terminology that is both defined by U.S. statute and denotes a general concept, e.g. "Attending Veterinarian", "Adequate Veterinary Care", and "Institutional Official". Even if these terms are not consistent with terms used by non-U.S. institutions, the underlying principles can still be applied. In all instances where *Guide* recommendations are different from applicable legal or policy requirements, the higher standard should apply.

Ethics and Animal Use

The decision to use animals in research requires critical thought, judgment and analysis. Using animals in research is a privilege granted by society to the research community with the expectation that such use will provide either significant new knowledge or lead to improvement in human and/or animal well-being (McCarthy 1999; Perry 2007). It is a trust that mandates responsible and humane care and use of these animals. The *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 B). These principles direct the research community to accept responsibility for the care and use of animals during all phases of the research effort. Other government agencies and professional organizations have published similar principles (NASA 2008; NCB 2005; NIH 2002, 2006; for additional references see Appendix A). Ethical considerations discussed here and in other sections of the *Guide* should serve as a starting point and readers are encouraged to go beyond these provisions. In certain situations, special considerations will arise during protocol review and planning. Several of these situations are discussed in more detail in Chapter 2. A practical method for implementation of these concepts is contained in the Three Rs principles.

The Three Rs

In 1959, W. M. S. Russell and R. L. Burch published a practical strategy, referred to as "the Three Rs," – replacement, refinement and reduction– for researchers to apply when considering experimental design in laboratory animal research (Russell and Burch 1959). Over the years, the Three Rs have evolved into an internationally accepted approach for researchers to employ when deciding to

use animals in research, and in designing humane animal research studies.

Replacement refers to methods that avoid using animals. The term includes absolute replacements (i.e., replacing animals with inanimate systems such as computer programs) as well as relative replacements (i.e., replacing animals, such as vertebrates, with animals that are lower on the phylogenic scale).

Refinement refers to modifications of husbandry or experimental procedures to enhance animal well-being and minimize or eliminate pain and distress. While institutions and investigators should take all reasonable measures to eliminate pain and distress through refinement, IACUCs should understand that with some types of studies, there could be either unforeseen or intended experimental outcomes that produce pain. These outcomes may or may not be eliminated based on the goals of the study.

Reduction includes strategies for obtaining comparable levels of information from the use of fewer animals or for maximizing the information obtained from any given number of animals (without increasing pain or distress) so that in the long run fewer animals are needed to acquire the same scientific information. This approach relies on an analysis of experimental design, applications of newer technologies, the use of appropriate statistical methods, and control of environmentally related variability in animal housing and study areas (see Appendix A).

Refinement and reduction goals should be balanced on a case-by-case basis. In other words, reduction should not serve as a rationale for reusing an animal or animals that have already undergone experimental procedures especially if the well-being of the animals would be compromised. Principal Investigators are strongly discouraged from advocating animal reuse as a reduction strategy. Studies that may result in severe or chronic pain or significant alterations in the animals' ability to maintain normal physiology, or adequately respond to stressors, should contain descriptions of appropriate humane endpoints or provide science-based justification as to why a particular, commonly accepted humane endpoint cannot be employed. Veterinary consultation must occur when pain or distress is beyond the level anticipated in the protocol description or when interventional control is not possible.

Key Terms Used in the **Guide**

The Committee to Update the Guide believes that the terms set out below are important for a full understanding of the Guide. Accordingly, we have defined these terms and concepts to provide the users of the Guide with additional assistance in implementing their responsibilities.

Humane Care

Humane care means those actions taken to assure that laboratory animals are treated according to high ethical and scientific standards. Implementing a humane care program, and creating a laboratory environment in which humane care and respect for animals is valued and encouraged, underlie the core requirements of the Guide and the system of self-regulation it supports (Klein and Bayne 2007).

Animal Care and Use Program

Animal care and use program ("Program") means the policies, procedures, standards, organizational structure, staffing and practices put into place by an institution to achieve humane care of animals in the laboratory and throughout the institution. This includes the establishment and support of an institution's animal care and use committee (IACUC) or equivalent ethical oversight committee and the maintenance of an environment in which the IACUC can function successfully to carry out its responsibilities under the Guide, U.S. laws and U.S. policies. Chapter 2 contains a more expansive discussion of the applicability to, and importance of, the Guide to animal care and use programs.

Engineering and Performance Standards

Engineering standard means a standard or guideline that specifies in detail a method, technology or technique for achieving a desired outcome, and does not provide for modification in the event that acceptable alternative methods are available or unusual circumstances arise. Engineering standards are prescriptive and provide limited flexibility for implementation. However, an engineering standard can be useful to establish a baseline, and are easier to use in evaluating compliance.

Performance standard means a standard or guideline that, while describing a desired outcome, provides flexibility in achieving this outcome by granting discretion to those with responsibility for managing the animal care and use program, the researcher, and the IACUC. The performance approach requires professional input, sound judgment and a team approach to achieve specific goals. It is essential that the desired outcomes and/or goals are clearly defined, and that appropriate performance measures are regularly monitored, in order to verify success of the process. This approach can be advantageous because many variables (such as the species and previous history of the animals, facilities, expertise of the people, and research goals) can be taken into consideration so that the implementation of the standard can be best tailored to meet the recommendations in the Guide.

Ideally, engineering and performance standards are balanced, setting a target for optimal practices, management and operations while encouraging flexibility and judgment, if appropriate, based on individual situations (Gonder et al. 2001). Scientists, veterinarians, technicians and others have extensive experience and information covering many of the topics discussed in the Guide. For those topics in which information is insufficient or incomplete, sustained research into improved methods of laboratory animal management, care and use is needed for the continued evaluation and improvement of performance and engineering standards.

Practice Standards

Practice standard means the application of professional judgment by qualified, experienced individuals to a task or process over time, which has been demonstrated to benefit or enhance animal care and use. Much of the basis for professional judgment comes from information obtained from the peer-reviewed scientific literature and textbooks. However, similar to many other disciplines, the application of professional judgment also relies on time-proven experiences in the field (for additional information see chapter 2). Therefore, in the absence of published scientific literature or other definitive sources, where experience has demonstrated that a particular practice improves animal care and use, such standards have been utilized in determining appropriate recommendations in the Guide. In most situations, the Guide is intended to provide flexibility so that institutions can modify practices and procedures with changing conditions and new information.

Policies, Principles and Procedures

Policies commonly derive from a public ag ency or private entity. Policies are generally practical statements of collect

Training. Federal Register, May 20, 1985. Washington: Office of Science and Technology Policy. Available at: http://oacu.od.nih.gov/regs/USGovt Prncpl.htm; accessed May 10, 2010.

Klein HJ, Bayne KA. 2007. Establishing a culture of care, conscience, and responsibility: Addressing the improvement of scientif ic discovery and animal welfare through science-based performance standards. ILAR J 48:3-11.

McCarthy CR. 1999. Bioethics of Laboratory Animal Research. ILAR J 40:1-37.

NASA [National Aeronautics and Space Administration]. 2008. NASA Principles for the Ethical Care and Use of Animals. NPR 8910.1B-Appendix A. May 28. Available at http://nodis3.gsfc.nasa.gov/displayDir.cfm?t=NPDandc=8910ands=1B; accessed May 10, 2010.

NCB [Nuffield Council on Bioethics]. 2005. The Ethics of Research Using Animals. London: NCB.

NIH [National Institutes of Health]. 2002. Memorandum of Understanding Between the Office of Research Compliance and Assurance, US Department of Veterans Affairs and the Office of Laboratory An imal Welfare, National Institutes of Health, US Department of Health and Human Services Concerning Laboratory Animal Welfare. December 2002. Rockville: Office of Extramural Research, NIH.

NIH. 2006. Memorandum of Understanding Among the Animal and Plant Health Inspection Service USDA and the Food and Drug Administration, US Department of Health and Human Services, and the National Institutes of Health Concerning Laboratory Animal Welfare. March 1, 2006. Rockville: Office of Extramural Research, NIH.

NRC [National Research Council]. 1992. Report on Responsible Science. Washington: National Academy Press.

Perry P. 2007. The Ethics of Animal Research: A UK Perspective. ILAR J 48:42-46.

PHS [Public Health Service]. 2002. Public Health Service Policy on Humane Care and Use of Laboratory Animals. Publication of the Department of Health and Human Services, National Institutes of Health, Office of Laboratory Animal Welfare. Available at: http://grants.nih.gov/ grants/olaw/references/phspol.htm; accessed June 9, 2008.

Russell WMS, Burch RL. 1959. The Principles of Humane Experimental Technique. London: Methuen and Co. [Reissued: 1992, Universities Federation for Animal Welfare, Herts, UK].

USDA [US Department of Agriculture]. 1985. 9 CFR 1A. (Title 9, Chapter 1, Subchapter A): Animal Welfare. Available at ht tp://ecfr.gpoaccess.gov/cgi/t/text/text-idx?sid=8314313bd7adf2c9f1964e2d82a88d92andc=ecfrandtpl=/ecfrbrowse/Title09/9cfrv1_02.tpl; accessed January 14, 2010.

Program Management

An effective Program requires clearly defined roles that align responsibility with regulatory and management authority. U.S. federal law creates a statutory basis for the Institutional Official (IO), the Attending Veterinarian (AV), and the Institutional Animal Care and Use Committee (IACUC). The Guide endorses these concepts as important operating principles for all U.S. and non-U.S. animal care and use programs. Effective leadership within and collaboration among these three components, which not only oversee but also support animal users, are necessary (Lowman 2008; Van Sluyters 2008). In addition, interactions with regulatory and funding agencies and accreditation organizations are an integral part of the Program.

As summarized here and discussed throughout the Guide, the primary oversight responsibilities within the Program rest with the IO, the AV and the IACUC. The roles fit within a defined organizational structure where the reporting relationships, authorities and responsibilities of each are clearly defined and transparent. Taken together they establish policies and procedures, ensure regulatory compliance, monitor Program performance and support high-quality science and humane animal use. A program that includes these elements, and establishes a balance among them, has the best chance of efficiently utilizing resources while attaining the highest standards of animal well-being and scientific quality (Bayne and Garnett 2008; Van Sluyters 2008).

Program Management Responsibility

The Institutional Official

Institutional Official – The individual who, as a representative of senior administration, bears ultimate responsibility for the Program, and is responsible for resource planning and ensuring alignment of Program goals with the institution's mission.

The Institutional Official (IO) bears ultimate responsibility for the Program, although overall direction of the Program should be a shared responsibility among the IO, AV and IACUC. The IO has the authority to allocate the needed resources and ensure the Program's overall effectiveness. Program needs should be clearly and regularly communicated to the IO by the AV, the IACUC and others associated with the Program

(facilities management, occupational health and safety, scientists, etc.). As a representative of senior administration, the IO is responsible for resource planning and ensuring alignment of Program goals of quality animal care and use, with the institution's mission.

The Attending Veterinarian

The Attending Veterinarian(AV) is responsible for the health and well-being of all laboratory animals used at the institution. The institution must provide the AV with sufficient authority, including access to all animals, and resources to manage the program of veterinary care. The AV should oversee other aspects of animal care and use(e.g., husbandry, housing) to ensure that the Program complies with the Guide.

Institutional mission, programmatic goals, including the nature of animal use at the institution, and Program size will determine whether full-time, part-time, or consultative veterinary services are needed. If a full-time veterinarian is not available on site, visits by a consulting or part-time veterinarian should be at intervals appropriate to programmatic needs. In such instances, there must be an individual with assigned respon sibility for daily animal care and use and facility management. While institutions with large animal care and use programs may employ multiple veterinarians, management of veterinary medicine, animal care, and facility operations by a single administrative unit is often an efficient mechanism to administer all aspects of the Program.

The Guideendorses the American College of Laboratory Animal Medicine's (ACLAM) "Guidelines for Adequate Veterinary Care" (ACLAM 1996). These guidelines include veterinary access to all animals and their medical records, regular veterinary visits to facilities where animals may be housed or used, provisions s tofals maysas and comvetent celidicad, preentative, andgemargncyf veterinary care, andah l anima, prcturement and rianportratiod.

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to work effectively, there should be clear and regular communication between the AV and the IACUC.

The Institutional Animal Care and Use Committee

The IACUC (or institutional equivalent) is responsible for assessment and oversight of the institution's Program components and facilities. The IACUC should have sufficient authority and be provided with resources (e.g., staff, training, computer resources) to fulfill th is responsibility. Detailed information on the role and function of the IACUC is provided later in this chapter.

Collaborations

Inter-institutional collaboration has the po tential to create ambiguities regarding responsibility for animal care and use. In cases of collaboration between institutions that involves animal use (beyond merely transporting animals), institutions should have a formal written understanding (e.g., contract, memorandum of understanding or inter- institutional agreement) between the institutions. The written agreement shou ld address the responsibility for offsite animal care and use, animal ownership and IACUC review and oversight (AAALAC 2003). In addition, IACUC's from both partic ipating institutions may choose to review protocols for the work being conducted.

Personnel Management

Training and Education

All personnel involved with the care an d use of animals must be adequately educated, trained and/or qualified in basic principles of laboratory animal science to help assure high quality scien ce and animal well-being. The number and qualifications of personnel required to conduct and support a Program depend on several factors, including th e type and size of institution, the administrative structure for providing ad equate animal care, the .;14sdfalgcrals

institution-sponsored discussion and trai ning programs and reference materials applicable to their jobs and the species being cared for, should be provided to each employee responsible for animal care (Kreger 1995). Coordinators of institutional training programs can seek assistance from the Animal Welfare Information Center (AWIC), the Laborat ory Animal Welfare and Training Exchange (LAWTE), AALAS 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 from other countries are valuable additions to the libraries of laboratory animal scientists (Appendix A).

Occupational Health and Safety of Personnel

Each institution must establish and maintain an Occupational Health and Safety Program (OHSP) as an essential part of the overall program of animal care and use (CFR 1984a, b, c; DHHS 2007; PHS 2002). The OHSP must be consistent with federal, state, and local regulations and should focus on maintaining a safe and healthy workplace (Gonder 2002; Newcomer 2002; OSHA 1998a). The nature of the OHSP will depend on the facility, research activities, hazards, and animal species involved. The National Research Council's publication Occupational Health and Safety in the Care and Use of Research Animals (NRC 1997) contains guidelines and references for establishing and maintaining an effective, comprehensive OHSP (also see Appendix A). An effective OHSP requires coordination between the research program (as represented by the investigator), the animal care and use program (as represented by the AV, IO and the IACUC), the environmental health and safety program, occupational-health services, and administration (e.g., human resources, finance, and facility-maintenance personnel). Establishment of a safety committee may facilitate communication and promote ongoing evaluation of health and safety in the workplace. In some cases there is a regulatory requirement for such a committee. Operational and day-to-day responsibility for safety in the workplace 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.

Control and Prevention Strategies

In developing a comprehensive OHSP a hierarchy of control and prevention strategies should be followed that begins with the identification of hazards and the assessment of risk associated with those hazards. Managing risk involves the following steps: first, the appropriate design and operation of facilities and use of appropriate safety equipment (engineering controls); second, the development of processes and standard operating procedures (SOPs; administrative controls); and finally, the provision of appropriate personal protective equipment (PPE) for employees. Managing risk, utilizing these strategies, requires that personnel be trained, adhere to good personal hygiene, be knowledgeable about the hazards in their work environment, understand the proper selection and use of equipment, follow established procedures, and utilize PPE provided.

Hazard Identification and Risk Assessment

The institutional OHSP should identify potential hazards in the work environment and conduct a critical assessment of the associated risks. An

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 (Frasier 2005; NIH 2002; DHHS 2007). When necessary, these facilities should be separated from other animal housing and support areas, research and clinical laboratories, and patient-care facilities. They should be appropriately identified, and access to them should be limited to authorized personnel.

Facilities, equipment, and procedures should also be designed, selected, and developed to reduce the potential of physical injury or health risk to personnel, (NIOSH 1997a, b). Engineering controls to address the potential for ergonomic injury should be considered in situations such as lifting of heavy equipment or animals (AVMA 2008). The potential for repetitive motion injuries in animal facilities (e.g., maintenance of large rodent populations and other husbandry activities) should be assessed. Engineering controls and equipment are frequently utilized to limit or control personnel exposure to animal allergens (Harrison 2001; Huerkamp et al. 2008).

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, the limitations or capabilities of the facilities, 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 utilized for appropriate bedding disposal. Safety equipment should be properly maintained and its function periodically validated. Appropriate methods should be used for assessing and monitoring exposure to potentially hazardous biologic, chemical, and physical agents where required (e.g., ionizing radiation), or where the possibility of exceeding permissible exposure limits (PELs) exists (CFR 1984b).

Personnel Training

Personnel at risk should be provided with clearly defined procedures, and in specific situations, personal protective equipment (PPE) to safely conduct their duties, understand the hazards involved, and be proficient in implementing the required safeguards. They should be trained regarding zoonoses, chemical, biologic and physical hazards (e.g., radiation and allergies), unusual conditions or agents that might be part of experimental procedures (e.g., the use of human tissue in immunocompromised animals), handling of waste materials, personal

attending veterinarian, animal care technician and occupational health and safety professionals may enhance compliance.

The BMBL (DHHS 2007) and the National Research Council (NRC 1997) 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. The use of highly pathogenic "select agents and toxins" in research requires that institutions develop a program and procedures for procuring, maintaining and disposing of

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 (e.g., PL 104-191).

A pre-employment health evaluation and/or a health-history evaluation before work assignment is advisable to assess potential risks for individual employees. Continuing periodic medical evaluations are advisable for personnel in specific risk categories. For example, personnel required to use respiratory protection may also require medical evaluation to ensure that they are physically and psychologically able to use the respirator properly (Sargent and Gallo 2003). An appropriate immunization schedule should be adopted. It is important to immunize animal-care personnel against tetanus (NRC 1997). In addition, pre-exposure immunization should be offered to people at risk of infection or exposure to specific agents such as rabies virus (e.g., if working with species at risk for infection) or hepatitis B virus (e.g., if working with human blood or human tissues, cell lines or stocks). Vaccination is recommended if research is to be conducted on infectious diseases for which effective vaccines are available. More specific recommendations can be found in the BMBL (DHHS 2007). Pre-employment or pre-exposure serum collection is advisable only in specific circumstances as determined by an occupational health and safety professional (NRC 1997). 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 federal and state laws.

Zoonosis surveillance should be a part of an OHSP (DHHS 2007; NRC 1997). 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 1997).

Laboratory animal allergy has become a significant issue for individuals in contact with laboratory animals (Bush and Stave 2003; Gordon 2001; Wolfle and Bush 2001; Wood 2001). The medical surveillance program should promote the early diagnosis of allergies (Bush 2001; Bush and Stave 2003; Seward 2001) and include evaluation of an individual's medical history for preexisting allergies. Personnel training should include information on laboratory animal allergies,

preventive control measures and proper techniques for working with animals (Gordon et at. 1997; Schweitzer et al. 2003; Thulin et al. 2002). PPE should be used to supplement, not replace, engineering or process controls (Harrison 2001; Reeb-Whitaker et al. 1999). If PPE for respiratory protection is necessary, appropriate fit testing and training should be provided.

Nonhuman primate diseases that are transmissible to humans can be serious hazards (NRC 2003a). Animal technicians, veterinarians, investigators, students, research technicians, maintenance workers and others who have contact with nonhuman primates, or their tissues and body fluids, or who have duties in nonhuman primate housing areas should be routinely screened for tuberculosis. Because of the potential for Macacine herpesvirus 1 (formerly Cercopithecine herpesvirus 1 or Herpes B virus) exposure, personnel who work with or handle biological samples (blood and tissues) from macaques should have access to and be instructed in the use of bite and scratch emergency-care stations (Cohen et al. 2002). Injuries associated with macaques, their tissues or body fluids, or caging and equipment with which the animals have had direct contact, should be carefully evaluated and appropriate post-exposure treatment and follow-up implemented (ibid; NRC 2003a). Medical care for bites, scratches, and puncture wounds from other animal species should also be available (Cohen et al. 2002; DHHS 2007).

Personnel Security

While contingency plans normally address natural disasters, institutions should also consider the threat that criminal activity, such as personnel harassment and assault, and facility trespassing, arson, and vandalism pose to laboratory animals, research personnel, equipment and facilities, and biomedical research within the institution. Preventive measures should be considered, including pre-employment screening, and physical and information technology security (Miller 2007).

Investigating and Reporting Animal Welfare Concerns

Safeguarding animal welfare is the responsibility of every individual associated with the Program. The institution must develop methods for reporting and investigating animal welfare concerns. In the U.S., responsibility for review and

are reported anonymously; taking corrective actions if deemed necessary; and providing a report of the issue, findings and actions taken to the IO. Reported concerns and any corrective actions taken should be documented.

Mechanisms for reporting concerns should be posted in prominent locations within the facility and on applicable institutional web site(s) with instructions on how to report the concern and to whom. Multiple points of contact, including senior management, IO, IACUC Chair and the AV are recommended. The process should include a mechanism for anonymity, compliance with applicable whistleblower policies, non-discrimination against the concerned/reporting party and protection from reprisals.

Training and regular communication with employees regarding the Institution's animal use activities may reduce potential concerns. Personnel, such as custodial, maintenance and administrative staff, who are farther removed from the animal use, should also be included.

Program Oversight

The Role of the IACUC

IACUC Constitution and Function

The responsibility of the IACUC is to oversee and routinely evaluate the Program. 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 their roles and responsibilities, and evaluating issues brought before the committee.

Committee membership includes the following:

- A Doctor of Veterinary Medicine certified (e.g., ACLAM, ECLAM, JCLAM, KCLAM) or with training and experience in laboratory animal science and medicine or in the use of the species at the institution.
- At least one practicing scientist experienced in research involving animals.
- At least one member from a nonscientific background, drawn from inside or outside the institution.
- At least one public member to represent general community interests in the proper care and use of animals.

Public members should not be laboratory animal users, be affiliated in any way with the institution, or be members of the immediate family of a person who is affiliated with the institution. While the public member may receive compensation for their participation and ancillary expenses (meals, parking, travel, etc.), the amount should be sufficiently modest that it does not become a substantial source of income, thus potentially compromising the association with the community and public at large.

For large institutions with many administrative units or departments, no more than three voting members should be associated with a single administrative unit of the institution (CFR 1985). The size of the institution and the nature and extent of the Program will determine the number of members of the committee and their terms of appointment. Institutions with broad research programs may need to choose scientists from a number of disciplines and experience to properly evaluate animal use protocols.

The committee is responsible for oversight and evaluation of the entire Program and its components as described in the Guide. Its oversight functions include review and approval of proposed animal use (protocol review); proposed significant changes to animal use; regular inspection of facilities and animal use areas; regular review of the Program; on-going assessment of animal care and use; and establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution. The committee must meet as often as necessary to fulfill its responsibilities. Records of committee meetings and results of deliberations should be maintained. Program review and facilities inspections should occur at least annually or more often as required (e.g., Animal Welfare Act and PHS Policy). After review and inspection, a written report (including any minority views) should be made to the IO on the status of the Program.

avoiding unnecessary animal use or duplication of experiments. For some IACUC questions, input from outside experts may be advisable or necessary. In the absence of evidence of a formal scientific merit review, the IACUC may

invasive experiments, the experimental and humane endpoints are closely linked (Wallace 2000) and should be carefully considered during IACUC protocol review. While all studies should employ endpoints that are humane, studies that commonly require special consideration include those that involve tumor models, infectious diseases, vaccine challenge, pain modeling, trauma, production of monoclonal antibodies, assessment of toxicologic effects, organ or system failure, and models of cardiovascular shock.

The Principal Investigator, with precise knowledge of both the objectives of the study and the proposed model, should identify, explain and include in his or her animal use protocol a study endpoint that is both humane and scientifically sound. The identification of humane endpoints is often challenging because multiple factors must be weighed, including the model, species (and sometimes strain or stock), animal health status, study objectives, institutional policy, regulatory requirements, and occasionally conflicting scientific literature. Determination of humane endpoints should involve the Principal Investigator, the veterinarian, and the IACUC, and should be defined when possible prior to the start of the study (Olfert and Godson 2000; Stokes 2000). Information that is critical to the IACUC's assessment of appropriate endpoint consideration within a protocol includes precisely defining the humane endpoint (including assessment criteria); the frequency of animal observation; training of personnel responsible for assessment and recognition of the humane endpoint; and the response required upon reaching the humane endpoint. An understanding of pre-emptive euthanasia (Toth 2000), behavioral or physiologic definitions of the moribund state (ibid), and the use of study-specific animal assessment records (Morton 2000; Paster et al. 2009) can aid the Principal Investigator and IACUC when considering or developing proposed endpoints. When novel studies are proposed or information for an alternative endpoint is lacking, the use of pilot studies is an effective method for identifying and defining humane endpoints and reaching consensus among the Principal Investigator, IACUC and veterinarian. A system for communication with the IACUC should be in place both during and after such studies. Numerous publications address specific proposals for the application and use of humane endpoints (e.g., CCAC 1998; ILAR 2000; OECD 1999; Toth 1997; UKCCCR 1997).

Unexpected Outcomes

Fundamental to scientific inquiry is the investigation of novel experimental variables. Because of the potential for unexpected outcomes that may affect animal well-being when highly novel variables are introduced, more frequent monitoring of animals may be required. With their inherent potential for unanticipated phenotypes, GMAs are an example of when increased monitoring

for unexpected outcomes could be implemented (Dennis 1999).

GMAs, particularly mice and fish, are important animal models, and new methods and combinations of genetic manipulation are constantly being developed (Gondo 2008). Regardless of whether genetic manipulation is targeted or random, the phenotype that initially results is often unpredictable and may lead to expected or unexpected outcomes that impact the animal's well-being or survival at any stage of life. For example, instances have occurred in which genetic modification has lead to unexpected immunodeficiency, requiring the GMA offspring to be held under specialized bio-exclusion conditions (Mumphrey et al. 2007). The promoter sequences used to direct expression of transgenes to specific tissues have varying degrees of specificity ("leakiness") that can lead to unexpected phenotypes (Moorehead et al. 2003). These examples illustrate the diversity of unanticipated outcomes and emphasize the need for diligent monitoring and professional judgment, to ensure the animals' well-being (Dennis 2000). The first offspring of a newly generated GMA line should be carefully observed from birth into early adulthood for signs of disease, pain or distress. Investigators may find that the phenotype precludes breeding of particular genotypes or that unexpected infertility occurs. Such situations could lead to increases in the numbers of animals used and revision of the animal use protocol. When the initial characterization of a GMA reveals a condition that negatively impacts animal well-being, this should be reported to the IACUC, and more extensive analysis may be required to better define the phenotype (Brown et al. 2000; Crawley 1999; Dennis 2000). This may help to determine whether proactive measures can be taken to circumvent or alleviate the impact of the genetic modification on the animal's well-being, and to establish humane endpoints specific to the GMA line.

Physical U-.001.0002 Tc79Rd

Prolonged restraint, including chairing of nonhuman primates, should be avoided unless it is essential for achieving research objectives and is specifically approved by the IACUC (NRC 2003b). Systems that do not limit an animal's ability to make normal postural adjustments, such as subcutaneous implantation of osmotic minipumps in rodents, back pack-fitted infusion pumps in dogs and nonhuman primates, and free-stall housing for farm animals, should be used when compatible with protocol objectives. Animals that do not adapt to necessary restraint systems should be removed from the study. 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 should not be considered a normal method of housing, and must be justified in the animal use protocol.
- Restraint devices should not be used simply as a convenience in handling or managing animals.
- Alternatives to physical restraint should be considered.
- 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 (with positive reinforcement) to adapt to the equipment and personnel.
- Animals that fail to adapt should be removed from the study.
- Provision should be made for observation of the animal at appropriate intervals, as determined by the IACUC.
- Veterinary care must 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.
- Clear explanation of the purpose of the restraint and its duration

animal training for a specific protocol-related task. Close monitoring of the animals should occur to ensure that food and fluid intake meets the animal's nutritional needs (Toth and Gardiner 2000). Body weights should be recorded at least weekly and more often for animals requiring greater restrictions (NRC 2003b). Written records should be maintained for each animal to document daily food and fluid consumption, hydration st atus, and any behavioral and clinical changes used as criteria for temporary or permanent removal of an animal from

Housing systems for agricultural animals used in biomedical research may or may not differ from those used in agricultural research. Animals used in either can be housed in cages, stalls, paddocks or pastures (ibid). 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 agricultural animals and defining standards for their care and use should be based on the researcher's goals 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 pain and distress are minimized.

The *Guide* applies to agricultural animals used in biomedical research, including those maintained in typical farm settings. For animals maintained in a farm setting, the Guide for the Care and Use of Agricultural Animals in Research and Teaching (FASS 2010) is a useful resource. In particular, information dealing with environmental enrichment, transport and handling may be helpful in both agricultural and biomedical research settings. Additional information regarding facilities and management of farm animals in an agricultural setting can be obtained from the Midwest Plan Service (1987) and from agricultural engineers or animal-science experts.

Post-Approval Monitoring

Continuing IACUC oversight of animal activities is required by federal laws, regulations and policies. A variety of mechanisms can be used to facilitate ongoing protocol assessment and regulatory compliance. Post-approval monitoring (PAM) is considered here in the broadest sense, consisting of all potential types of protocol monitoring following initial protocol approval by the IACUC. PAM helps ensure the well-being of the animals and may also provide opportunities to refine research procedures. Methods include continuing protocol review; laboratory inspections (as part of regular facilities' inspections or conducted separately); veterinary or IACUC observation of select procedures; observation of animals by animal care, veterinary, and IACUC staff and members; and external regulatory inspections and assessments. The IACUC, veterinary, animal care and compliance staff may all conduct PAM, which may also be used as an educational tool.

Disaster Planning and Emergency Preparedness

Animal facilities may be subjected to unexpected conditions that result in the catastrophic failure of critical systems or significant personnel absenteeism, or other unexpected events that severely compromise on-going animal care and well-being (ILAR 2010). Facilities must have a disaster plan. The plan should define the actions necessary to prevent animal pain, distress, and deaths due to loss of systems such as those controlling ventilation, cooling, heating, or provision of potable water. If possible the plan should describe how the facility will preserve animals necessary for critical research activities or that are irreplaceable. The geographic locale may provide guidance as to the probability of a particular type of disaster.

Disaster plans should be established in conjunction with the responsible investigator(s) taking into consideration both the priorities for triaging animal populations and institutional needs and resources. Animals that cannot be protected from the consequences of the disaster or relocated must be humanely euthanized. The disaster plan should identify essential personnel who should be trained in advance in its implementation. Efforts should be taken to assure personnel safety and provide access to essential personnel during or immediately following disasters. Such plans should be approved by the institution and be part of the overall institutional disaster response plan that is coordinated by the IO or another senior level administrator. Law enforcement and emergency personnel should be provided with a copy of the plan for comment and integration into broader, area-wide planning (Vogelweid 1998).

Chapter 2 References

Colby LA, Turner PV, Vasbinder MA. 2007. Training strategies for laboratory animal veterinarians: Challenges and opportunities. ILAR J 48:143-155.

Collins JG. 2008. Postapproval monitoring and the IACUC. ILAR J 49:388-392.

Conarello SL, Shepard MJ. 2007. Training strategies for research investigators and technicians. ILAR J 48:120-130.

Crawley JN. 1999. Behavioral phenotyping of transgenic and knockout mice: Experimental design and evaluation of general health, sensory functions, motor abilities, and specific behavioral tests. Brain Res 835:18-26.

Dale WE. 2008. Postapproval monitoring and the role of the compliance office. ILAR J 49:393-401.

Dennis MB. 1999. Institutional animal care and use committee review of genetic engineering. In: Gonder JC, Prentice ED, Russow L-M, eds. Genetic Engineering and Animal Welfare: Preparing for the 21st Century. Greenbelt MD: Scientists Center for Animal Welfare.

Dennis MB. 2000. Humane endpoints for genetically engineered animal models. ILAR J 41:94-98.

DHHS [Department of Health and Human Services]. 2007. Biosafety in Microbiological and Biomedical Laboratories, 5th ed. Chosewood LC, Wilson DE, eds. Washington: Government Printing Office.

FASS [Federation of Animal Science Societies]. 2010. Guide for the Care and Use of Agricultural Animals in Research and Teaching, 3rd ed. Champlain IL: FASS.

Fechter LD. 1995. Combined effects of noise and chemicals. Occup Med 10:609-621.

Foshay WR, Tinkey PT. 2007. Evaluating the effectiveness of training strategies: Performance goals and testing. ILAR J 48:156-162.

Frasier D, Talka J. 2005. Facility design considerations for select agent animal research. ILAR J 46:23-33.

Gonder JC. 2002. Regulatory compliance. In

OSHA. 1998d. Occupational Safety and Health Standards. Subpart I, Personal Protective Equipment, Respiratory Protection (29 CFR 1910.134). Washington: Department of Labor.

Paster EV, Villines KA, Hickman DL. 2009. Endpoints for mouse abdominal tumor models: Refinement of current criteria. Comp Med 59:234-241.

Perret-Gentil M, Sinanan M, Dennis MB Jr, Horgan S, Weyhrich J, Anderson D, Hudda K. 1999. Videoendoscopy: An effective and efficient way to perform multiple visceral biopsies in small animals. J Invest Surg 12:157-165.

Perret-Gentil MI, Sinanan MN, Dennis MB Jr, Anderson DM, Pasieka HB, Weyhrich JT, Birkebak TA. 2000. Videoendoscopic techniques for collection of multiple serial intra-abdominal biopsy specimens in HIV-negative and HIV-positive pigtail macaques (Macaca nemestrina). J Invest Surg 13:181-195.

PHS [Public Health Service]. 2002. Public Health Service Policy on Humane Care and Use of Laboratory Animals. Publication of the Department of Health and Human Services, National Institutes of Health, Office of Laboratory Animal Welfare. Available at http://grants.nih.gov/grants/olaw/references/phspol.htm; accessed January 14, 2010.

PL [Public Law] 104-191. 1996. Health Insurance Portability and Accountability Act (HIPAA) of 1996. Washington: Government Printing Office.

PL 107-56. 2001. The Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA PATRIOT) Act of 2001. Washington: Government Printing Office. October 26.

PL 107-188. 2002. Public Health Security and Bioterrorism Preparedness and Response Act of 2002. Washington: Government Printing Office. June 12.

Plante A, James ML. 2008. Program oversight enhancements (POE): The big PAM. ILAR J 49:419-425.

Prescott MJ, Buchanan-Smith HM. 2003. Training nonhuman primates using positive reinforcement techniques. J Appl Anim Welf Sci 6:157-161.

Pritt S, Duffee N. 2007. Training strategies for animal care technicians and veterinary technical staff. ILAR J 48:109-119.

Reeb-Whitaker CK, Harrison, DJ, Jones RB, Kacergis JB, Myers DD, Paigen B. 1999. Control strategies for aeroallergens in an animal facility. J Allergy Clin Immunol 103:139-146.

Reinhardt V. 1991. Training adult male rhesus monkeys to actively cooperate during in-homecage venipuncture. Anim Technol 42:11-17.

Reinhardt V. 1995. Restraint methods of laboratory non-human primates: A critical review. Anim Welf 4:221-238.

Richmond JY, Hill RH, Weyant RS, Nesby-O'Dell SL, Vinson PE. 2003. What's hot in animal biosafety? ILAR J 44:20-27.

Rowland NE. 2007. Food or fluid restriction in common laboratory animals: Balancing welfare considerations with scientific inquiry. Comp Med 57:149-160.

Sargent EV, Gallo F. 2003. Use of personal protective equipment for respiratory protection. ILAR J 44:52-56.

Sass N. 2000. Humane endpoints and acute toxicity testing. ILAR J 41:114-123.

Sauceda R, Schmidt MG. 2000. Refining macaque handling and restraint techniques. Lab Anim 29:47-49.

Schweitzer IB, Smith E, Harrison DJ, Myers DD, Eggleston PA, Stockwell JD, Paigen B, Smith AL. 2003. Reducing exposure to laboratory animal allergens. Comp Med 53:487-492.

Seward JP. 2001. Medical surveillance of allergy in laboratory animal handlers. ILAR J 42:47-54.

Silverman J, Sukow MA, Murthy S, eds. 2007. The IACUC Handbook, 2nd ed. Boca Raton FL: CRC Press.

Stokes WS. 2000. Reducing unrelieved pain and distress in laboratory animals using humane endpoints. ILAR J 41:59-61.

Stokes WS. 2002. Humane endpoints for laborato

Yeates JW, Main DCJ. 2009. Assesment of positive welfare: A review. Vet Rev 175:293-300.

Vogelweid CM. 1998. Developing emergency management plans for university laboratory animal programs and facilities. Contemp Top Lab Anim Sci 37:52-56.

Wallace J. 2000. Humane endpoints and cancer research. ILAR J 41:87-93.

Wolff MS, Garnett N, Potkay S, Wigglesworth C, Doyle D, Thornton, D. 2003. Frequently asked questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Lab Anim 32:33-36.

Wolfle TL, Bush RK. 2001. The science and prevasiveness of laboratory animal allergy. ILAR J 42:1-3.

Wood RA. 2001. Laboratory animal allergens. ILAR J 42:12-16.

CHAPTER 3. Environment, Housing, and Management

This chapter provides guidelines for th e environment, housing, and management

Terrestrial Animals

Terrestrial Environment

Microenvironment and Macroenvironment

The microenvironment of an animal is the physical environment immediately surrounding it; that is, the primary enclosure such as the cage, pen, or stall. It contains all the resources with which the animals directly contact and also provides the limits of the animals' immediate environment. The microenvironment is characterized by many factors, including illumination, noise, vibration, temperature, humidity, and gaseous and particulate composition of the air. The physical environment of the secondary enclosure, such as a room, a

Temperature and Humidity

Maintenance of body temperature within normal circadian variation is necessary for animal well-being and animals should be housed within temperature and humidity ranges appropriate for the species, to which they can adapt with minimal stress and physiologic alteration. The ambient temperature range in which thermoregulation occurs without the need to increase metabolic heat production is called thermoneutral zone (TNZ) and is bounded by the upper (UCT) and lower critical temperatures (L CT). To maintain body temperature under a given environmental temperat ure animals adjust physiologically (including metabolism) and behaviorally (including their activity level and resource use). For example, the thermoneutral zone of mice ranges between 26°C and 34°C (Gordon 1993). At lower temperatures, building nests and huddling for resting and sleeping allows them to thermoregulate by behaviorally controlling their microclimate. Although mice choose temperatures below their LCT of 26°C during activity periods, they strongly prefer temperatures above LCT for maintenance and resting beha

The dry-bulb temperatures listed in Table 3.1 are broad and generally

macroenvironment, e.g., static filter-top (isolator) cages. Some species may require conditions with high relative humidity (e.g., selected species of nonhuman primates, tropical reptiles, and amphibians; Olson and Palotay 1983). In mice, both abnormally high and low humidity may increase pre-weaning mortality (Clough 1982). In rats, low relative humidity, especially in combination with temperature extremes, may lead to ringtail, a condition involving ischemic necrosis of the tail and sometimes toes (Crippa et al. 2000; Njaa 1957; Totten 1958). For some species, elevated relative humidity may impact an animal's ability to cope with thermal extremes. Elevated microenvironmental relative humidity may also lead to high intra-cage ammonia concentrations in rodent isolator cages (Corning and Lipman 1991; Hasenau et al. 1993), which can be irritating to the nasal passages and alter some biological responses (Gordon et al. 1980; Manninen et al. 1998). In climates where it is difficult to provide a sufficient level of environmental relative humidity, animals should be closely monitored for negative effects such as excessively flaky skin in

in optimizing ventilation of micro- and macroenvironments (Hughes and Reynolds 1995).

Direct exposure of animals to air moving at high velocity (drafts) should be avoided as the speed of air to which animals are exposed affects the rate at which heat and moisture are removed from an animal. For example, air at 20°C moving at 60 linear feet per minute (18.3 m/min) has a cooling effect of approximately 7°C (Weihe 1971). Drafts can be particularly problematic for neonatal homeotherms, which may be hairless and have poorly developed mechanisms for thermoregulatory control, for mutants lacking fur, and for semi-aquatic amphibians that can desiccate.

Provision of 10-15 fresh-air changes per hour in animal housing rooms is an acceptable guideline to maintain macroenvironmental air quality by constant volume systems and may also ensure microenvironmental air quality. Although this range is effective in many animal-housing settings, it does not take into account the range of possible heat loads; the species, size, and number of animals involved; the type of primary enclosure and bedding utilized; the frequency of cage-changing; the room dimensions; or the efficiency of air distribution within the macroenvironment and between it and the microenvironment. In some situations, the use of such a broad guideline might overventilate a macroenvironment containing few animals, thereby wasting energy, or underventilate a microenvironment containing many animals, allowing heat, moisture, and pollutants to accumulate.

Modern heating, ventilation, and air conditioning (HVAC) systems, e.g., variable air volume (VAV) systems, allow ventilation rates to be set in accordance with heat load and other variables (see Chapter 5). These systems offer considerable advantages with respect to flexibility and energy conservation, but should always provide a minimum amount of air exchange, as recommended for general use laboratories (Bell 2008; DiBerardinis et al. 2008).

Individually ventilated cages and other types of specialized primary enclosures, that either directly ventilate the enclosure using filtered room air or are ventilated independently of the room, can effectively address animals' ventilation requirements without the need to increase macroenvironmental ventilation. However, cautions mentioned above regarding high velocity air should be considered (Baumans et al. 2002; Krohn et al. 2003). Nevertheless, the macroenvironment should be ventilated sufficiently to address heat loads, particulates, odors, and waste gases released from primary enclosures (Lipman 1993).

If ventilated primary enclosures contain adequate filtration to address contamination risks, air exhausted from the microenvironment may be returned to the room in which animals are housed, although it is generally preferable to exhaust these systems directly into the building's exhaust system to reduce heat load and macroenvironmental contamination.

Static isolation caging (without forced ventilation), such as that used in some types of rodent housing, restricts ventilation (Keller et al. 1989). To compensate, it might be necessary to adjust husbandry practices, including sanitation and cage change frequency; selection of contact bedding; placement of cages in a secondary enclosure; animal densities within cages; and/or decrease of macroenvironmental relative humidity to improve the microenvironment and heat dissipation.

The use of recycled air to ventilate animal rooms may save energy but entails risks. Because many animal pathogens can be airborne or travel on fomites (e.g., dust), exhaust air recycled into heating, ventilation, and air conditioning (HVAC) systems that serve multiple rooms presents a risk of cross contamination. Recycling air from non-animal use areas (e.g., some human occupancy areas and food, bedding, and supply storage areas) may require less intensive filtration or conditioning and pose less risk of infection. The risks in some situations, however, might be too great to consider recycling (e.g., in the case of nonhuman primates and biohazard areas). The exhaust air to be recycled should be filtered, at minimum, with 85- 95% ASHRAE efficient filters to remove airborne particles before it is recycled (NAFA 1996). Depending on the air source, composition and proportion of recycled air utilized (e.g., ammonia and other gases emitted from excrement in recirculating air from animal rooms), consideration should also be given to filtering volatile substances. In areas that require filtration to ensure personnel and/or animal safety (e.g., hazardous containment holding), filter efficiency, loading, and integrity should be assessed. The successful operation of any HVAC system requires regular preventive maintenance and evaluation, including measurement of its function at the level of the secondary enclosure. Such measurements should include supply- and exhaust-air volumes, fluctuation in temperature and relative humidity, air pressure differentials between spaces, as well as critical mechanical operating parameters.

Illumination

Light can affect the physiology, morphology, and behavior of various animals (Azar et al. 2008, Brainard et al. 1986; Erkert and Grober 1986; Newbold et al. 1991; Tucker et al. 1984). Potential photostressors include inappropriate

photoperiod, photointensity, and spectral quality of the light (Stoskopf 1983). Numerous factors can affect animals' needs for light and should be considered when an appropriate illumination level is being established for an animal holding room. These include light intensity and wavelength, duration of the animal's current and prior exposure to light; pigmentation; circadian rhythm; body temperature; hormonal status; age; species; sex; and stock or strain of animal (Brainard 1989; Duncan and O'Steen 1985; O'Steen 1980; Saltarelli and Coppola 1979; Semple-Rowland and Dawson 1987; Wax 1977). More recent studies in rodents and primates have shown the importance of intrinsically photosensitive retinal ganglion cells, distinct from rods and cones, for neuroendocrine, circadian and neurobehavioral regulation (Berson et al. 2002; Hanifin and Brainard 2007). These cells can respond to light wavelengths that may differ from other photoreceptors and may influence the type of lighting, light intensity and wavelength selected for certain types of research.

In general, lighting should be diffused throughout an animal holding area and provide sufficient illumination for the animals' well-being while permitting good housekeeping practices, adequate animal inspection including the bottom-most cages in racks, and safe working conditions for personnel. Light in animal holding rooms should provide for adequate vision and for neuroendocrine regulation of diurnal and circadian cycles (Brainard 1989).

Photoperiod is a critical regulator of reproductive behavior in many animal species (Brainard et al. 1986; Cherry 1987), therefore inadvertent light

light intensity under which it was raised has been reported to be near the threshold of retinal damage in some individual albino rats according to histologic, morphometric, and electrophysiologic evidence (Semple-Rowland and Dawson 1987). Some guidelines recommend a light intensity as low as 40 lux at the position of the animal in midcage (NASA 1988). Rats and mice generally prefer cages with low light intensity (Blom et al. 1993), and albino rats prefer areas with a light intensity of less than 25 lux (Schlingmann et al. 1993a). Young mice prefer much lower illumination than adults (Wax 1977). Thus, for animals that have been shown to be susceptible to phototoxic retinopathy, light should be between 130 and 325 lux in the room at cage level.

Light intensity decreases with the square of the distance from its source. Therefore, the location of a cage on a rack impacts the intensity of light to which animals contained within are exposed. Light intensity may differ by as much as 80-fold in transparent cages from the top to the bottom of a rack, while differences up to 20-fold have been recorded within a cage (Schlingman et al. 1993a, b). Management practices, such as rotating cage position relative to the light source (Greenman et al. 1982) or providing animals with ways to control their own light exposure by behavioral means (e.g., nesting or bedding material adequate for tunneling), can be used to reduce inappropriate light stimulation. Variable-intensity lights are often used to accommodate the needs of research protocols, certain animal species, and energy conservation. However, such a system should also provide for the observation and care of the animals. Caution should be exercised since increasing daytime room illumination for maintenance purposes has been shown to change photoreceptor physiology and can alter circadian regulation (NRC 1996; Remé et al. 1991; Terman et al. 1991).

Noise and Vibration

Noise produced by animals and animal-care activities is inherent in the operation of an animal facility (Pfaff and Stecker 1976) and noise control should be considered in facility design and operation (Pekrul 1991). Assessment of the potential effects of noise on an animal warrants consideration of the intensity, frequency, rapidity of onset, duration, and vibration potential of the sound and the hearing range, noise-exposure history, and sound-effect susceptibility of the species, stock, or strain. Similarly, occupational exposure to animal or animal care practices generating noise may also be of concern for personnel and if of sufficient intensity may warrant hearing protection.

Separation of human and animal areas minimizes disturbances to both human and animal occupants of the facility. Noisy animals such as dogs, swine, goats, nonhuman primates, and some birds (e.g., zebra finches), should be

housed away from quieter animals, such as rodents, rabbits, and cats. Environments should be designed to accommodate animals that make noise, rather than resorting to methods of noise reduction. Exposure to sound louder than 85 dB can have both auditory

Terrestrial Housing

Microenvironment (Primary Enclosure)

All animals should be housed under conditions that provide sufficient space as well as supplementary structures and resources required to meet physical, physiologic, and behavioral needs. Environments that fail to meet the animals' needs may result in abnormal brain development, physiologic dysfunction and behavioral disorders (Garner 2005; van Praag et al. 2000; Würbel 2001) that potentially compromise both animal well-being and scientific validity. The primary enclosure or space may need to be enriched to prevent such effects and improve animal well-being (see also section on Environmental Enrichment, page 107).

An appropriate housing space or enclosure should also account for the animals' social needs. Social animals should be housed in stable pairs or groups of compatible individuals unless they must be housed alone for experimental reasons or because of social incompatibility (see also section on Behavioral and Social Management, page 126). Structural adjustments are frequently required for social housing (e.g., perches, visual barriers, refuges), and important resources (e.g., food, water, and shelter) should be provided in such a way that they cannot be monopolized by dominant animals (see also section on Environmental Enrichment, page 107).

The primary enclosure should provide a secure environment that does not permit animal escape and should be made of durable materials that resist corrosion, withstand the rigors of cleaning and regular handling, and are not detrimental to the health and research use of the animals. The enclosure should be designed and manufactured to prevent accidental entrapment of animals or their appendages and should be free of sharp edges or projections that could cause injury to the animals or personnel. It should have smooth, impervious surfaces with minimal ledges, angles, corners, and overlapping surfaces so that accumulation of dirt, debris, and moisture is minimized and cleaning and disinfecting are not impaired. All enclosures should be kept in good repair to prevent escape of or injury to animals, promote physical comfort, and facilitate sanitation and servicing. Rusting or oxidized equipment that threaten the health or safety of animals need to be repaired or replaced. Less durable materials, such as wood, may be appropriate in select situations, e.g., outdoor corrals, perches, climbing structures, resting areas, and perimeter fences for primary enclosures. Wooden items may need to be replaced periodically because of damage or difficulties with sanitation. Painting or sealing wood surfaces with non-toxic materials may improve durability in many instances.

Flooring should be solid, perforated or sl atted with a slip-resistant surface. In the case of perforated or slatted floors, the holes and slats should have smooth edges. Their size and spacing need tobe commensurate with the size of the housed animal to minimize injury and the development of foot lesions. If wire-mesh flooring is used, a solid resting area

1994). Novelty of enrichment through rotation or replacement of items should also be a consideration; however, changing the animal environment too frequently may be stressful.

Enrichment programs should be reviewed by the IACUC, researchers and veterinarian on a regular basis to ensure that they are beneficial to animal well-being and consistent with the goals of animal use. They should be updated as needed to ensure that they reflect current knowledge. Personnel responsible for animal care and husbandry should receive training in the behavioral biology of the species they work with to appropriately monitor the effects of enrichment, as well as identify the development of adverse or abnormal behaviors.

Like other environmental factors (such as space, light, noise, temperature, and animal care procedures), enrichment affects animal phenotype and may impact the experimental outcome. Thus, it should be considered an independent variable and appropriately controlled.

Some scientists have raised concerns that environmental enrichment may compromise experimental standardization by introducing environmental variability, adding not only diversity to the animals' behavioral repertoire but also variation to the animals' responses to experimental treatments (e.g., Bayne 2005; Eskola et al. 1999; Gärtner 1999; Tsai et al. 2003). A systematic study in mice did not find evidence to support this viewpoint (Wolfer et al. 2004), indicating that housing conditions can be enriched without compromising the precision or reproducibility of experimental results. However, further research in other species may be needed to confirm this conclusion. Moreover, it has been

such as an indoor portion of a run. Shelters should be large enough to accommodate all animals housed in the enclosure, should be accessible at all times to all animals, have sufficient ventilation, and be designed to prevent build-up of waste materials and excessive moisture. Houses, dens, boxes, shelves, perches, and other furnishings should be constructed in a manner and made of materials that allow cleaning or replacement in accord with generally accepted husbandry practices.

Floors or ground-level surfaces of outdoor housing facilities can be covered with dirt, absorbent bedding, sand, gravel, grass, or similar material that can be removed or replaced when needed to ensure appropriate sanitation. Excessive build-up of animal waste and stagnant water should be avoided by, for example, using contoured or drained surfaces. Other surfaces should be able to withstand the elements and be easily maintained.

Successful management of outdoor housing relies on stable social groups of compatible animals; sufficient and species-adequate feeding and resting places; an adequate acclimation period in advance of seasonal changes when animals are first introduced to outdoor housing; training of animals to cooperate with veterinary and investigative personnel; (e.g., to enter chutes or cages for restraint or transport); and adequate security via a perimeter fence or other means.

Naturalistic Environments

Areas such as pastures and islands afford opportunities to provide a suitable environment for maintaining or producing animals and for some types of research. Their use results in the loss of some control over nutrition, health care and surveillance, and pedigree management. These limitations should be balanced against the benefits of having the animals live in more natural conditions. Animals should be added to, removed from, and returned to social groups in this setting with appropriate consideration of the effects on the individual animals and on the group. Adequate supplies of food, fresh water, and natural or constructed shelter should be ensured.

Space

General Considerations for all Animals

An animal's space needs are complex, and consideration of only the animal's body weight or surface area may be inadequate. Important considerations for determining space needs include the age and sex of the animals; the number of

enrichment devices (e.g., novel objects, toys, foraging devices) should not be considered part of the floor space.

The space recommendations presented here are based on professional judgment and experience. They should be considered the minimum for animals housed under conditions commonly found in laboratory animal housing facilities. Adjustments to the amount and arrangement of space recommended in the following tables should be reviewed and approved by the IACUC. They should be based on performance indices related to animal well-being and research quality as described in the preceding paragraphs with due consideration of the AWRs and PHS Policy and other applicable regulations and standards.

It is not within the scope of the Guide to discuss the housing requirements of all species used in research. For species not specifically indicated, advice should be sought from the scientific literature and from species-relevant experts.

Laboratory Rodents

Table 3.2 lists recommended minimum space for commonly used laboratory rodents housed in groups. If they are housed singly or in small groups, or exceed the weights in the table more space per animal may be required, while larger groups may be housed at slightly higher densities.

Space needs and the effects of social housing, group size and density

TABLE 3.2 Recommended Minimum Space for Commonly Used Laboratory Rodents Housed in Groups

Animals	Weight (g)	Floor Area/Animal [a]		Height [b]		Comments
		in^2	cm^2	in	cm	
Mice in Groups[c]	<10					

[d] Other considerations may include culling of litters or separation of litters from the breeding group, as well as other methods of more intensive management of available space to allow for the safety and well-being of the breeding group. Sufficient space should be allocated for mothers with litters to allow the pups to develop to weaning without detrimental effects to the mother or the litter.

Other Common Laboratory Animals

Tables 3.3 and 3.4 list recommended minimum space for other common laboratory animals and for avian species. These allocations are based, in general, on the needs of pair- or group-housed animals. Space allocations should be re-evaluated to provide for enrichment or to accommodate animals that exceed the weights in the tables, and should be based on species characteristics, behavior, compatibility of the animals, number of animals, and goals of the housing situation (Held et al. 1995; Lupo et al. 2000; Raje 1997; Turner et al. 1997). Singly housed animals may require more space per animal than that recommended for group-housed animals, while larger groups may be housed at slightly higher densities. For cats, dogs and some rabbits, housing enclosures that allow greater freedom of movement and less restricted vertical space are preferred (e.g., kennels, runs, or pens instead of cages). Dogs and cats, especially when housed individually or in smaller enclosures (Bayne 2002), should be allowed to exercise and provided with positive human interaction. Species-specific plans for housing and management should be developed. Such plans should also include strategies for environmental enrichment.

TABLE 3.3 Recommended Minimum Space for Rabbits, Cats and Dogs Housed in Pairs or Groups

Animals	Weight Kg[a]	Floor Area/Animal[b] ft^2	m^2	Height[c] in	cm	Comments
Rabbits	<2	1.5	0.14	16	40.5	Larger rabbits may require more cage height to allow animals to sit up.
	Up to 4	3.0	0.28	16	40.5	
	Up to 5.4	4.0	0.37	16	40.5	
	>5.4[c]	≥5.0	≥0.46	16	40.5	
Cats	≤4	3.0	0.28	24	60.8	For cats vertical space with perches is preferred and may require additional cage height.
	>4[d]	≥4.0	≥0.37	24	60.8	
Dogs[e]	<15	8.0	0.74		-[f]	Cage height should be sufficient for the animals to comfortably stand erect with their feet on the floor.
	Up to 30	12.0	1.2		-[f]	
	>30[d]	≥24.0	≥2.4		-[f]	

[a] To convert kilograms to pounds, multiply by 2.2.

[b] Singly housed animals may require more space per animal than recommended for pair- or group-housed animals.

[c] From cage floor to cage top.

[d] Larger animals might require more space to meet performance standards (see text).

[e]

If it is necessary to house animals singly (for example, when justified for experimental purposes; for provision of veterinary care; or for incompatible animals), it should be for the shortest duration possible. If single animals are housed in small enclosures an opportunity for periodic release into larger enclosures with additional enrichment items should be considered, particularly for animals housed singly for extended periods of time. Singly housed animals may require more space per animal than recommended for pair- or group-housed housed animals, while larger groups may be housed at slightly higher densities. Because of the many physical and behavioral characteristics of nonhuman primate species and the many factors to consider when using these animals in a biomedical research setting, species-specific plans for housing and management should be developed. Such plans should include strategies for environmental and psychological enrichment.

TABLE 3.5 Reccomended Minimum Space for Nonhuman Primates Housed in Pairs or Groups

Animals	Weight Kg[a]	Floor Area/Animal[b] ft^2	m^2	Height[c] in	cm	Comments

Animals/Enclosure	Weight, kg [a]	Floor Area/Animal [b]	
		ft^2	m^2
	>50[c]	≥15.0	1.35
Swine			
1	<15	8.0	0.72
	Up to 25	12.0	1.08
	Up to 50	15.0	1.35
	Up to 100	24.0	2.16
	Up to 200	48.0	4.32
	>200[c]	≥60.0	5.4
2-5	<25	6.0	0.54
	Up to 50	10.0	0.9
	Up to 100	20.0	1.8
	Up to 200	40.0	3.6
	>200[c]	≥52.0	4.68
>5	<25	6.0	0.54
	Up to 50	9.0	0.81
	Up to 100	18.0	1.62
	Up to 200	36.0	3.24
	>200[c]	≥48.0	4.32
Cattle			
1	<75	24.0	2.16
	Up to 200	48.0	4.32
	Up to 350	72.0	6.48
	Up to 500	96.0	8.64
	Up to 650	124.0	11.16
	>650[c]	≥144.0	12.96
2-5	<75	20.0	1.8
	Up to 200	40.0	3.6
	Up to 350	60.0	5.4
	Up to 500	80.0	7.2
	Up to 650	105.0	9.45
	>650[c]	≥120.0	10.8
>5	<75	18.0	1.62
	Up to 200	36.0	3.24
	Up to 350	54.0	4.86
	Up to 500	72.0	6.48
	Up to 650	93.0	8.37
	>650[c]	≥108.0	9.72
Horses	--	144.0	12.96
Ponies			
1-4	--	72.0	6.48
>4/Pen	≤200	60.0	5.4
	>200[c]	≥72.0	6.48

[a] To convert kilograms to pounds, multiply by 2.2.

Terrestrial Management

Behavioral and Social Management

Activity

Animal activity typically implies motor activity but also includes cognitive activity and social interaction. Animals maintained in a laboratory environment are generally restricted in their activities compared to free-ranging animals. The animals' natural behavior and activity profile should be considered during evaluation of suitable housing or behavioral assessment. Forced activity for reasons other than attempts to meet therapeutic or approved protocol objectives should be avoided. High levels of repetitive, unvarying behavior (stereotypies, compulsive behaviors) may reflect disruptions of normal behavioral control mechanisms due to housing conditions or management practices (Garner 2005; NRC 1998a).

Dogs, cats, rabbits, and many other animals benefit from positive human interaction (Augustsson et al. 2002; Bayne et al. 1993; McCune 1997; Poole 1998; Rennie and Buchanan-Smith 2006; Rollin 1990). Dogs can be given additional opportunities for activity by being walked on a leash, having access to a run, or being moved into areas for social contact, play, or exploration (Wolff and Rupert 1991). Loafing areas, exercise lots, and pastures are suitable for large farm animals, such as sheep, horses, and cattle.

Social Environment

Appropriate social interactions among members of the same species (conspecifics) are essential to normal development and well-being (Bayne et al. 1995; Hall 1998; Novak et al. 2006). When selecting a suitable social environment, attention should be given to whether the animals are naturally territorial or communal and whether they should be housed singly, in pairs, or in groups. An understanding of species-typical natural social behavior (e.g., natural social composition, population density, ability to disperse, familiarity and social ranking) is key to successful social housing.

Not all members of a social species are necessarily socially compatible. Social housing of incompatible animals can induce chronic stress, injury and even death. In some species, social incompatibility may be sex biased; for example, male mice are generally more prone to aggression than female mice, and female hamsters are generally more aggressive than male hamsters. These risks of social incompatibility are greatly reduced if the animals to be grouped are raised together from a young age, if group composition remains stable, and if

design of the animals' enclosure and environmental enrichment facilitate the avoidance of social conflicts. Social stability should be carefully monitored and in cases of severe or prolonged aggression, incompatible individuals need to be separated.

For some species, developing a stable social hierarchy will entail agonistic interactions between pair or group members, particularly for animals introduced as adults. Animals may have to be introduced to each other over a period of time and they should be monitored closely during this introductory period and thereafter to ensure compatibility.

Single housing of social species should be the exception and should be justified based on experimental requirements or veterinary-related concerns regarding animal well-being. In these cases, single housing of social animals should be limited to the minimum period necessary, and where possible, visual, auditory, olfactory and tactile contact with compatible conspecifics should be provided. In the absence of other animals, enrichment should be offered such as positive interaction with the animal care staff and additional enrichment items or addition of a companion animal in the room or housing area. The need for single housing should be reviewed on a regular basis by the IACUC and veterinarian.

Procedural Habituation and Training of Animals

Habituating animals to routine husbandry or experimental procedures should be encouraged, whenever possible, as it may assist the animal to better cope with a captive environment by reducing stress associated with novel procedures or people. The type and duration of habituation needed will be determined by the complexity of the procedure being performed. In most cases, principles of operant conditioning may be employed during training sessions, using progressive behavioral shaping, to induce voluntary cooperation with procedures (Bloomsmith et al. 1998; Laule et al. 2003; NRC 2006a; Reinhardt 1997).

Husbandry

Food

Animals should be fed palatable, uncontaminated diets that meet their nutritional and behavioral needs at least daily, or according to their particular requirements, unless the protocol in which they are being used requires otherwise. Subcommittees of the National Research Council Committee on Animal Nutrition have prepared comprehensive reports of the nutrient

requirements of laboratory animals (NRC 1977, 1982, 1993, 1994, 1995a, 1998b, 2000, 2001, 2003a, 2006b, 2006c, 2007). These publications consider issues of quality assurance, freedom from chemical or microbial contaminants and presence of natural toxicants in feedstuffs, bioavailability of nutrients in feeds, and palatability. There are three types of diets classified by the degree of refinement of their ingredients. Natural-ingredient diets are formulated with

stored off the floor on pallets, racks, or carts in a manner that facilitates sanitation. Opened bags of food should be stored in vermin-proof containers to minimize contamination and to avoid potential spread of pathogens. Exposure to elevated storage room temperatures, extremes in relative humidity, unsanitary conditions, insects and other vermin hastens food deterioration. Storage of natural ingredient diets at less than 21°C (70° F) and below 50% relative humidity is recommended. Precautions should be taken if perishable items—such as meats, fruits, and vegetables and some specialty diets (for example, select medicated or high fat diets)—are fed, because storage conditions may lead to variation in food quality.

Most natural-ingredient, dry laboratory-animal diets stored properly can be used up to 6 months after manufacture. Non-stabilized vitamin C in manufactured feeds generally has a shelf-life of only 3 months, but commonly employed stabilized forms can extend the shelf-life of feed. Refrigeration preserves nutritional quality and lengthens shelf-life, but food-storage time should be reduced to the lowest practical period and the manufacturers' recommendations should be considered. Purified and chemically defined diets are often less stable than natural-ingredient diets, and their shelf-life is usually less than 6 months (Fullerton et al. 1982); these diets should be stored at 4°C (39°F) or lower.

Irradiated and fortified autoclavable diets are commercially available and are commonly used for axenic, microbiologically-defined rodents, and immunodeficient animals (NRC 1996). The use of commercially fortified autoclavable diets ensures that labile vitamin content is not compromised by steam and/or heat (Caulfield et al. 2008; NRC 1996). Consideration should also be given to the impact of autoclaving on pellet hardness, which may affect palatability, as well as chemical alteration of ingredients (Thigpen et al. 2004; Twaddle et al. 2004). The date of sterilization should be recorded and the diet used quickly.

Feeders should be designed and placed to allow easy access to food and minimize contamination with urine and feces, and should be maintained in good condition. When animals are housed in groups, there should be enough space and enough feeding points to minimize competition for food and ensure access to food for all animals, especially if feed is restricted as part of the protocol or management routine. Food-storage containers should not be transferred between areas that pose different risks of contamination without appropriate treatment, and they should be cleaned and sanitized regularly.

Management of caloric intake is an accepted practice for long-term housing of some species, such as some rodents, rabbits and nonhuman primates, and as an adjunct to some clinical, experimental and surgical procedures (for

more discussion on food and fluid regu lation as an experimental tool see Chapter 2 and NRC 2003b). Benefits acured by moderate caloric restriction in

Softwood beddings have been used, but the use of untreated softwood shavings and chips is contraindicated for some protocols because they can affect metabolism (Vesell 1967; Vessell et al. 1973, 1976). Cedar shavings are not recommended, because they emit aromatic hydrocarbons that induce hepatic microsomal enzymes and cytotoxicity (Torronen et al. 1989; Weichbrod et al. 1986, 1988). Prior treatment with high heat (kiln-drying or autoclaving) may, depending on the material used and the concentration of aromatic hydrocarbon constituents present, reduce the concentration of volatile organic compounds; however, the amounts remaining may be sufficient to affect specific protocols (Cunliffe-Beamer et al. 1981; Nevalainen and Vartiainen 1996).

Manufacturing, monitoring, and storage methods used by vendors should be considered when purchasing bedding products. Bedding may be contaminated with toxins and other substances, bacteria, fungi, and vermin. Bedding should be transported and stored off the floor on pallets, racks, or carts in a fashion consistent with maintenance of quality and avoidance of contamination. Bags should be stored sufficiently away from walls to facilitate cleaning. During autoclaving, bedding can absorb moisture and as a result lose absorbency and support the growth of microorganisms. Therefore, appropriate drying times and storage conditions should be used or alternatively, gamma-irradiated materials utilized if sterile bedding is indicated.

Bedding should be used in amounts sufficient to keep animals dry between cage changes, and, in the case of small laboratory animals, care should be taken to keep the bedding from coming into contact with the sipper tubes, because such contact could cause leakage of water into the cage.

Sanitation

Sanitation—the maintenance of environmental conditions conducive to health and well-being—involves bedding change (as appropriate), cleaning, and disinfection. Cleaning removes excessive amounts of excrement, dirt and debris, and disinfection reduces or eliminates unacceptable concentrations of microorganisms.

The frequency and intensity of cleaning and disinfection should depend on what is needed to provide a healthy environment for an animal. Methods and frequencies of sanitation will vary with many factors, including the normal physiologic and behavioral characteristics of the animals; the type, physical characteristics, and size of the enclosure; the type, number, size, age, and reproductive status of the animals; the use and type of bedding materials;

caging and husbandry practices used, including the use of regularly changed contact or noncontact bedding, regular flushing of suspended catch pans, and the use of wire-bottom or perforated-bottom cages. In general, enclosures and accessories, such as tops, should be sanitized at least once every 2 weeks. Solid-bottom caging, bottles, and sipper tubes usually require sanitation at least once a week. Some types of cages and housing systems might require less-frequent cleaning or disinfection; these might include large cages with very low animal density and frequent bedding changes; cages that house animals in gnotobiotic conditions with frequent bedding changes; individually ventilated cages; and cages used for special situations. Other circumstances, such as filter-topped cages without forced air ventilation, animals that urinate excessively (e.g., diabetic or renal patients), or densely populated enclosures, might require more frequent sanitation.

The increased use of individually ventilated cages (IVCs) for rodents has led to investigations regarding the maintenance of a suitable microenvironment with extended cage sanitation intervals and/or increased housing densities

rooms) should be regularly cleaned and disinfected as appropriate to the circumstances and at a frequency based on the use of the area and the nature of likely contamination. Vaporized hydrogen peroxide or chlorine dioxide are effective compounds for room decontamination, particularly following completion of studies with highly infectious agents (Krause et al. 2001) or contamination with adventitious microbial agents.

Cleaning implements should be constructed of materials that resist corrosion and withstand regular sanitation. They should be assigned to specific areas and should not be transported between areas with different risks of contamination without prior disinfection. Worn items should be replaced regularly. The implements should be stored in a neat, organized fashion that facilitates drying and minimizes contamination or harborage of vermin.

Assessing the Effectiveness of Sanitation

Monitoring of sanitation practices should fit the process and materials being cleaned and may include visual inspection and microbiological and water temperature monitoring (Compton et al. 2004 a, b; Ednie et al. 1998; Parker et al. 2003). The intensity of animal odors, particularly that of ammonia, should not be used as the sole means of assessing the effectiveness of the sanitation program. A decision to alter the frequency of cage-bedding changes or cage-washing should be based on such factors as ammonia concentration; bedding condition; appearance of the cage and animals; and the number and size of animals housed in the cage.

Mechanical washer function should be evaluated regularly and include examination of mechanical components such as spray arms and moving headers as well as spray nozzles to ensure they are functioning appropriately. If sanitation is temperature dependent, the use of temperature sensing devices (e.g., thermometers, probes, or temperature sensitive indicator strips), is recommended to ensure that the equipment being sanitized is exposed to the desired conditions.

Whether the sanitation process is automated or manual, regular evaluation of sanitation effectiveness is recommended. This can be performed by evaluating processed materials by microbiologic culture or the use of soil detection systems (e.g., ATP bioluminescence) and/or by confirming the removal of artificial soil applied to equipment surfaces before washing.

Pest Control

Programs designed to prevent, control, or eliminate the presence of or infestation by pests, are essential in an animal environment. A regularly scheduled and documented program of control and monitoring should be implemented. The ideal program prevents the entry of vermin into and eliminates harborage within the facility (Anadon et al. 2009; Easterbrook et al. 2008). For animals in outdoor facilities, consideration should also be given to eliminating or minimizing the potential risk associated with pests and predators. Pesticides can induce toxic effects on research animals and interfere with experimental procedures

Population Management

Identification

Animal records are useful and variable, ranging from limited information on identification cards to detailed computerized records for individual animals (Field et al. 2007). Means of animal identification include room, rack, pen, stall, and cage cards with written or bar-coded or radio frequency identification (RFID) information. Identification cards should include the source of the animal, the strain or stock, names and contact information for the responsible investigators, pertinent dates, and protocol number, when applicable. Where applicable, genotype information should be included in the identification, and consistent, unambiguous abbreviations should be used where the full genotype nomenclature (see below) is too lengthy.

Further, the animals may wear collars, bands, plates, or tabs; be marked by colored stains; ear notches/punches and tags; tattoos; subcutaneous transponders; and freeze brands. As a method of identification of small rodents, toe-clipping should be used only when no other individual identification method is feasible. It may be the preferred method for neonatal mice up to 7 days of age as it appears to have few adverse effects on behavior and well-being at this age (Castelhano-Carlos et al. 2010; Schaefer et al. 2010), especially if toe-clipping and genotyping can be combined. Under all circumstances aseptic practices should be followed. Use of anesthesia or analgesia should be commensurate with the age of the animals (Hankenson et al. 2008).

on experimental use, and necropsy findings where applicable. Basic demographic information and clinical hist ories enhance the value of individual animals for both breeding and research and should be readily accessible to investigators, veterinary staff, and animal-care staff.

Cryopreservation of fertilized embryos, ova, ovaries, or spermatozoa should also be considered as a safeguard against alterations in transgenes over time or accidental loss of GMA lines (Conner 2002; Liu 2009). When animals with multiple genetic alterations are required, this often involves crossing different GMA lines and can lead to the production of offspring with genotypes that are not of interest to the researcher, either as experimental or control animals as well as unexpected phenotypes. Carefully designed breeding strategies and accurate genotype assessment can help to minimize the generation of animals with unwanted genotypes (Linder 2003). Newly generated genotypes should be carefully monitored and new phenotypes that negatively impact well-being should be reported to the IACUC and managed in a manner to ensure the animals' health and well being.

Accurate recording, with standardized nomenclature h si

Aquatic Environment

Microenvironment and Macroenvironment

As with terrestrial systems, the microenvironment of an animal is the physical environment immediately surrounding it; that is, the primary enclosure such as the tank, raceway or pond. It contains all the resources with which the animals are in direct contact and also provides the limits of the animals' immediate environment. The microenvironment is characterized by many factors, including

The specific parameters and frequency

advanced containing biological filters (biofilters) that promote conversion of ammonia to nitrite and nitrate via nitrifying bacteria, protein skimmers (foam fractionators) and particulate filters to remove undissolved and dissolved proteins and particulate matter, carbon filters to remove dissolved chemicals, and ultraviolet or ozone units to disi nfect the water. The systems generally contain components to aerate and degas the water to prevent gas over-saturation, heat or cool the water, and automated dosing systems to maintain appropriate pH and conductivity. Not all elements are found on all systems and some components may accomplish multiple funct ions. Re-circulating systems may be designed so that multiple individual ta nks are supplied with treated water from a single source, as is the case with "rack" systems utilized for zebrafish (Danio rerio) and Xenopus laevis and tropicalis, as examples (Fisher 2000; Koerber 2009; Schultz 2003).

The development and maintenance of the biofilter is critical for limiting ammonia and nitrite accumulation in re-cir culating systems. The biofilter must be of sufficient size (i.e., contain a sufficient quantity of bacteria) to be capable of processing the bioload (level of nitrog enous waste) entering the system. The microorganisms supported by the biofilter require certain water quality parameters. Alterations in the aquatic environment, such as rapid changes in salinity, temperature, and pH, as well as the addition of chemicals or anti-microbials, may significantly impact th e microbial ecology of the system, and therefore water quality and animal well-being. If damaged, biofilter recovery may take weeks (Fisher 2000). Changes in water quality parameters (such as pH, ammonia, and nitrite) may negatively impact animal health and the efficiency of the biofilter, therefore species sensitive to change in water quality outside of a narrow range require more frequent monitoring.

Continuous or timed flow-through systems can be utilized where suitable water is available to support the species to be housed (e.g., aquaculture facilities). These systems may utilize extremely large volumes of water, as water is not reused. The water may be used "as is" or processed before use, for example by removing sediments, excessive dissolved gases, chlorine or chloramines, and by disinfecting with UV or ozone (Fisher 2000; Overstreet 2000). Static systems vary in size from small tanks to large in-g round ponds. These systems may utilize mechanical devices to move and aerate water.

Temperature, Humidity and Ventilation

The general concepts discussed in the Terrestrial Animals section also apply to the aquatic setting. The majority of aquatic or semi aquatic species (fish, amphibians and reptiles) used in research are poikilotherms. Poikilotherms

depend, for the most part, on the temperature of their environment to sustain physiologic processes, such as metabolism, reproduction, and feeding behavior (Browne and Edwards 2003a; Fraile 1989; Maniero 1997; Pough 1991). Temperature requirements are based on the natural history of the species and can vary across life stage (Green 2002; Pough 1991; Schultz 2003). Water temperature may be controlled at its source, within the life support system, or by controlling the macroenvironment. Some semi-open systems depend on source water temperature and thus enclosure water temperature will vary with that of the source water (e.g., raceways by a river).

The volume of water contained within a room can impact room temperature, temperature stability and relative humidity. Likewise the thermal load produced by chiller/heater systems can affect the stability of the macroenvironmental temperature. Air handling systems need to be designed to compensate for these thermal and moisture loads. Macroenvironmental relative humidity levels are generally defined by safety issues and staff comfort, since room humidity is not critical for aquatic species; however, excessive moisture may result in condensation on walls, ceilings, and tank lids, which may support microbial growth and serve as a source of contamination or create a conducive environment for metal corrosion. In a dry environment (e.g., indoor heating during cold weather or outdoor housing in some climates/seasons), evaporation rates may be increased, potentially requiring the addition of large quantities of water to the system and monitoring for increases in salinity/conductivity, contaminants or other water quality aberrations. Semi-aquatic species (e.g., some amphibians and reptiles) may need elevated microenvironmental humidity (in excess of 50%-70% relative humidity), which may require maintaining elevated macroenvironmental humidity levels (Pough 1991; St. Claire 2005).

Room air exchange rates are typically governed by thermal and moisture loads. For fish and some aquatic amphibians, the microenvironmental air quality may impact water quality (i.e., gas exchange), however, appropriate life support system design may reduce its importance. Air borne particulates and compounds (e.g., volatile organic compounds and ammonia) may dissolve in tank water and impact animal health (Koerber 2009). As the aerosolization of water can lead to spreading of aquatic animal pathogens (e.g., protozoa, bacteria) within or throughout an aquatic animal facility, this process should be minimized as much as feasibly possible (Roberts-Thomson et al. 2006; Wooster and Bowser 2007; Yanong 2003)

- Allow access to adequate food and removal of food waste.
- Restrict escape or accidental entrapment of animals or their appendages.
- Are free of sharp edges and/or projections that could cause injury.
- Allow for observation of the animals with minimal disturbance.
- Are constructed of non-toxic materials that do not leach toxicants or chemicals into the aquatic environment
- Do not present electrical hazards directly or indirectly

Environmental Enrichment and Social Housing

Environmental enrichment strategies for many aquatic species are not well established. The implications of a barren versus an enriched environment on well-being, general research, growth and development are unknown or poorly defined. This also applies to individual vs. group (social) housing for many species. When utilized, enrichment should elicit species appropriate behaviors and be evaluated for safety and utility.

Generally, schooling fish species are housed with conspecifics, and many amphibians, especially anuran speciesmay be group-housed. Aggression in aquatic animals does occur (van de Nieuwegiessen et al. 2008; Speedie and Gerlai 2007) and, as for terrestrial animals, appropriate monitoring and intervention may be necessary (Matthews 2002; Torreilles 2007). Some species need appropriate substrate (e.g., gravel) to reproduce or need substrate variety to express basic behaviors and maintain health (Overstreet 2000). Improved breeding success in enriched environments has been reported but further research in this area is needed (Carfagnini 2009). For many species, visual barriers, hides and shading are appropriate as, for example, for Xenopus laevis (Alworth 2009; Torreilles 2007). Most semi-aquatic reptiles spend some time on land (e.g., basking, feeding, digesting, and ovipositing) and terrestrial areas should be provided as appropriate for the species.

Sheltered, Outdoor, and Naturalistic Housing

Animals utilized in aquaculture are often housed in situations that mimic agricultural rearing and may be in outdoor and/or sheltered raceways, ponds, or pens with high population densities. In these settings, where natural predation and mortalities occur, it may be appropriate to measure animal “numbers” by utilizing standard aquaculture techniques such as final production biomass (Borski 2003).

Space

Space recommendations and housing density varies extensively with the species, age/size of the species, life support system, and type of research (Browne et al.

Husbandry

Food

The general principles relating to feeding of terrestrial animals are applicable to aquatic animals. Food should be stored in a type-appropriate manner to preserve nutritional content, minimize contamination and prevent entry of pests.

Pest Control

Terrestrial animal pest control principl

animals are maintained utilizing group (vs. individual) identification, detailed animal records still need to be maintained. General animal information that may routinely be captured, particularly in biomedical research with fish, includes: species; genetic information (parental stock identification, genetic composition); stock source; stock numbers in system; tank identification; system life support information; breeding; deaths; illnesses; animal transfers within and out of the facility; and fertilization/hatching information (ibid; Matthews 2002). Feeding records should also be maintained for aquatic animals (e.g., food offered, acceptance) as well as an accurate tracking of non-expired food supplies to ensure sustainance of nutritional profile. Records should also be maintained for any live cultures (e.g., hatch rates and information to ensure suppliers' recommendations are being met; ibid).

Records of water quality testing for system and source water and maintenance activities of the life support system components are important in tracking and maintaining water quality. The exact water quality parameters tested and testing frequency should be clearly established and will vary with such factors as the type of life support system, animals, and research as discussed in the Water Quality section (page 160). Detailed tracking of animal numbers in aquatic systems is often possible if accurate records of transfers, breeding and mortalities are maintained (ibid). In some cases where animals are housed in large groups (e.g., some *Xenopus* colonies) periodic censuses may be undertaken to obtain an exact count. In large-scale aquaculture research it may be more appropriate to measure biomass of the system vs. actual numbers of animals (Borski 2003).

Chapter 3 References

Alworth LC, Harvey SB. 2007. IACUC issues associated with amphibian research. ILAR J 48:278-289.

Alworth LC, Vazquez VM. 2009. A novel system for individually housing bullfrogs. Lab Anim 38:329-333.

Ames BN, Shigenaga MK, Hagen TM. 1993. Review: Oxidants, antioxidants, and the degenerative diseases of aging. Proc Natl Acad Sci U S A 90:7915-7922.

Anadon A, Martinez-Larranaga MR, Martinez MA. 2009. Use and abuse of pyrethrins and synthetic pyrethroids in veterinary medicine. Vet J (UK) 182:7-20.

Andrade CS, Guimaraes FS. 2003. Anxiolytic

Armstrong KR, Clark TR, Peterson MR. 1998.Use of corn-husk nesting material to reduce aggression in caged mice.Contemp Top Lab Anim Sci 37:64-66.

Augustsson H, Lindberg L, Hoglund AU, Dahl born K. 2002. Human-animal interactions and animal welfare in conventionally and pen-housed rats. Lab Anim 36:271-281.

Azar TA, Sharp JL, Larson DM. 2008. Effect ofhousing rats in dim light or long nights on heart rate. JAALAS 47:25-34.

Baer LA, Corbin BJ, Vasques MF, GrindelandRE. 1997. Effects of the use of filtered microisolator tops on cage microenviron ment and growth rate of mice. 1997 Lab

Bergmann P, Militzer K, Büttner D. 1994. Environmental enrichment and aggressive behaviour: influence on body weight and body fat in male inbred HLG mice. J Exp Anim Sci 37:59-78.

Berson DM, Dunn FA, Takao M. 2002. Phototransduction by retinal ganglion cells that set the circadian clock. Science 295:1070-1073.

Besch EL. 1980. Environmental quality within animal facilities. Lab Anim Sci 30:385-406.

Blaustein A, Marco A, Quichano C. 1999. Sensitivity to nitrate and nitrite in pond-breeding amphibians from the Pacific Northwest, USA. Environ Toxicol Chem J 18:2836-2839.

Blom HJM, Van Tintelen G, Van V. 1996. Preferences of mice and rats for types of bedding material. Lab Anim 30:234-244.

Bloomsmith MA, Stone AM, Laule GE. 1998. Positive reinforcement training to enhance the voluntary movement of group-housed chimpanzees within their enclosures. Zoo Biol 17:333-341.

Bly JE, Quiniou SM, Clem LW. 1997. Environmental effects on fish immune mechanisms. Dev Biol Stand 90:33-43.

Borski R, Hodson RG. 2003. Fish research and the institutional animal care and use committee. ILAR J 44:286-294.

Bracke MBM, Metz JHM, Spruijt BM, Schouten WGP. 2002. Decision support system for overall welfare assessment in pregnant sows. B: Validation by expert opinion. J Anim Sci 80:1835-1845.

Brainard GC. 1989. Illumination of laboratory animal quarters: Participation of light irradiance and wavelength in the regulation of the neuroendocrine system. In: Science and Animals: Addressing Contemporary Issues. Greenbelt MD: Scientists Center for Animal Welfare. p 69-74.

Brainard GC, Vaughan MK, Reiter RJ. 1986. Effect of light irradiance and wavelength on the Syrian hamster reproductive system. Endocrinology 119:648-654.

Brenner FJ, Brenner PE. 1969. The influence of light and temperature on body fat and reproductive conditions of Rana pipiens. Ohio J Sci 69:305-312.

Briese V, Fanghanel J, Gasow H. 1984. Effect of pure sound and vibration on the embryonic development of the mouse. Zentralbl Gynokol 106:378-388.

Broderson JR, Lindsey JR, Crawford JE. 1976. The role of environmental ammonia in respiratory mycoplasmosis of rats. Amer J Path 85:115-127.

Brown AM, Pye JD. 1975. Auditory sensitivity at high frequencies in mammals. Adv Comp Physiol Biochem 6:1-73.

Browne RK, Edwards DL. 2003a. The effect of temperature on the growth and development of green and golden bell frogs (Litoria aurea). J Therm Biol 28:295-299.

Browne RK, Pomering M, Hamer AJ. 2003b. High density effects on the growth, development and survival of Litoria aurea tadpoles. Aquaculture 215:109-121.

Browne RK, Odum RA, Herman T, Zippel K. 2007a. Facility design and associated services for the study of amphibians. ILAR J 48:188-202.

Browne RK, Zippel K. 2007b. Reproduction and larval rearing of amphibians. ILAR J 48:214-234.

Buddaraju AKV, Van Dyke RW. 2003. Effect of animal bedding on rat liver endosome acidification. Comp Med 53:616-621.

Carfagnini AG, Rodd FH, Jeffers KB, Bruce AEE. 2009. The effects of habitat complexity on aggression and fecundity in zebrafish (Danio rerio). Environ Biol Fish 86:403-409.

Carissimi AS, Chaguri LCAA, Teixeira MA , Mori CMC, Macchione M, Sant'Anna ETG, Saldiva PHN, Souza NL, Merusse JBL. 2000. Effects of two ventilation systems and bedding change frequency on cage environmental factors in rats (Rattus norvegicus). Anim Tech 51:161-170.

Carman RA, Quimby FW, Glickman GM. 2007. The effect of vibration on pregnant laboratory mice. Noise-Con Proc 209:1722-1731.

Castelhano-Carlos MJ, Sousa N, Ohl F, Baumans V. 2010. Identification methods in newborn C57BL/6 mice: A developmenta l and behavioural evaluation. Lab Anim 4:88-103.

Caulfield CD, Cassidy JP, Kelly JP. 2008. Effects of gamma irradiation and pasteurization on the nutritive composition of commerc ially available animal diets. JAALAS 47:61-66.

CFR [Code of Federal Regulation]. 2009. Title 21, Part 58. Good Laboratory Practice for Nonclinical Laboratory Studies. Wash ington: Government Printing Office. Available at: www.accessdata.fda.gov/scripts/cdrh/cf docs/cfcfr/CFRSearch.cfm?CFRPart=58andshowFR=1; accessed April 1, 2010.

Chapillon P, Manneche C, Belzung C, Caston J1999 Rearing environmental enrichment in two inbred strain of mice: 1. Effects on emotional reactivity. Behav Genet 29:41-46.

Cherry JA. 1987. The effect of photoperiod on development of sexual behavior and fertility in golden hamsters. Physiol Behav 39:521-526.

Chmiel DJ, Noonan M. 1996. Preference of laboratory rats for potentially enriching stimulus objects. Lab Anim 30:97-101.

Clarence WM, Scott JP, Dorris MC, Paré M.2006. Use of enclosures with functional vertical space by captive rhesus monkeys (Macaca mulatta) involved in biomedical research. JAALAS 45:31-34.

Festing MFW. 2002. Laboratory animal genetics and genetic quality control. In: Hau J, Van Hoosier GL Jr, eds. Handbook of Laboratory Animal Science. Boca Raton FL: CRC Press. p 173-203.

Festing MFW, Kondo K, Loosli R, Poiley SM, Spiegel A. 1972. International standardized nomenclature for outbred stocks of laboratory animals. ICLA Bull 30:4-17.

Fidler IJ. 1977. Depression of macrophages in mice drinking hyperchlorinated water. Nature 270:735-736.

Field K, Bailey M, Foresman LL, Harris RL, Motzel SL, Rockar RA, Ruble G, Suckow MA. 2007. Medical records for animals used in research, teaching and testing: Public statement from the American College of Laboratory Animal Medicine. ILAR J 48:37-41.

Fisher JP. 2000. Facilities and husbandry (large fish model). In: Ostrander GK, ed. The Laboratory Fish. San Francisco: Academic Press. p 13-39.

Fletcher JL. 1976. Influence of noise on animals. In: McSheehy T, ed. Control of the Animal House Environment. Laboratory Animal Handbooks 7. London: Laboratory Animals Ltd. p 51-62.

Fraile B, Paniagua R, Rodrigues MC, Saez J. 1989. Effects of photoperiod and temperature on spermiogenesis in marbeled newts (Triturus marmoratus marmoratus). Copeia 1989:357-363.

Fullerton PM, Gilliatt RW. 1967. Pressure neuropathy in the hind foot of the guinea pig. J Neurol Neurosurg Psychiat 30:18-25.

Fullerton FR, Greenman DL, Kendall DC. 1982. Effects of storage conditions on nutritional qualities of semipurified (AIN-76) and natural ingredient (NIH-07) diets. J Nutr 112:567-473.

Garg RC, Donahue WA. 1989. Pharmacologic profile of methoprene, an insect growth regulator, in cattle, dogs, and cats. JAVMA 194:410-412.

Garner JP. 2005. Stereotypies and other abnormal repetitive behaviors: Potential impact on validity, reliability, and replicability of scientific outcomes. ILAR J 46:106-117.

Gonder JC, Laber K. 2007. A renewed look at laboratory rodent housing and management. ILAR J 48:29-36.
Gonzalez RR, Kiuger MJ, Hardy JD. 1971. Partitional calorimetry of the New Zealand white rabbit at temperatures of 5-35°C. J Appl Physiol 31:728.
Gordon AH, Hart PD, Young MR. 1980. Ammonia inhibits phagosome-lysosome fusion in macrophages. Nature 286:79-80.
Gordon CJ. 1990. Thermal biology of the laboratory rat. Physiol Behav 47:963-991.
Gordon CJ. 1993. Temperature Regulation in Laboratory Animals. New York: Cambridge University Press.
Gordon CJ. 2004. Effect of cage bedding on temperature regulation and metabolism of group-housed female mice. Comp Med 54:63-68.
Gordon CJ, Becker P, Ali JS. 1998. Behavioral thermoregulatory responses of single- and group-housed mice. Physiol Behav 65:255-262.
Green EL. 1981. Genetics and Probability in Animal Breeding Experiments. New York: Oxford University Press.
Green SL. 2002. Factors affecting oogenesis in the South African clawed frog (Xenopus laevis). Comp Med 52:307-312.
Green SL. 2009. The Laboratory Xenopus sp. (Laboratory Animal Pocket Reference). Boca Raton FL: CRC Press.
Greenman DL, Bryant P, Kodell RL, Sheldon W. 1982. Influence of cage shelf level on retinal atrophy in mice. Lab Anim Sci 32:353-356.
Gresens J. 2004. An introduction to the Mexican Axolotl (Ambystoma mexicanum). Lab Anim 33:41-47.
Groen A. 1977. Identification and genetic monitoring of mouse inbred strains using biomedical polymorphisms. Lab Anim (London) II:209-214.
Gunasekara AS, Rubin AL, Goh KS, Spurlock FC, Tjeerdema RS. 2008. Environmental fate and toxicology of carbaryl. Rev Env Contam Toxicol (United States) 196:95-121.
Gutleb AC, Bronkhorst M, van den Berg JHJ, Musrk AJ. 2001. Latex laboratory gloves: An unexpected pitfall in amphibian toxicity assays with tadpoles. Environ Toxicol Pharmacol 10:119-121.
Haemisch A, Voss T, Gärtner K. 1994 Effects of environmental enrichment on aggressive behaviour, dominance hierarchies and endocrine states in male DBA/2J mice. Physiol Behav 56:1041-1048.
Hall FS. 1998. Social deprivation of neonatal, adolescent, and adult rats has distinct neurochemical and behavioural consequences. Crit Rev Neurobiol 12:129-162.
Hall JE, White WJ, Lang CM. 1980. Acidification of drinking water: Its effects on selected biologic phenomena in male mice. Lab Anim Sci 30:643-651.
Hanifin JP, Brainard GC. 2007.Photoreception for circadian, neuroendocrine, and neurobehavioral regulation. J Physiol Anthropol 26:87-94.
Hartl DL. 2000. A Preimier of Population Genetics, 3rd ed. Sunderland MA: Sinauer Associates.
Hasenau JJ, Baggs RB, Kraus AL. 1993. Microenvironments in microisolation cages using BALB/c and CD-1 Mice. Contemp Top Lab Anim Sci 32:11-16.
Hedrich HJ. 1990. Genetic Monitoring of Inbred Strains of Rats. New York: Gustav Fischer Verlag.
Heffner HE, Heffner RS. 2007. Hearing ranges of laboratory animals. JAALAS 46:20-22.

Held SDE, Turner RJ, Wootton RJ. 1995. Choices of laboratory rabbits for individual or group-housing. Appl Anim Behav Sci 46:81-91

Hermann LM, White WJ, Lang CM. 1982. Prolonged exposure to acid, chlorine, or tetracycline in drinking water: Effects on delayed-type hypersensitivity, hemagglutination titers, and reticuloendothelial clearance rates in mice. Lab Anim Sci 32:603-608.

Hess SE, Rohr S, Dufour BD, Gaskill BN, Pajor EA, Garner JP. 2008. Home improvement: C57BL/6J mice given more naturalistic nesting materials build better nests. JAALAS 47:25-31.

Hill D. 1999. Safe handling and disposal of laboratory animal waste. Occ Med 14:449-468.

Hilken G, Dimigen J, Iglauer F. 1995. Growth of Xenopus laevis under different laboratory rearing conditions. Lab Anim 29:152-62.

Hoffman HA, Smith KT, Crowell JS, Nomura T, Tomita T. 1980. Genetic quality control of laboratory animals with emphasis on genetic monitoring. In: Spiegel A, Erichsen S, Solleveld HA, eds. Animal Quality and Models in Biomedical Research. Stuttgart: Gustav Fischer Verlag. p 307-317.

Homberger FR, Pataki Z, Thomann PE. 1993. Control of Pseudomonas aeruginosa infection in mice by chlorine treatment of drinking water. Lab Anim Sci 43:635-637.

Hotchkiss CE, Paule MG. 2003. Effect of pair-housing on operant behavior task performance by rhesus monkeys. Contemp Top Lab Anim Sci 42:38-41.

Hubrecht RC. 1993. A comparison of social and environmental enrichment methods for laboratory housed dogs. Appl Anim Behav Sci 37: 345-361.

Hughes HC, Reynolds S. 1995. The use of computational fluid dynamics for modeling air flow design in a kennel facility. Contemp Top Lab Anim Sci 34:49-53

Ikemoto S, Panksepp J. 1992. The effect of early social isolation on the motivation for social play in juvenile rats. Dev Psychobiol 25:261-274.

Ivy AS, Brunson KL, Sandman C, Baram TZ. 2008. Dysfunctional nurturing behavior in rat dams with limited access to nesting material: A clinically relevant model for early-life stress. Neuroscience 154:1132-1142.

Jacobs BB, Dieter DK. 1978. Spontaneous hepatomas in mice inbred from Ha:ICR Swiss stock: Effects of sex, cedar shavings in bedding, and immunization with fetal liver or hepatoma cells. J Natl Cancer Inst 61:1531-1534.

Jones DM. 1977. The occurrence of dieldrin in sawdust used as bedding material. Lab Anim 11:137.

Karolewicz B, Paul IA. 2001. Group housing of mice increases immobility and antidepressant sensitivity in the forced swim and tail suspension tests. Eur J Pharmacol 415:97-201.

Kaufman BM, Pouliot AL, Tiefenbacher S, Novak MA. 2004. Short- and long-term effects of a substantial change in cage size on individually housed, adult male rhesus monkeys (Macaca mulatta). Appl Anim Beh Sci 88:319-330.

Kaye GI, Weber PB, Evans A, Venezia RA. 1998. Efficacy of alkaline hydrolysis as an alternative method for treatment and disposal of infectious animal waste. Contemp Top Lab Anim Sci 37:43-46.

Keenan KP, Smith PF, Soper KA. 1994. Effect of dietary (caloric) restriction on aging, survival, pathobiology and toxicology. In: Notter W, Dungworth DL, Capen CC, eds. Pathobiology of the Aging Rat, vol 2. Washington: International Life Sciences Institute. p 609-628.

Liu L, Nutter LMJ, Law N, McKerlie C. 2009. Sperm freezing and in vitro fertilization on three substrains of C57BL/6 mice. JAALAS 48:39-43.

Lupo C, Fontani G, Girolami L, Lodi L, Muscettola M. 2000. Immune and endocrine aspects of physical and social environmental variations in groups of male rabbits in seminatural conditions. Ethol Ecol Evol 12:281-289.

Lutz CK, Novak MA. 2005 Environmental enrichment for nonhuman primates: Theory and application. ILAR J 46:178-191.

MacCluer JW, VandeBerg JL, Read B, Ryder OA. 1986. Pedigree analysis by computer simulation. Zoo Biol 5:147-160.

MacLean EL, Roberts Prior S, Platt ML, Brannon EM. 2009. Primate location preference in a double-tier cage: The effects of illumination and cage height. J Anim Welf Sci 12:73-81.

Macrì S, Pasquali P, Bonsignore LT, Pieretti S, Cirulli F, Chiarotti F, Laviola G. 2007 Moderate neonatal stress decreases within-group variation in behavioral, immune and HPA responses in adult mice. PLoS One 2(10):e1015.

Maniero GD, Carey C. 1997. Changes in selected aspects of immune function in leopard frog, Rana pipiens, associated with exposure to cold. J Comp Physiol B 167:256-263.

Manninen AS, Antilla S, Savolainen H. 1998. Rat metabolic adaptation to ammonia inhalation. Proc Soc Biol Med 187:278-281.

Manser CE, Elliott H, Morris TH, Broom DM. 1996. The use of a novel operant test to determine the strength of preference for flooring in laboratory rats. Lab Anim 30:1-6.

Manser CE, Broom DM, Overend P, Morris TM. 1997. Operant studies to determine the strength of preference in laboratory rats for nest boxes and nest materials. Lab Anim 32:36-41.

Manser CE, Broom DM, Overend P, Morris TM. 1998. Investigations into the preferences of laboratory rats for nest boxes and nesting materials. Lab Anim 32:23-35.

Manser CE, Morris TH, Broom DM. 1995. An investigation into the effects of solid or grid cage flooring on the welfare of laboratory rats. Lab Anim 29:353-363.

Martin B, Ji S, Maudsley S, Mattson MP. 2010. "Control" laboratory rodents are metabolically morbid: Why it matters. Proc Nat Acad Sci U S A 107:6127-6133.

Mason G, Littin KE. 2003. The humaneness of rodent pest control. Anim Welf 12:1-37.

Matthews M, Trevarrow B, Matthews J. 2002. A virtual tour of the guide for zebrafish users. Lab Anim 31:34-40.

McCune S. 1997. Enriching the environment of the laboratory cat: A review. In: Proceedings of the second international conference on environmental enrichment,

Memarzadeh F, Harrison PC, Riskowski GL, Henze T. 2004. Comparisons of environment and mice in static and mechanically ventilated isolator cages with different air velocities and ventilation designs. Contemp Top Lab Anim Sci 43:14-20.

MGI [Mouse Genome Informatics]. 2009. Guidelines for Nomenclature of Genes, Genetic Markers, Alleles, and Mutations in Mouse and Rat. International Committee on Standardized Genetic Nomenclature for Mice and Rat Genome and Nomenclature Committee. Available at www.informatics.jax.org/mgihome/nomen/gene.shtml; accessed May 10, 2010.

Moore BJ. 1987. The California diet: An inappropriate tool for studies of thermogenesis. J Nutrit 117:227-231.

Murphy RGL, Scanga JA, Powers BE, Pilon JL, VerCauteren KC, Nash PB, Smith GC, Belk KE. 2009. Alkaline hydrolysis of mouse-adapted scrapie for inactivation and

NRC [National Research Council]. 1974. Amphibians: Guidelines for the Breeding, Care and Management of Laboratory Animals. Washington: Printing and Publishing Office, NAS.
NRC. 1977. Nutrient Requirements of Rabbits, 2nd rev ed. Washington: National Academy Press.
NRC. 1979a. Laboratory Animal Records. Washington: National Academy Press.
NRC. 1979b. Laboratory animal management: Genetics. ILAR News 23(1):A1-A16.
NRC. 1982. Nutrient Requirements of Mink and Foxes, 2nd rev ed. Washington: National Academy Press.
NRC. 1989. Biosafety in the Laboratory: Prudent Practices for the Handling and Disposal of Infectious Materials. Washington: National Academy Press.
NRC. 1993. Nutrient Requirements of Fish. Washington: National Academy Press.
NRC. 1994. Nutrient Requirements of Poultry, 9th rev ed. Washington: National Academy Press.
NRC. 1995a. Nutrient Requirements of Laboratory Animals, 4th rev ed. Washington: National Academy Press.
NRC. 1995b. Prudent Practices in the Laboratory: Handling and Disposal of Chemicals. Washington: National Academy Press.
NRC. 1996. Laboratory Animal Management: Rodents. Washington: National Academy Press.
NRC. 1998a. Psychological Well-being of Nonhuman Primates. Washington: National Academy Press.
NRC. 1998b. Nutrient Requirements of Swine, 10th rev ed. Washington: National Academy Press.
NRC. 2000. Nutrient Requirements of Beef Cattle, 7th rev ed: Update 2000. Washington: National Academy Press.
NRC. 2001. Nutrient Requirements of Dairy Cattle, 7th rev ed. Washington: National Academy Press.
NRC. 2003a. Nutrient Requirements of Nonhuman Primates, 2nd rev ed. Washington: National Academies Press.
NRC. 2003b. Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research. Washington: National Academies Press.
NRC. 2006a. Preparation of Animals for Use in the Laboratory. ILAR J 43:281-375.
NRC. 2006b. Nutrient Requirements of Dogs and Cats. Washington: National Academies Press.
NRC. 2006c. Nutrient Requirements of Horses, 6th rev ed. Washington: National Academies Press.
NRC. 2007. Nutrient Requirements of Small Ruminants: Sheep, Goats, Cervids, and New World Camelids. Washington: National Academies Press.
Olivier B, Molewijk E, van Oorschot R, van der Poel G, Zethof T, van der Heyden J, Mos J. 1994. New animal models of anxiety. Eur Neuropsychopharmacol 4:93-102.
Olson LC, Palotay JL. 1983. Epistaxis and bullae in cynomolgus macaques (Macaca fascicularis). Lab Anim Sci 33:377-379.
Olsson IA, Dahlborn, K. 2002. Improving housing conditions for laboratory mice: A review of “environmental enrichment”. Lab Anim 36:243-270.
OSHA [Occupational Safety and Health Administration]. 1998. Occupational Safety and Health Standards. Subpart G, Occupational Health and Environmental Controls,

Occupational Noise Exposure (CFR 29 1910.95). Washington: Department of Labor.

O'Steen WK. 1980. Hormonal influences in retinal photodamage. In: Williams TP, Baker BN, eds. The Effects of Constant Light on Visual Processes. New York: Plenum Press. p 29-49.

Chapter 3: Environment, Housing, and Manao1tent,

Thigpen JE, Setchell KDR, Saunders HE, Haseman JK, Grant MG, Forsythe DB. 2004. Selecting the appropriate rodent diet for endocrine disruptor research and testing studies. ILAR J 45:401-416.

Tompkins JA, Tsai C. 1976. Survival time and lethal exposure time for the blacknose dace exposed to free chlorine and chloramines. Trans Am Fish Soc 105:313-321.

Torreilles SL, Green SL. 2007. Refuge cover decreases the incidence of bite wounds in laboratory South African clawed frogs (*Xenopus laevis*). JAALAS 46:33-36.

Torronen R, Pelkonen K, Karenlampi S. 1989. Enzyme-inducing and cytotoxic effects of wood-based materials used as bedding for laboratory animals: Comparison by a cell culture study. Life Sci 45:559-565.

Totten M. 1958. Ringtail in newborn Norway rats: A study of the effect of environmental temperature and humidity on incidence. J Hygiene 56:190-196.

Tsai PP, Stelzer HD, Hedrich HJ, Hackbarth H. 2003. Are the effects of different enrichment designs on the physiology and behaviour of DBA/2 mice consistent? Lab Anim 37:314-27.

Tsutsui S, Tasumi S, Suetake H, Kikuchi K, Suzuki Y. 2005. Demonstration of the mucosal lectins in the epithelial cells of internal and external body surface tissues in pufferfish (*Fugu rubripes*). Dev Comp Immun 29:243-253.

Tucker HA, Petitclerc D, Zinn SA. 1984. The influence of photoperiod on body weight gain, body composition, nutrient intake and hormone secretion. J Anim Sci 59:1610-1620.

Turner RJ, Held SD, Hirst JE, Billinghurst G, Wootton RJ. 1997. An immunological assessment of group-housed rabbits. Lab Anim 31:362-372.

Turner JG, Bauer CA, Rybak LP. 2007. Noise in animal facilities: Why it matters. JAALAS 46:10-13.

Twaddle NC, Churchwell MI, McDaniel LP, Doerge DR. 2004. Autoclave sterilization produces acrylamide in rodent diets: Implications for toxicity testing. J Agricul Food Chem 52:4344-4349.

van de Nieuwegiessen PG, Boerlage AS, Verreth JAJ, Schrama AW. 2008. Assessing the effects of a chronic stressor, stocking density, on welfare indicators of juvenile African catfish, *Clarias gariepinus* Burchell. Appl Anim Behav Sci 115:233-243.

van den Bos R, de Cock Buning T. 1994. Social behaviour of domestic cats (*Felis lybica catus* L.): A study of dominance in a group of female laboratory cats. Ethology 98:14-37.

Van Loo PL, Mol JA, Koolhaas JM, Van Zutphen BM, Baumans V. 2001. Modulation of aggression in male mice: Influence of group size and cage size. Physiol Behav 72:675-83.

Van Loo PL, Van de Weerd HA, Van Zutphen LF, Baumans V. 2004. Preference for social contact versus environmental enrichment in male laboratory mice. Lab Anim 38:178-188.

Van Praag H, Kempermann G, Gage FH. 2000. Neural consequences of environmental enrichment. Nat Rev Neurosci 1:191-198.

Verma RK. 2002. Advances on cockroach control. Asian J Microbiol, Biotech Env Sci 4:245-249.

Vesell ES. 1967. Induction of drug-metabolizing enzymes in liver microsomes of mice and rats by softwood bedding. Science 157:1057-1058.

Vesell ES, Lang CM, White WJ, Passananti GT, Tripp SL. 1973. Hepatic drug metabolism in rats: Impairment in a dirty environment. Science 179:896-897.

Vesell ES, Lang CM, White WJ, Passananti GT, Hill RN, Clemen TL, Liu DL, Johnson WD. 1976. Environmental and genetic factors affecting response of laboratory animals to drugs. Fed Proc 35:1125-1132.

Vlahakis G. 1977. Possible carcinogenic effects of cedar shavings in bedding of C3H-A^{vy}fB mice. J Natl Cancer Inst 58:149-150.

Vogelweid CM. 1998. Developing emergency management plans for university laboratory animal programs and facilitie s. Contemp Top Lab Anim Sci 37:52-56.

Waiblinger E. 2002. Comfortable quarters for gerbils in research institutions. In: Reinhardt V, Reinhardt A, eds. Comfortable Quarters for Laboratory Animals, 9 th ed. Washington: Animal Welfare Institute. p 18-25.

Wardrip CL, Artwohl JE, Bennett BT. 1994. A review of the role of temperature versus

Wolfer DP, Litvin O, Morf S, Nitsch RM, Lipp HP, Würbel H. 2004. Laboratory animal welfare: Cage enrichment and mouse behaviour. Nature 432:821-822.

Wolff A, Rupert G. 1991. A practical assessment of a nonhuman primate exercise program. Lab Anim 20:36-39.

Wooster GA, Bowser PR. 2007. The aerobiological pathway of a fish pathogen: Survival and disseminaton of Aeromonas salmonicida in aerosols and its implications in fish

immobilization, sedation, analgesia, anesthesia, and euthanasia. In addition, the veterinarian should provide guidance and oversight to surgery programs and perioperative care involving animals.

Animal Procurement and Transportation

Animal Procurement

All animals must be acquired lawfully , and the receiving institution should ensure that all procedures involving animal procurement are conducted in a lawful manner. Prior to procuring anim als, the Principal Investigator should confirm that there are sufficient facilities and expertise to house and manage the species being acquired. Procurement of animals should be linked to the prior

does not pose risks to animal well-being or personnel safety. During times of extreme temperatures animal transport may not be possible if an appropriately heated or cooled means of

inadvertently introduced; a comprehensive ongoing program for evaluating animals' health status, including access to all animals; and containment and eradication –if desired- of introduced infectious agents. Related program components include procedures for evaluating and selecting appropriate animal suppliers (these may include quarantine and confirmation of animal health status if unknown); treatment of animals or their products at entry to minimize disease risks (e.g., surface disinfection of fish eggs); establishment of a comprehensive pest control program that may include evaluation of the health status of feral animals; procedures to ensure that all biologicals administered to animals are free of contamination; and development of appropriate procedures for intra- and inter-facility animal transport. For example, transport of animals to laboratory and other facilities outside of the animal facility can present challenges to animal biosecurity (Balaban and Hampshire 2001). Additional details pertaining to these topics can be found in other sections of the Guide.

Quarantine and Stabilization

Quarantine is the separation of newly received animals from those already in the facility, in a way that prevents potential spread of contaminants, until the health and possibly the microbial status of the newly received animals have been determined. Transportation of animals can be stressful and may induce recrudescence of subclinical infections harbored by an animal. An effective quarantine program minimizes the risk of introduction of pathogens into an established colony. The veterinary medical staff should implement procedures for evaluating the health and, if appropriate, the pathogen status of newly received animals, and the procedures should reflect acceptable veterinary medical practice and federal and state regulations applicable to zoonoses (Butler et al. 1995). Effective quarantine procedures are particularly helpful in limiting human exposure to zoonotic infections from nonhuman primates, such as mycobacterial infections which necessitate specific guidelines for handling of these animals (Lerche et al. 2008; Robertstad and Andrews 2008). Information from suppliers on animal quality should be sufficient to enable a veterinarian to determine the length of quarantine, to define the potential risks to personnel and animals within the colony, to determine whether therapy is required before animals are released from quarantine, and,

animals from other shipments to preclude transfer of infectious agents between groups.

Depending on the health status of the colony animals and consistent with the animal biosecurity program in place, rodents or other animals being moved outside of an animal facility for procedures, such as imaging or behavioral testing, may need to be held separately from their colony of origin until their health status is evaluated.

Regardless of whether the animals are quarantined, newly received animals should be given a period for physiologic, behavioral, and nutritional acclimation before their use (Obernier and Baldwin 2006). The length of time for acclimation will depend on the type and duration of animal transportation, the species involved, and the intended use of the animals. For animals not typically housed in research settings, considerations should be given to providing means to assist with animal acclimation, for example, shearing sheep before they are brought indoors. The need for an acclimation period has been demonstrated in mice, rats, guinea pigs, nonhuman primates, and goats; it is likely important for other species as well (Conour et al. 2006; Capitanio et al. 2006; Kagira et al. 2007; Landi et al. 1982; Prasad et al. 1978; Sanhouri et al. 1989; Tuli et al. 1995).

Separation by Health Status and Species

Physical separation of animals by species is recommended to prevent interspecies disease transmission and to eliminate the potential for anxiety and physiologic and behavioral changes due to interspecies conflict (Arndt et al. 2010). Such separation is usually accomplished by housing different species in separate rooms. In some instances, however, this might be accomplished with cubicles, laminar-flow units, cages that

- As a rule, New World (South and Central American), Old World African, and Old World Asian species of nonhuman primates should be housed in separate rooms. Simian hemorrhagic fever (Renquist 1990) and simian immunodeficiency virus (Hirsch et al. 1991; Murphy-Corb et al. 1986), for example, cause only subclinical infections in African species but induce clinical disease in Asian species.
- Some species should be housed in separate rooms even though they are from the same geographic region. For example, squirrel monkeys (*Saimiri sciureus*) and tamarins (*Saguinus oedipus*) might be latently infected with herpesviruses (*Herpesvirus saimiri* and *Herpesvirus tamarinus*, respectively), which could be transmitted to and cause a fatal epizootic disease in owl monkeys (*Aotus trivirgatus*) (Barahona et al. 1975; Hunt and Melendez 1966; Murphy et al. 1971).

Intraspecies separation might be essential when animals obtained from multiple sites or sources, either commercial or institutional, differ in pathogen status, e.g., rat theilovirus in rats, mouse hepatitis virus in mice, bacterial gill disease in rainbow trout, *Pasteurella multocida* in rabbits, Macacine herpesvirus (B virus) in macaque species, and *Mycoplasma hyopneumoniae* in swine.

Surveillance, Diagnosis, Treatment, and Control of Disease

All animals should be observed for signs of illness, injury, or abnormal behavior by a person trained to recognize such signs. As a rule, this should occur at least daily, but more frequent observations may be required, such as during postoperative recovery, when animals are ill or have a physical deficit, or when animals are approaching a study endpoint. Professional judgment should be used to ensure that the frequency and character of observations minimize risks to individual animals and does not compro

Procedures for disease prevention, diagnosis, and therapy should be those currently accepted in veterinary and laboratory animal practice. Health monitoring programs also include veterinary herd/flock health programs for livestock, and colony health monitoring programs for aquatic and rodent species. Access to diagnostic laboratory services facilitate veterinary medical care and can include gross and microscopic pathology, hematology, microbiology, parasitology, clinical chemistry, molecular diagnostics, and serology. If a disease or infectious agent is identified within a facility or colony, the choice of therapy should be made by the veterinarian in consultation with the investigator. If the animal is to continue on study, the selected treatment plan should be therapeutically sound and, when possible, should interfere minimally with the research process.

Subclinical microbial infections (see Appendix A, Pathology, Clinical Pathology, and Parasitology) occur frequently in conventionally maintained rodents but also can occur in facilities designed and maintained for production and use of pathogen-free rodents if the microbial barrier is breached. Examples of infectious agents that can be subclinical but which may induce immunologic changes or alter physiologic, pharmacologic, or toxicologic responses are noroviruses, parvoviruses, mouse hepatitis virus, lymphocytic choriomeningitis virus, and *Helicobacter* spp (Besselsen et al. 2008; Clifford and Watson 2008; NRC 1991 a, b, c). Scientific objectives of a particular protocol, the consequences of infection within a specific strain of rodent, the potential for zoonotic disease, and the adverse effects that infectious agents might have on other animals or protocols in a facility should determine the characteristics of rodent health-surveillance programs and strategies for keeping rodents free of specific pathogens.

The principal method for detecting microbial infections in animal populations is serologic testing, flow cytometric bead immunoassays or immunofluorescent assays. Other methods of detecting infections, such as DNA analysis using a polymerase chain reaction (PCR), microbial culture, clinical chemistry (e.g., LDH virus), histopathology, and other validated emergent technologies can also be used to make or confirm a diagnosis. Transplantable tumors, hybridomas, cell lines, blood products, and other biologic materials can be sources of murine viruses that can contaminate rodents as well as human viruses that may pose risks to laboratory personnel (Nicklas et al. 1993). Rapid and effective assays are available to monitor microbiologic contamination and should be considered prior to introducing such material into animals (Peterson 2008). Because health monitoring programs are dependent on the size and complexity of the Program, the species involved, and the institutional research focus, it is beyond the scope of the *Guide* to go into details about health monitoring programs for all species. Additional references can be found in

Appendix A (Disease Surveillance, Diagnosis and Treatment; Pathology, Clinical Pathology and Parasitology; and under Species-Specific References).

Clinical Care and Management

Healthy, well cared for animals are a prerequisite for good quality animal-based science. The structure of the veterinary care program, including the number of qualified veterinarians should be appropriate to fulfill the program's requirements. This will vary by institution, species used, and the nature of the animal use. To be effective in providing clinical care, the veterinarian should be familiar with the species, the various uses of animals in the institutional research, teaching, testing, or production programs and have access to medical and experimental treatment records.

Medical Management

There should be a timely and accurate method for communication of any abnormalities or concerns regarding animal health, behavior, and well-being to the veterinarian or the veterinarian's designee. The responsibility for bringing these concerns forward rests with all those involved with as2gshu7(exso7 0 TDc)3 Tc .0003 Tw (ab

Emergency Care

Procedures must be in place to provide for emergency veterinary care both during and outside of regularly scheduled hours. Such procedures must enable timely reporting of animal injury, illness, or death by animal care and research staff. A veterinarian or the veterinarian's designee must be available to expeditiously assess the animal's condition, treat the animal, investigate an unexpected death, or advise on euthanasia. In the case of a pressing health problem, if the responsible person (e.g., investigator) is not available or if consensus between the investigator and veterinary staff cannot be reached concerning treatment, the veterinarian

the procedures will be conducted; and perioperative animal health assessment and care (Brown and Schofield 1994). Aveterinarian should be involved in discussions surrounding the selection of anesthetic agents and doses to be used as well as the plan for perioperative analgesic use. If a nonsterile part of an animal, such as the gastrointestinal tract, is to be surgically exposed or if a se. immunosuppes ions,proeperative anatib-1628(i)1(oic s maybe s]TJ -0-1.24 TD -0001 Tc -.0001

Surgical Procedures

In general, surgical procedures are categorized as major or minor and, in the laboratory setting, can be further divided into survival and nonsurvival. As a general guideline, major survival surgery penetrates and exposes a body cavity or produces substantial impairment of physical or physiologic functions (such as laparotomy, thoracotomy, joint replacement, and limb amputation), or involves extensive tissue dissection or transection(Brown et al. 1993). Minor survival surgery does not expose a body cavity and causes little or no physical impairment (such as wound suturi ng; peripheral vessel cannulation; percutaneous biopsy; routine agricultural animal procedures such as castration, and most procedures routinely done on an “outpatient” basis in veterinary clinical practice). Typically, animals re covering from these minor procedures do not show significant signs of postope rative pain, have minimal complications,

In non-survival surgery, an animal is euthanatized before recovery from anesthesia. It might not be necessary to follow all the techniques outlined in this section if nonsurvival surgery is performed; however, at a minimum, the surgical site should be clipped, the surgeon should wear gloves, and the instruments and surrounding area should be clean (Slattum et al. 1991). For non-survival procedures of extended duration, attention to aseptic technique may be more important in order to ensure stability of the model and a successful outcome.

Aseptic Technique

Aseptic technique is used to reduce microbial contamination to the lowest possible practical level (Mangram et al. 1999). No procedure, piece of equipment, or germicide alone can achieve that objective (Schonholtz 1976). Aseptic technique requires the input and cooperation of everyone who enters the surgery area (Belkin 1992; McWilliams 1976). The contribution and importance of each practice varies with the procedure. Aseptic technique, regardless of the species, includes preparation of the patient, such as hair or feather removal and disinfection of the operative site (Hofmann 1979); preparation of the surgeon, such as the provision of appropriate surgical attire, face masks, and sterile surgical gloves (Chamberlain and Houang 1984; Pereira et al. 1990; Schonholtz 1976); sterilization of instruments, supplies, and implanted materials (Bernal et al. 2009; Kagan 1992b); and the use of operative techniques to reduce the likelihood of infection (Ayliffe 1991; Kagan 1992a; Ritter and Marmion 1987; Schofield 1994; Whyte 1988).

While the species of animal may influence the manner in which principles of aseptic technique are achieved (Brown 1994; Cunliffe-Beamer 1983), inadequate or improper technique may lead to subclinical infections that can cause adverse physiologic and behavioral responses (Beamer 1972; Bradfield et al. 1992; Cunliffe-Beamer 1990; Waynforth 1980, 1987) affecting surgical success, animal well-being, and research results (Cooper et al 2000). General principles of aseptic technique should be adhered to for all survival surgical procedures (ACLAM 2001).

Specific sterilization methods should be selected on the basis of physical characteristics of materials to be sterilized (Callahan et al. 1995; Schofield 1994). Autoclaving and plasma and gas sterilization are effective methods most commonly used to sterilize instruments and materials. Sterilization indicators should be used to validate that materials have been properly sterilized (Berg 1993). Alternative methods, used primarily for rodent surgery, include liquid chemical sterilants and dry heat sterilization. Liquid chemical sterilants should

care of surgical incisions. Appropriate medical records should also be maintained. After recovery from anesthesia, monitoring is often less intense but should include attention to basic biologic functions of intake and elimination, behavioral signs of postoperative pain, monitoring for postsurgical infections, monitoring of the surgical incision site for dehiscence, bandaging as appropriate, and timely removal of skin sutures, clips, or staples (UFAW 1989).

Pain and Distress

An integral component of veterinary medical care is prevention or alleviation of pain associated with procedural and surgical protocols. Pain is a complex experience that typically results from stimuli that damage tissue or have the potential to damage tissue. The ability to experience and respond to pain is

physiologic, and biochemical indicato rs of well-being (Dubner 1987; Karas 2002;

procedures. Neuromuscular blocking agents (e.g., pancuronium) are sometimes used to paralyze skeletal muscles during surgery in which general anesthetics have been administered (Klein 1987). When these agents are used during surgery or in any other painful procedure, many signs and reflexes used to assess anesthetic depth are eliminated because of the paralysis. However, autonomic nervous system changes (e.g., sudden changes in heart rate and blood pressure) can be indicators of pain related to an inadequate depth of anesthesia. It is imperative that any proposed use of neuromuscular blocking drugs be carefully evaluated by the veterinarian and the

The selection of specific agents and methods for euthanasia will depend on the species involved, the animal's age, and the objectives of the protocol. Generally, chemical agents (such as barbiturates and non-explosive inhalant anesthetics) are preferable to physical methods (such as cervical dislocation, decapitation, and use of a penetrating captive bolt); however, scientific considerations might preclude the use of chemical agents for some protocols.

Although carbon dioxide (CO_2) is a commonly used method for rodent euthanasia, there is ongoing controversy regarding its aversive characteristics as an inhalant euthanasia agent. This is an area of active research (Conlee et al. 2005; Danneman et al. 1997; Hackbarth et al. 2000; Kirkden et al. 2008; Leach et al. 2002; Niel et al. 2008) and further study is needed to optimize the methods for CO_2 euthanasia in rodents (Hawkins et al. 2006). Its acceptability as a euthanasia agent for small rodents should be evaluated as new data becomes available. Because neonatal rodents are resistant to the hypoxia-inducing effects of CO_2 and require longer exposure times to the agent (Artwohl et al. 2006), alternative methods should be considered (e.g., injection with chemical agents, cervical dislocation, or decapitation; Klaunberg et al. 2004; Pritchett-Corning 2009).

It is essential that euthanasia be

NRC. 1991b. Individual disease agents and their effects on research. In: Infectious Diseases of Mice and Rats. Washington: National Academy Press. p 31-256.
NRC. 1991c. Health Surveillance Programs. In: Infectious Diseases of Mice and Rats. Washington: National Academy Press. p 21-27.
NRC. 1996. Rodents: Laboratory Animal Management. Washington: National Academy Press.
NRC. 2003. Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research. Washington: National Academies Press.
NRC. 2006. Guidelines for the Humane Transportation of Research Animals. Washington: National Academies Press.
NRC. 2008. Recognition and Alleviation of Distress in Laboratory Animals. Washington: National Academies Press.
NRC. 2009a. Recognition and Alleviation of Pain in Laboratory Animals. Washington: National Academies Press.
NRC. 2009b. Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research. Washington: National Academies Press.
Obernier JA, Baldwin RL. 2006. Establishing an appropriate period of acclimatization following transportation of laboratory animals. ILAR J 47:364-369.
Otto G, Tolwani RJ. 2002. Use of microisolator caging in a risk-based mouse import and quarantine program: a retrospective study. Contemp Top Lab Anim Sci 41(1):20-27.
Paul-Murphy J, Ludders JW, Robertson SA, Gaynor JS, Hellyer PW, Wong PL. 2004. The need for a cross-species approach to the study of pain in animals. JAVMA 224:692-697.
Pereira L J, Lee GM, Wade KJ. 1990. The effect of surgical handwashing routines on the microbial counts of operating room nurses. Am J Inf Control 18:354-364.
Perret-Gentil M, Sinanan M, Dennis MB Jr, Horgan S, Weyhrich J, Anderson D, Hudda K. 1999. Videoendoscopy: An effective and efficient way to perform multiple visceral biopsies in small animals. J Invest Surg 12:157-165.
Perret-Gentil MI, Sinanan MN, Dennis MB Jr, Anderson DM, Pasieka HB, Weyhrich JT, Birkebak TA. 2000. Videoendoscopic techniques for collection of multiple serial intra-abdominal biopsy specimens in HIV-negative and HIV-positive pigtail macaques (Macaca nemestrina). J Invest Surg 13:181-195.
Peterson NC. 2008. From bench to cageside: Risk assessment for rodent pathogen contamination of cells and biologics. ILAR J 49:310-315.
Prasad SB, Gatmaitan R, O'Connell RC. 1978. Effect of a conditioning method on general safety test in guinea pigs. Lab Anim Sci 28:591-593.
Pritchett-Corning KR. 2009. Euthanasia of neonatal rats with carbon dioxide. JAALAS 48:23-27.
Pritchett-Corning KR, Chang FT, Festing MF. 2009. Breeding and housing laboratory rats and mice in the same room does not affect the growth or reproduction of either species. JAALAS 48:492-498.
Renquist D. 1990. Outbreak of simian hemorrhagic fever. J Med Primatol 19:77-79.
Ritter MA, Marmion P. 1987. The exogenous so

Robertshaw D. 2004. Temperature regulation and the thermal environment. In: Duke's Physiology of Domestic Animals, 12th ed. WO Reese, ed. Ithaca, NY: Cornell

Tuli JS, Smith JA, Morton DB. 1995. Stress measurements in mice after transportation. Lab Anim 29:132-138.

UFAW [Universities Federation for Animal Welfare]. 1989. Surgical procedures. In: Guidelines on the Care of Laboratory Animals and Their Use for Scientific Purposes III. London. p 3-15.

USDA [US Department of Agriculture]. 1985. 9 CFR 1A. (Title 9, Chapter 1, Subchapter

CHAPTER 5. Physical Plant

A well-planned, well-designed, well-constructed, properly maintained and managed facility is an important element of humane animal care and use, as it facilitates efficient, economical, and safe operation (see Appendix A, Design and Construction of Animal Facilities). The design and size of an animal facility depend on the scope of institutional research activities, the animals to be housed, the physical relationship to the rest of the institution, and the geographic location. Effective planning and design should include input from personnel experienced with animal-facility design, engineering and operation, as well as from representative users of the proposed facility. Use of computational fluid dynamics (CFD), building information modeling and literature on post-occupancy analysis of space use may provide benefits when designing facilities and caging (Eastman et al. 2008; Reynolds 2008; Ross et al. 2009). An animal facility should be designed and constructed in accord with all applicable building codes. In areas with substantial seismic activity the recommendations of the Building Seismic Safety Council should be incorporated into building planning and design (BSSC 2001; Vogelweid et al. 2005). As animal model development and use would be expected to change during the life cycle of an animal facility, facilities should be designed to accommodate changes in utilization. Modular units (such as custom-designed trailers or prefabricated structures) should comply with construction guidelines described in this chapter.

Building materials should be selected to facilitate efficient and hygienic operation of animal facilities. Durable, moisture- and vermin-proof, fire-resistant, seamless materials are most desirable for interior surfaces. Surfaces should be highly resistant to the effects of cleaning agents, scrubbing, high-pressure sprays, and impact. Paints and glazes should be nontoxic if used on surfaces with which animals will have direct contact. In the construction of outdoor facilities, consideration should be given to surfaces that withstand the elements and can be easily maintained.

Location

Quality animal management and human comfort and health protection require separation of animal facilities from personnel areas, such as offices and conference rooms. Separation can be accomplished by having the animal quarters in a separate building, wing, floor, or room. Careful planning should

make it possible to place animal-housing areas next to or near research laboratories but separated from them by barriers, such as entry locks, corridors, or floors. Additional considerations include the impact of noise and vibration generated from within the facility and from surrounding areas of the building, as well as security of the facility. Animals should be housed in facilities dedicated to or assigned for that purpose and should not be housed in laboratories merely for convenience. If animals must be maintained in a laboratory to satisfy the scientific aims of a protocol, then that space should be appropriate to house and care for the animals and its use limited to the period during which it is required. If needed, measures should be taken to minimize occupational hazards related to exposure to animals both while in the research area and during transport to and from the area.

Centralization versus Decentralization

In a physically centralized animal facility, support, care, and use areas are adjacent to the animal-housing space. When decentralized, animal housing and use occurs in space that is not solely dedicated to animal care or support, or is physically separated from the support areas and animal care personnel. Centralization often reduces operating costs, providing a more efficient flow of animal care supplies, equipment and personnel; more efficient use of environmental controls; and, less duplication of support services. Centralization generally reduces the needs for transporting animals between housing and study sites, thereby minimizing the risks of transport stress and exposure to disease agents, and generally provides greater security by providing the opportunity to control facility access and increases the ease of monitoring staff and animals.

Decentralized animal facilities generally cost more to construct because of the requirement for specialized environmental systems and controls in multiple sites. Duplicate equipment (for example, cage washers) may be needed, or soiled materials may need to be moved distances for processing. Decentralization may be preferred for certain specialized research services such as imaging, quarantine, and proximity to research facilities, or for biosecurity reasons. Decentralization may be needed to accommodate large or complex equipment, such as magnetic resonance imaging, or to permit space sharing by users from multiple facilities or institutions. The opportunity for exposure to disease agents is much greater in these situations and special consideration should be given to biosecurity including transportation to and from the site, quarantine before or after utilizing the specialized research area, and environmental and equipment decontamination. In any event, the decisions leading to a selection of physically

centralized vs. decentralized animal facilities should be made early and carefully,

- Space for administrative and supervisory personnel, including space for training and education of staff
- Showers, sinks, lockers, toilets, and break areas for personnel
- Security features, such as card-key systems, electronic surveillance, and alarms
- Areas for maintenance and repair of specialized animal housing systems and equipment

Construction Guidelines

Corridors

Corridors should be wide enough to facilitate the movement of personnel and equipment. Corridors 6-8 ft wide can accommodate the needs of most facilities. Floor-wall junctions should be designed to facilitate cleaning. Protective rails or bumpers are recommended and, if provided, should be sealed or manufactured to prevent access to vermin. In corridors leading to dog or swine housing facilities, cage-washing facilities and other high-noise areas, double-door entry vestibules or other noise traps should be considered. Similar entries are advisable for areas leading to non-human primate housing as a means to reduce the potential for escape. Double-door entry vestibules also permit air-locks in these and other areas where directional airflow is critical for containment or protection. Wherever possible, water lines, drainpipes, reheat coils and valves, electric-service connections, and other utilities should be accessible via interstitial space or through access panels or chases in corridors outside the animal rooms. Fire alarms, fire extinguishers, and telephones should be recessed, installed high enough, or be protected by protective guards to prevent damage from the movement of large equipment.

Animal-Room Doors

For safety, doors should open into animal rooms; however, if it is necessary that they open toward a corridor, there should be recessed vestibules. Doors with viewing windows may be needed for safety and other reasons. However, the ability to cover viewing windows might be considered in situations where exposure to light or hallway activities would be undesirable, e.g., to avoid disturbing the circadian rhythm. Red-tinted windows, which do not transmit specific wavelengths of visible light between corridors and animal rooms, have proved useful for mouse and rat holding rooms as both species have a limited ability to detect light in the red portions of the spectra (Jacobs et al. 2001;

Drainage

Where floor drains are used, the floors should be sloped and drain traps kept filled with liquid. To minimize prol onged increases in humidity, drainage should allow rapid removal of water and drying of surfaces (Gorton and Besch 1974). Drainpipes should be at least 4 in(10.2 cm) in diameter. In some areas, such as dog kennels and agricultural-animal facilities, larger drainpipes (>_ 6 in) are recommended. A rim- and/or trap-fl ushing drain or an in-line comminutor may be useful for the disposal of solid waste. When drains are not in use for long periods, they should be capped and sealed to prevent backflow of sewer gases, vermin, and other contaminants; lockable drain covers might be advisable for this purpose in some circumstances.

Floor drains are not essential in all animal rooms, particularly those housing rodents. Floors in such rooms can be sanitized satisfactorily by wet vacuuming or mopping with appropriate cl eaning compounds or disinfectants. However, floor drains capped when not in use may provide flexibility for future housing of non-rodent species.

Walls and Ceilings

Walls and ceilings should be smooth, moisture-resistant, nonabsorbent, and resistant to damage from impact. They should be free of cracks, of unsealed utility penetrations, and of imperfect junc tions with doors, ceilings, floors, walls, and corners. Surface materials should becapable of withstanding cleaning with

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Heating, Ventilation and Air-Conditioning (HVAC)

A properly designed and functioning HV AC system is essential to provide environmental and space pressurization control. Temperature and humidity control minimizes variations due either to changing climatic conditions or to differences in the number and kind of animals and equipment in animal holding space, i.e., room or cubicle. Pressurization assists in controlling airborne contamination and odors by providing directional airflow between spaces. Areas for quarantine, housing and use of animals exposed to hazardous materials, and housing of non-human primates should be kept under relative negative pressure, whereas areas for surgery or clean-equipment storage should be kept under relative positive pressure with clean air. HVAC systems should be designed for reliability (including re

Temperature is best regulated by having thermostatic control for each holding space. Use of zonal control for multiple spaces can result in temperature variations between spaces in the zone because of differences in animal densities within the spaces and heat gain or loss in ventilation ducts and other surfaces within the zone. Individual space control is generally accomplished by providing each space with a dedicated reheat coil. Valves controlling reheat coils should fail closed and steam coils should be avoided or be equipped with a high temperature cut-off system to prevent space overheating and animal loss with valve failure. Humidification is generally controlled and supplemented on a system or zone basis. Control of humidification in individual holding spaces may be desirable for select species with reduced tolerance for low relative (e.g, non-human primates) or high humidity (e.g ., rabbits). Holding spaces should be designed to minimize drafts and temperature gradients.

Most HVAC systems are designed for average high and low temperatures and humidities experienced in a geographic area within ±5% variation (ASHRAE 2009). Moderate fluctuations in temperature and relative humidity outside suggested ranges are generally well tolerated by most species commonly used in research as long as they are brief and infrequent. Consideration should be given to measures that minimize fluctuations in temperature and relative humidity outside the recommended ranges due to extremes in the external ambient environment. Such measures can include partial redundancy, partial air recirculation, altered ventilation rates, or the use of auxiliary equipment. In the event of an HVAC system or component failure, systems should at the minimum supply facility needs at a reduced level, address the adverse effects of loss of temperature control, and, where necessary, maintain critical pressurization gradients. It is essential that life-threatening heat accumulation or loss be prevented during mechanical failure. Temporary needs for ventilation of sheltered or outdoor facilities can usually be met with auxiliary equipment.

Air handling system intake locations should avoid entrainment of fumes from vehicles, equipment, and system exhaust. While 100% outside air is typically provided, when recirculated air is used, its quality and quantity should be in accord with recommendations in Chapter 3. The type and efficiency of supply and exhaust air treatment should be matched to the quantity and types of contaminants and to the risks that they pose. Supply air is usually filtered with 85 – 95% dust spot efficient filters (ASHRAE 2008). In select instances, higher efficiency filters, for example, HEPA, may be beneficial for recirculated supply air, and air supplied to or exhausted from specialized areas such as surgical and containment facilities (Kowalsky et al. 2002).

Power and Lighting

The electrical system should be safe and provide appropriate lighting, a sufficient number of power outlets, and suitable amperage for specialized equipment. In the event of power failure, an alternative or emergency power supply should be available to maintain critical services (e.g, the HVAC system, power to ventilated caging systems (Huerkamp et al. 2003), or life support systems for aquatic species) or support functions (e.g., freezers and isolators) in animal rooms, operating suites, and other essential areas. Consideration should be given to outfitting moveable equipment for which an uninterrupted power is essential, for example, ventilated racks, with twist-lock plugs to prevent accidental removal from the power supply.

Light fixtures, timers, switches, and outlets should be properly sealed to prevent access to vermin. Recessed energy-efficient fluorescent lights are commonly used in animal facilities. Spectral quality of lights may be important for some species when maintained in the laboratory. In these cases full spectrum lamps may be appropriate. A time-controlled lighting system should be used to ensure a uniform diurnal lighting cycle. Override systems should be equipped with automatic timeout or a warning light to indicate the system is in override mode. System performance and override functions should be regularly evaluated to ensure proper cycling. Dual-level lighting may be considered when housing species that are sensitive to high light intensity, such as albino rodents. Low intensity lighting is provided during the light phase of the diurnal cycle, whereas higher intensity lighting is provided, as needed (e.g., when personnel require enhanced visibility). Light bulbs or fixtures should be equipped with protective covers to ensure the safety of the animals and personnel. Moisture-resistant switches and outlets and ground-fault interrupters should be used in areas with high water use, such as cage-washing areas and aquarium-maintenance areas.

Storage Areas

Adequate space should be provided for storage of equipment, supplies, food, bedding, and refuse. Corridors are not appropriate storage areas. Storage space can be decreased when delivery of materials and supplies is reliable and frequent; however, it should be ample enough to accommodate storage of essential commodities to ensure the animals' uninterrupted husbandry and care (e.g., should delivery be delayed). Bedding and food should be stored in a separate area free from vermin and protected from the risk of contamination

from toxic or hazardous substances. Areas used for food storage should not be subject to elevated temperatures or relative humidity for prolonged periods. Refuse-storage areas should be separated from other storage areas. Refrigerated storage, separated from other cold storage, is essential for storage of dead animals and animal-tissue waste; this storage area should be kept below 7°C (44.6°F) to reduce putrefaction of wastes and animal carcasses. These areas should be constructed in a manner that facilitates cleaning.

Noise Control

Noise control is an important consideration in an animal facility and should be addressed during the planning stages of new facility design or renovation (see Chapter 3). Noise-producing support functions, such as cage-washing, are commonly separated from housing and experimental functions. Masonry walls, due to their density, generally have excellent sound attenuating properties; however, similar sound attenuation can be achieved using many different materials and partition designs. Generally, acoustic materials applied directly to the ceiling or as part of a suspended ceiling of an animal room present problems for sanitation and vermin control and are not recommended. However, sanitizable sound-attenuating materials bonded to walls or ceilings might be appropriate for noise control in some situations. Experience has shown that well-constructed corridor doors, sound-attenuating doors, or double-door entry vestibules can help to control the transmission of sound along corridors. An excellent resource on partition design for sound control may be found in the publication, Noise Control in Buildings: A Practical Guide for Architects and Engineers (Warnock and Quirt 1994).

Attention should be paid to attenuating noise generated by equipment (ASHRAE 2007b). Fire and environmental-monitoring alarm systems and public-address systems should be selected and positioned to minimize potential animal disturbance. The location of equipment capable of generating sound at ultrasonic frequencies is important as some species can hear such high frequencies. Selecting equipment for rodent facilities that does not generate noise in the ultrasonic range should be considered.

Vibration Control

Vibration may arise from mechanical equipment, electrical switches and other building components, or from remote sources with ground-borne transmission to

the inside. Regarding the latter, special consideration should be given to the building structure type especially if th e animal facility will be located over, under, or adjacent to subways, trains, or automobile and truck traffic. Like noise, different species can detect and be affected by vibrations of different frequencies and wavelengths. Therefore, attempts should be made to identify all vibration sources and isolate or dampen them with vibration suppression systems (ASHRAE 2007b).

Facilities for Sanitizing Materials

A dedicated, central area for sanitizing cages and ancillary equipment should be provided. Mechanical cage-washing equipment is generally needed and should be selected to match the types of caging and equipment used. Consideration should be given to such factors as:

- Location with respect to animal rooms and waste-disposal and storage areas
- Ease of access, including doors of sufficient width to facilitate movement of equipment
- Sufficient space for staging and maneuvering of equipment
- Provision for soiled waste disposal and prewashing activities
- Ease of cleaning and disinfection of the area
- Traffic flow that separates animals and equipment moving between clean and soiled areas
- Air pressurization between partitioned spaces to reduce the potential of cross contamination between soiled and clean equipment
- Insulation of Ef <0e
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Environmental Monitoring

Monitoring of environmental conditions within animal holding spaces and other environmentally sensitive areas within the facility should be considered. Automated monitoring systems, which notify personnel of excursions in environmental conditions, including temperature and photoperiod, are advisable to prevent animal loss or physiologic changes which may occur as a result of system malfunction. If provided, system function and accuracy should be regularly verified.

Special Facilities

Surgery

The design of a surgical facility should accommodate the species to be operated on and the complexity of the procedures to be performed (Hessler 1991; see also Appendix A, Design and Construction of Animal Facilities). For most survival surgery performed on rodents and other small species such as aquatics and birds, an animal procedure laboratory, dedicated to surgery and related activities when used for this purpose and managed to minimize contamination from other activities conducted within the room at other times, is recommended. The surgical facility, including that used for rodents, by necessity becomes larger and more complex as the number and size of animals or the complexity of procedures increase. For instance, a larger facility may be required for procedures on agricultural species, to accommodate large surgical teams, imaging devices, robotic surgical systems, and/or laparoscopic equipment towers. Surgical facilities for agricultural species may additionally require floor drains, special restraint devices and hydraulic operating tables. The association of surgical facilities with diagnostic laboratories, imaging facilities, animal housing, staff offices, and so on should be considered in the overall context of the complexity of the surgical program. Surgical facilities should be sufficiently separate from other areas to minimize unnecessary traffic and decrease the potential for contamination (Humphreys 1993). Centralized surgical facilities are cost-effective in equipment, conservation of space and personnel resources, and reduced transit of animals. They also sustain enhanced personnel safety and enhanced professional oversight of both facilities and procedures.

For most surgical programs, functional components of aseptic surgery include surgical support, animal preparation, surgeon's scrub, operating room,

and postoperative recovery. The areas that support those functions should be designed to minimize traffic flow and separate the related, nonsurgical activities from the surgical procedure in the operating room. The separation is best achieved by physical barriers (AORN 1993) but might also be achieved by distance between areas or by the timing of appropriate cleaning and disinfection between activities. The number of personnel and their level of activity have been shown to be directly related to the level of bacterial contamination and the incidence of postoperative wound infection (Fitzgerald 1979). Traffic in the operating room itself can be reduced by the installation of an observation window, a communication system (such as an intercom system), and judicious location of doors.

Control of contamination and ease of cleaning should be key considerations in the design of a surgical facility. The interior surfaces should be constructed of materials that are monolithic and impervious to moisture. Ventilation systems supplying filtered air at positive pressure can reduce the risk of postoperative infection (Ayscue 1986; Bartley 1993; Schonholtz 1976). Careful location of air supply and exhaust ducts and appropriate room-ventilation rates are also recommended to minimize contamination (Ayliffe 1991; Bartley 1993; Holton and Ridgway 1993; Humphreys 1993). To facilitate cleaning, the operating rooms should have as little fixed equipment as possible (Schonholtz 1976; UFAW 1989). Other features of the operating room to consider include surgical lights to provide adequate illumination (Ayscue 1986), sufficient electric outlets for support equipment, gases to support anesthesia, surgical procedures, and gas-powered equipment, vacuum, and gas-scavenging capability.

The surgical-support area should be designed for washing and sterilizing instruments and for storing instruments and supplies. Autoclaves are commonly placed in this area. It is often desirable to have a large sink in the animal-preparation area to facilitate cleaning of the animal and the operative site. A dressing area should be provided for personnel to change into surgical attire; a multipurpose locker room can serve this function. There should be a scrub area for surgeons, equipped with foot, knee, or electric-eye surgical sinks (Knecht et al. 1981). To minimize the potential for contamination of the surgical site by aerosols generated during scrubbing, the scrub area should usually be outside the operating room and animal preparation area.

A postoperative-recovery area should provide the physical environment to support the needs of the animal during the period of anesthetic and immediate postsurgical recovery and should be so placed as to allow adequate observation of the animal during this period. The electric and mechanical requirements of monitoring and support equipment should be considered. The type of caging and support equipment will depend on the species and types of procedures but

Imaging

In vivo imaging offers non-invasive methodology for evaluating structure and function at the level of the whole animal, tissue, or cell, and allows for the sequential study of temporal events (Chatham and Blackband 2001; Cherry and Gambhir 2001). Imaging devices vary in the technology used to generate an image, body targets imaged, resolution, hazard exposure and requirements for use. Imaging devices may be self shielded and require no modifications of the surrounding structure to operate safely, or they may require concrete, solid core masonry, lead-, steel-, or copper-lined walls, or other construction features to operate safely or minimize interference with devices and activities in adjacent areas. As these devices are often expensive to acquire and maintain, and may require specialized support space and highly trained personnel to operate, shared animal imaging resources may be preferable. Consideration should be given to the location of the imaging resource. Whether located within the animal facility or in a separate location, cross contamination between groups of animals, different animal species, or between animals and humans (if the device is used for both animal and human subjects) is possible because these devices may be difficult to sanitize (Klaunberg and Davis 2008; Lipman 2006). If the imaging resource is located outside of the animal facility, appropriate transportation methods and routes should be developed to avoid inappropriate exposure of humans to animals in transit. If possible, animals should not be moved past offices, lunch rooms, or public areas where people are likely to be present.

As imaging may require the subject to be immobile, often for extended time periods during image acquisition, provision should be made for delivery of anesthetics and carrier gas and to scavenge waste anesthetic gas and provision for adequate animal monitoring (Balaban and Hampshire 2001). Remote storage of gas tanks is generally required in facilities using magnetic resonance (MR) scanners as the magnetic field requires ferrous materials to be maintained a safe distance away from the magnet. Site selection of MR scanners requires special attention because of their weight, the fringe field generated (especially from

emit ionizing or magnetic radiation. Imaging devices with difficult to sanitize components should be covered with a disposable or sanitizable material when not in use.

Whole Body Irradiation

Total body irradiation of small laboratory animals may be accomplished using devices that emit either gamma- or X-rays. Devices are usually self shielded and, as a result of the shielding material weight, may require special site considerations. Devices containing gamma-emitting sources are subject to regulations, which require adherence to specific security, monitoring, and personnel clearance requirements (NRC 2008). The site selected for irradiators should also take into consideration whether they are to be used for animals and biologics, as well as the source and microbial status of the animals to be irradiated. Locating them within the animal facility may require access be provided to personnel who would normally not require it or necessitate bringing animals into a facility where they are not normally housed.

Hazardous Agent Containment

The goal of containment is to "reduce or eliminate exposure of laboratory workers, other persons, and the outside environment to potential hazardous agents" (DHHS 2007). This is accomplished by employing appropriate practices and equipment, vaccinating personnel if a vaccine is available, and through the proper design and operation of the physical plant. Animal facilities used to study biological agents that are infectious to humans are categorized into different biosafety levels of escalating

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Lieberman D. 1995. Biohazards Management Handbook, 2nd ed. New York: Marcel Dekker.

Lipman NS. 2006. Design and management ofresearch facilities for mice. In: Fox J,

Vogelweid CM, Hill JB, Shea RA, Johnson DB 2005. Earthquakes and building design: A primer for the laboratory animal professional. Lab Anim (NY) 34:35-42.

Warnock ACC, Quirt JD. 1994. Chapter 5: Airborne Sound Insulation and Appendix 5 Tables on Sound Transmission Loss. In: Harris CM, ed. Noise Control in Buildings: A Practical Guide for Archit ects and Engineers. Columbus OH: McGraw-Hill. p 5.1-5.32; 5.33-5.77.

APPENDIX A: Additional Selected References

USE OF LABORATORY ANIMALS
- x Alternatives
- x Ethics and Welfare
- x Experimental Design and Statistics
- x Research and Testing Methodology

PROGRAM MANAGEMENT
- x General References
- x Laws, Regulations and Policies
- x Education
- x Monitoring the Care and Use of Animals
- x Occupational Health and Safety

ENVIRONMENT, HOUSING and MANAGEMENT
- x General References
- x Environmental Enrichment
- x Genetics and Genetically Modified Animals
- x Species-Specific References – Environment, Housing and Management
    - o Agricultural Animals
    - o Amphibians, Reptiles and Fish
    - o Birds
    - o Cats and Dogs
    - o Exotic, Wild and Zoo Animals
    - o Nonhuman Primates
    - o Rodents and Rabbits
    - o Other Animals

VETERINARY CARE
- x Transportation
- x Anesthesia, Pain and Surgery
- x Disease Surveillance, Diagnosis and Treatment
- x Pathology, Clinical Pathology, and Parasitology
- x Species-Specific References – Veterinary Care
    - o Agricultural Animals
    - o Amphibians, Reptiles and Fish
    - o Birds
    - o Cats and Dogs

- Exotic, Wild and Zoo Animals
- Nonhuman Primates
- Rodents and Rabbits

DESIGN and CONSTRUCTION of ANIMAL FACILITIES

USE of LABORATORY ANIMALS

Alternatives

Alternative Methods for Toxicity Testing: Regulatory Policy Issues. EPA 230/12 85 029. NTIS PB8 6 113404/AS. Washington: Office of Policy, Planning and Evaluation, US Environmental Protection Agency 20460.

Alternatives to Animal Use in Research, Testing, and Education. 1986. Office of Technology Assessment (OTA BA 273). Washington: Government Printing Office.

Alternatives to Current Uses of Animals in Research, Safety Testing, and Education. 1986. Stephens ML. Washington: Humane Society of the United States.

Alternatives to Pain in Experiments on Animals. 1980. Pratt D. Argus Archives.

Alternative Toxicological Methods. 2003. Salem H, Katz S. Boca Raton FL: CRC Press.

Animals and Alternatives in Testing: History, Science, and Ethics. 1994. Zurlo J, Rudacille D, Goldberg AM. New York: Mary Ann Liebert Publishers.

Future improvements: Replacement in vitro methods. 2002. Balls M. ILAR J 43(Suppl):S69-S73.

ICCVAM Recommendations on In Vitro Method s for Assessing Acute Systemic Toxicity. 2001. Available at: http://iccvam.niehs.nih.gov/docs/acutetox_docs/finalrpt//finappi2.pdf; accessed January 24, 2010.

Regulatory Testing and Animal Welfare. 2002. ILAR J 43(Supplement).

Implementation of the 3Rs (refinement, reduction, and replacement): Validation and regulatory acceptance considerations for alternative toxicological test methods. 2002. Schechtman L. ILAR J 43:S85-S94.

Incorporating the 3Rs into regulatory scientif ic practices. 2002. Sterling S, Rispin A. ILAR J 43:S18-S20.

Refinement, reduction, and replacement of animal use for regulatory testing: Future improvements and implementation with in the regulatory framework. 2002. Richmond J. ILAR J 43:S63-S68.

The Role of the Interagency Coordinating Committee on the Validation of Alternative

Ethics and Welfare

An additional "R": Remembering the animals. 2002. Iliff SA. ILAR J 43:38-47.
Animal Liberation, 2nd ed. 1990. Singer P. New York: New York Review Book (distributed by Random House).
Animal Rights and Human Obligations, 2nd ed. 1989. Regan T, Singer P. Englewood Cliffs NJ: Prentice-Hall.
Animal Welfare: Competing Conceptions and Their Ethical Implications. 2008. Haynes RP. Springer.
Animals and Why They Matter. 1983. Midgley M. University of Georgia Press.
Applied Ethics in Animal Research: Philosophy, Regulation, and Laboratory Applications. 2002. Gluck JP, DiPasqualeT, Orlans FB. West Lafayette IN: Purdue University Press.
The Assessment and 'Weighing' of Costs. In: Lives in the Balance: The Ethics of Using Animals in Biomedical Research. 1991. Smith JA, Boyd K, eds. London: Oxford University Press.
Bioethics, animal research, and ethicaltheory. Russow L-M. 1999. ILAR J 40:15-21.
Cost of Caring: Recognizing Human Emotions in the Care of Laboratory Animals. 2001. American Association for Laboratory Animal Science, Memphis, TN.
Ethics and pain research in animals. Tannenbaum J. 1999. ILAR J 40:97-110.
Ethical aspects of relationships between humans and research animals. Herzog H. 2002. ILAR J 43:27-32.
Ethical implications of the human-animal bond in the laboratory. Russow L-M. 2002. ILAR 43:33-37.
Ethical scores for animal procedures. 1992. Porter D. Nature 356:101-102.
Fish and welfare: Do fish have the capacity for pain perception and suffering? 2004. Braithwaite VA, Huntingford FA. Anim Welf 13:S87-S92.
Guidance notes on retrospective review: A discussion document prepared by the LASA Ethics and Training Group. 2004. Jennings M, Howard B. Tamworth UK: Laboratory Animal Science Association.
Guidelines for the ethical use of animals in applied ethology studies. 2003. Sherwin CM, Christiansen SB, Duncan IJ, Erhard HW, Lay DC Jr, Mench JA, O'Connor CE, Petherick JC. Appl Anim Behav Sci 81:291-305.
Guidelines to Promote the Wellbeing of Animals Used for Scientific Purposes: The Assessment and Alleviation of Pain and Distress in Research Animals. 2008. National Health and Medical Research Council, Australian Government. Available at: www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/ea18.pdf; accessed January 24, 2010.
How and why animals matter. Donnelley S. 1999. ILAR J 40:22-28.
In the Name of Science: Issues in Responsible Animal Experimentation. 1993. Orlans FB. New York: Oxford University Press.
International Guiding Principles for Biomedical Research Involving Animals. 1985. Council for International Organizations of Medical Sciences (CIOMS). Available at: www.cioms.ch/frame_1985_texts_of_guidelines.htm; accessed May 21, 2010.

Moral Status: Obligations to Persons and Other Living Things. 1997. Warren MA. Gloucestershire UK: Clarendon Press.
Of Mice, Models, and Men: A Critical Evalua tion of Animal Research. 1984. Rowan AN. Albany: State University of New York Press.
Painful dilemmas: The ethics of animal-based pain research. 2009. Magalhaes-Sant'Ana M, Sandoe P, Olsson IAS. Anim Welf 18:49-63
Principles and guidelines for the developm ent of a science-based decision making process facilitating the implementation of the 3Rs by governmental regulators. 2002. Gauthier C. ILAR J 43(Suppl):S99-S104.
Principles and practice in ethical review of animal experiments across Europe: Summary of the report of the FELASA Working Gr oup on Ethical Evaluation of Animal Experiments. 2007. Smith JA, van den Broek FAR, Canto Martorell J, Hackbarth H, Ruksenas O, Zeller W. Lab Anim 41:143-160.
Recognition and Alleviation of Distress in La boratory Animals. 2008. National Research Council. Washington: National Academies Press.
Refinement of the use of non-human primates in scientific research, Part I: The influence of humans. 2006. Rennie AE, Buchanan-Smith HM. Anim Welf 15:203-213.
Review of Cost-benefit Assessment in the Use of Animals in Research. 2003. Animal Procedures Committee. London. Available at: http://apc.homeoffice.gov.uk/reference/ costbenefit.pdf; accessed January 24, 2010.
Roots of concern with non-human animals in biomedical ethics. Sideris L, McCarthy CR, Smith DH. 1999. ILAR J 40:3-14.
Science, Medicine, and Animals. 2004. National Research Council. Washington: National Academies Press.
Taking Animals Seriously: Mental Life and Moral Status. 1996. DeGrazia D. Cambridge University Press.
The Ethics of Research Involving Animals. 2005. Nuffield Council on Bioethics. London.
The Experimental Animal in Biomedical Research, vol I: A Survey of Scientific and Ethical Issues for Investigators. 1990. Rollin BE, Kesel ML, eds. Boca Raton FL: CRC Press.
The Frankenstein Syndrome: Ethical and Social Issues in the Genetic Engineering of Animals. 1995. Rollin BE. New York: Cambridge University Press.
The regulation of animal research and the emergence of animal ethics: A conceptual history. 2006. Rollin BE. Theor Med Bioeth 27:285-304.
The Three Rs: A journey or a destination? Richmond J. 2000. ATLA 28:761-773.

Experimental Design and Statistics

Animal welfare and the statistical consultant. 1993. Engeman RM, Shumake SA. Am Statistician 47:229-233.
Appropriate animal numbers in biomedical research in light of animal welfare considerations. 1991. Mann MD, Crouse DA, Prentice ED. Lab Anim Sci 41:6-14.
Common errors in the statistical analysis of experimental data. 2002. Festing MFW. In: Balls M, van Zeller A-M, Halder ME, eds. Progress in the Reduction, Refinement and Replacement of Animal Experiment ation: Developments in Animal and Veterinary Science. vol 31a. Amsterdam: Elsevier. p 753-758.

Experimental Design and Statistics in Biomedical Research. 2002. ILAR J 43(4).
Experimental design and statistics in biomedical research. Festing MFW. 2002. ILAR J 43:191-258.
Guidelines for the design and statistical analysis of experiments using laboratory animals. 2002. Festing MFW, Altman DG. ILAR J 43:244-258.
Practical aspects to experimental design in animal research. 2002. Johnson PD, Besselsen DG. ILAR J 43:202-206.
Sample size determination. 2002. Dell RB, Holleran S, Ramakrishnan R. ILAR J 43:207-213.
The control of variability. 2002. Howard BR. ILAR J 43:194-201.
The role of ancillary variables in the design, analysis, and interpretation of animal experiments. 2002. Gaines Das R. ILAR J 43:214-222.
The use of factorial designs to optimize animal experiments and reduce animal use. 2002. Shaw R, Festing MFW, Peers I, Furlong L. ILAR J 43:223-232.
Primer of Biostatistics, 6th ed. 2005. Glantz SA. New York: McGraw-Hill.
Sample Size Determination (Appendix A). 2003. National Research Council. In: Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research. Washington: National Academies Press. p 175-180.
Statistical Methods, 8th ed. 1989. Snedecor GW, Cochran WG. Ames: Iowa State Press.
The Design and Analysis of Long-Term Animal Experiments. 1986. Gart JJ, Krewski D, Lee PN, Tarone RE, Wahrendorf J. Lyon: International Agency for Research on Cancer.
The Design of Animal Experiments: Reducing the Use of Animals in Research through Better Experimental Design. 2002. Festing MFW, Overend P, Gaines Das R, Cortina Borja M, Berdoy M. London: Royal Society of Medicine Press.
What is it like to be a rat? Rat sensory perception and its implications for experimental design and rat welfare. 2008. Burn CC. Appl Anim Behav Sci 112: 1-32.

Research and Testing Methodology

Adjuvants and Antibody Production. 1995. ILAR J 37(3).
Advanced Physiological Monitoring in Rodents. 2002. ILAR J 43(3).
Mechanical ventilation for imaging the small animal. Hedlund LW, Johnson GA. 2002. ILAR J 43:159-174.
Miniaturization: An overview of biotechnologies for monitoring the physiology and pathophysiology of rodent animal models. 2002. Goode TL, Klein HJ. ILAR J 43:136-146.
Casarett and Doull's Toxicology: The Basic Science of Poisons, 8th ed. 2007. Klaassen CD. New York: McGraw-Hill.
Categorising the Severity of Scientific Procedures on Animals: Summary and Reports from Three Roundtable Discussions. 2004. Smith JA, Jennings M, eds. West Sussex UK: RSPCA, Research Animals Department. Available at: www.boyd-group.demon.co.uk/severity_report.pdf; accessed January 24, 2010.
Clinical considerations in rodent bioimaging. 2004. Colby LA, Morenko BJ. Comp Med 54:623-30.

Effects of Freund's complete adjuvant on the physiology, histology, and activity of New Zealand white rabbits. 2004. Halliday LC, Artwohl JE, Bunte RM, Ramakrishnan V, Bennett BT. Contemp Top Lab Anim Sci 43:8-13.

Ethological research techniques and methods. 1998. Novak MA, West M, Bayne KL, Suomi SJ. In: Hart L, ed. Responsible Conduct of Research in Animal Behavior. New York: Oxford University Press. p 51-66.

Genetic Engineering and Animal Welfare: Preparing for the 21st Century. 1999. Gonder JC, Prentice ED, Russow L-M, eds. Greenbelt MD: Scientists Center for Animal Welfare.

Guidance for Industry and Other Stakeholders : Toxicological Principles for the Safety

Integration of safety pharmacology endpoints into toxicology studies. 2002. Luft J, Bode G. Fundam Clin Pharmacol 16:91-103.
Methods and Welfare Considerations in Behavio

The International Symposium on Regulatory Testing and Animal Welfare: Recommendations on best scientific practices for animal care in regulatory toxicology. 2002. Morris T, Goulet S, Morton D. ILAR J 43:S123-S125.

The International Symposium on Regulatory Testing and Animal Welfare: Recommendations on best scientific practices for biologicals: Safety and potency evaluations. 2002. Cussler K,Kulpa J, Calver J. ILAR J 43:S126-S128.

The International Symposium on Regulatory Testing and Animal Welfare: Recommendations on best scientific practices for subchronic/chronic toxicity and carcinogenicity testing. 2002. Combes R, Schechtman L, Stokes WS, Blakey D. ILAR J 43:S112-S117.

The safety assessment process: Setting the scene—An FDA perspective. 2002. Schechtman L. ILAR J 43:S5-S10.

Tiered testing strategies: Acute local toxicity. 2002. Stitzel K. ILAR J 43:S21-S26.

The use of laboratory animals in toxicologic research. 2001. White WJ. In: Principles and Methods in Toxicology, Hays AW, ed. Philadelphia: Taylor and Francis. p 773-818.

The use of radiotelemetry in small laboratory animals: Recent advances. 2001. Kramer K, Kinter L, Brockway BP, Voss HP, Remie R, VanZutphen BL. Contemp Top Lab Anim Sci 40:8-16.

PROGRAM MANAGEMENT

General References

Cost Analysis and Rate Setting Manual for Animal Resource Facilities. 2000. National Center for Research Resources. Available at: www.ncrr.nih.gov/publications/comparative_medicine/CARS.pdf; accessed January 24, 2010.

Disaster Planning and Management. 2010. ILAR J 51(2).

Crisis planning to manage risks posed by animal rights extremists. 2010. Bailey MR, Rich BA, Bennett BT. ILAR J 51:138-148.

Disaster preparedness in biocontainmnet animal research facilities: Developing and implementing an incident response plan (IPR). 2010. Swearengen JR, Vargas KJ, Tate MK, Linde NS. ILAR J 51:120-126.

Introduction: Disaster planning and management: A practicum. 2010. Bayne KA. ILAR J 51:101-103.

IACUC considerations: You have a disaster plan but are you really prepared? 2010. Wingfield WE, Rollin BE, Bowen RA. ILAR J 51:164-170.

Management of rodent viral disease outbreaks: One institution's (r)evolution. 2010. Smith AL. ILAR J 51:127-137.

Tropical storm and hurricane recovery and preparedness strategies. 2010. Goodwin BS Jr, Donaho JC. ILAR J 51:104-119.

Verification of poultry carcass composting research through application during actual avian influenza outbreaks. 2010. Flory GA, Peer RW. ILAR J 51:149-157.

Wildlife evacuation: Ou trunning the witch's curse—One animal center's experience. 2010. Arms MM, Van Zante JD. ILAR J 51:158-163.

Available at: www.rspca.org.uk/ImageLocator/LocateAsset?asset=documentandassetId=1232713599355andmode=prd; accessed January 24, 2010.

Animal Care and Use Committees Bibliography . 1992. Allen T, Clingerman K. Beltsville MD: US Department of Agriculture, National Agricultural Library (Publication #SRB92 16).

Best practices for animal care committees andanimal use oversight. 2002. De Haven R. ILAR J 43(Suppl):S59-S62.

Community representatives and nonscientists on the IACUC: What difference should it make? 1999. Dresser R. ILAR J 40:29-33.

Effective animal care and use committees.1987. Orlans FB, Simmonds RC, Dodds WJ, eds. In: Laboratory Animal Science, Special Issue, January 1987. Published in

animal use oversight. 2002. Richmond J, Fletch A, Van Tongerloo R. ILAR J 43(Suppl):S129-S132.

Occupational Health and Safety

Air quality in an animal facility: Particulates , ammonia, and volatile organic compounds. 1996. Kacergis JB, Jones RB, Reeb CK, Turner WA, Ohman JL, Ardman MR, Paigen B. Am Ind Hyg Assoc J 57:634-640.

Facilities; Part 265, Interim Status Standards for Owners and Operators of Hazardous Waste Treatment, Storage, and Disposal Facilities; and Part 270, EPA-Administered Permit Programs: The Hazardous Waste Permit Program. Washington: Office of the Federal Register. (Part 260 updated April 1994; 261 and 270 updated August 1994; 264 and 265 updated June 1994; 262 and 263 updated 1993)

Evaluation of individually ventilated cage sy stems for laboratory rodents: Occupational health aspects. 2001. Renstrom A, Bjoring G, Hoglund AU. Lab Anim 35:42-50.

Industrial Biocides. 1988. Payne KR, ed. New York: Wiley.

Infectious Disease Research in the Age of Biodefense. ILAR J 46(1).

Issues related to the use of animals in biocontainment research facilities. Copps J. 2005. ILAR J 46:34-43.

Select agent regulations. Gonder JC. 2005. ILAR J 46:4-7.

Laboratory safety for arboviruses and certain other viruses of vertebrates. 1980. Subcommittee on Arbovirus Safety, American Committee on Arthropod-Borne Viruses. Am J Trop Med Hyg 29:1359-1381.

Mechanism and epidemiology of laboratory animal allergy. 2001. Bush RD. ILAR J 42:4-11.

National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses.

The growing pains of biodefense. 2003. Birmingham K. J Clin Invest 112:970-971.
Zoonoses and Communicable Diseases Common to Man and Animals. 2003. Acha PN, Szyfres B. Washington: Pan American Health Organization.

ENVIRONMENT, HOUSING and MANAGEMENT

General References

Biomedical Investigator's Handbook for Researchers Using Animal Models. 1987. Washington: Foundation for Biomedical Research.
Disinfection in Veterinary and Farm Animals Practice. 1987. Linton AH, Hugo WB, Russell AD, eds. Oxford: Blackwell Scientific Publications.
Efficacy of vaporized hydrogen peroxide against exotic animal viruses. 1997. Heckert RA, Best M, Jordan LT, Dulac GC, Eddington DL, Sterritt WG. Appl and Envir Micro 63:3916-3918.
The Experimental Animal in Biomedical Research, vol II: Care, Husbandry, and Well-being: An Overview by Species. 1995.Rollin BE, Kesel ML, eds. Boca Raton FL: CRC Press.
Guidelines for the treatment of animals in behavioral research and teaching. 1995. Animal Behavior Society. Anim Behav 49:277-282.
Handbook of Disinfectants and Antiseptics. 1996. Ascenzi JM, ed. New York: Marcel Dekker.
Handbook of Laboratory Animal Science, 2nd ed. 2003. Essential Principles and Practices, vol 1. Boca Raton FL: CRC Press.
IESNA Lighting Handbook, 9th ed. 2000. Illuminating Engineering Society of North America. New York.
Laboratory Animals. 1995. Tuffery AA. London: John Wiley.
Laboratory Animals: An Annotated Bibliography of Informational Resources Covering Medicine, Science (Including Husbandry), Technology. 1971. Cass JS, ed. New York: Hafner Publishing.
Laboratory Animals: An Introduction for New Experimenters. 1987. Tuffey AA, ed. Chichester: Wiley Interscience.
Managing the Laboratory Animal Facility, 2nd ed. 2009. Silverman J, ed. Boca Raton FL: CRC Press.
Microbiological Aspects of Biofilms and Drinking Water. 2000. Percival SL, Walker JT, Hunter PR. Boca Raton FL: CRC Press.
Pheromones and Reproduction in Mammals. 1983. Vandenbergh JG, ed. New York: Academic Press.
Practical Animal Handling. 1991. Anderson RS, Edney ATB, eds. Elmsford NY: Pergamon.
Recent advances in sterilization. 1998. Lagergren ER. J Infect Control (Asia) 1:11-30.
UFAW Handbook on the Care and Management of Laboratory Animals, 7th ed, vol 1: Terrestrial Vertebrates. 1999. Universities Federation for Animal Welfare. Blackwell.

Environmental Enrichment

A novel approach for documentation and evalua tion of activity patterns in owl monkeys during development of environmental enrichment programs. 2003. Kondo SY, Yudko EB, Magee LK. Contemp Top Lab Anim Sci 42:17-21.

A review of environmental enrichment for pi gs housed in intensive housing systems. 2009. van de Weerd HA, Day JEL. Appl Anim Behav Sci 116:1-20.

A review of environmental enrichment stra tegies for single-caged nonhuman primates. 1989. Fajzi K, Reinhardt V, Smith MD. Lab Anim 18:23-35.

A targeted approach to developing envi ronmental enrichment for two strains of laboratory mice. 2008. Nicol CJ, Brockleb ank S, Mendl M, Sherwin C. Appl Anim Behav Sci 110:341-353.

Annotated Bibliography on Refinement an d Environmental Enrichment for Primates Kept in Laboratories, 8th ed. 2005. Reinhardt V, Reinhardt A. Washington: Animal Welfare Institute.

Artificial turf foraging boards as enviro nmental enrichment fo r pair-housed female squirrel monkeys. 2000. Fekete JM, Norcross JL, Newman JD. Contemp Top Lab Anim Sci 39:22-26.

Assessment of the use of two commercially available environmental enrichments by laboratory mice by preference testing. 2005. Van Loo PL, Blom HJ, Meijer MK, Baumans V. Lab Anim 39:58-67.

Behavioural effects of environmental enrich ment for individually caged rabbits. 1997. Lidfors L. Appl Anim Behav Sci 52:17-169.

Can puzzle feeders be used as cognitive screening instruments? Differential performance of young and aged female monkeys on a puzzle feeder task. 1999. Watson SL, Shively CA, Voytko ML. Am J Primatol 49:195-202.

Effectiveness of video of conspecifics as a reward for socially housed bonnet macaques (Macaca radiata). 2004. Brannon E, Andrews M, Rosenblum L. Percept Motor Skills 98(3-1):849-858.

Effects of a cage enrichment program on heart rate, blood pressure, and activity of male Sprague-Dawley and spontaneously hypertensive rats monitored by radiotelemetry. 2005. Sharp J, Azar T, Lawson D. Contemp Top Lab Anim Sci 44:32-40.

Effects of different forms of environmental enrichment on behavioral, endocrinological, and immunological parameters in male mice. 2003. Marashi V, Barnekow A, Ossendorf E, Sachser N. Horm Behav 43:281-292.

Effects of environmental enrichment for mice : Variation in experimental results. 2002. Van de Weerd HA, Aarsen EL, Mulder A, Kruitwagen CL, Hendriksen CF, Baumans V. J Appl Anim Welf Sci 5:87-109.

Effects of environmental enrichment on males of a docile inbred strain of mice. 2004. Marashi V, Barnekow A, Sachser N. Physiol-Behav 82:765-776.

Effects of puzzle feeders on pathological behavior in individually housed rhesus monkeys. 1998. Novak MA, Kinsey JH, Jorgensen MJ, Hazen TJ. Am J Primatol 46:213-227.

Enriching the environment of the laboratory cat. 1995. AWIC Resource Series, No. 2: Environmental Enrichment Informatio n Resources for Laboratory Animals—

Birds, Cats, Dogs, Farm Animals, Ferrets, Rabbits, and Rodents. McCune S. p 27-33.

Enrichment and aggression in primates. 2006. Honess PE, Marin CM. Neurosci Biobehav Rev 30:413-436.

Enrichment of laboratory caging for rats: A review. 2004. Patterson-Kane EF. Anim Welf 13:209-214.

Enrichment strategies for laboratory animals. 2005. ILAR J 46(2).

Enrichment and nonhuman primates: “First, do no harm.” 2005. Nelson RJ, Mandrell TD. ILAR J 46:171-177.

Environmental enrichment for laboratory rodents and rabbits: Requirements of rodents, rabbits, and research. 2005. Baumans V. ILAR J 46:162-170.

Environmental enrichment for nonhuman primates. Lutz CK, Novak MA. 2005. ILAR J 46:178-191.

Environmental Enrichment Information Resources for Nonhuman Primates: 1987-1992. 1992. National Agricultural Library, National Library of Medicine, and Primate Information Center. Beltsville MD: National Agricultural Library.

Environmental Enrichment for Captive Animals. 2003. Young RJ. Oxford: Blackwell Science.

Environmental Enrichment for Caged Rhesus Macaques, 2

Genetically Engineered Mice Handbook. 2006. Sundberg JP, Ichiki T, eds. Boca Raton FL: CRC Press.

Genetically modified animals: What welfare problems do they face? 2003. Buehr M, Hjorth JP. J Appl Anim Welf Sci 6:319-338.

Genetics and Probability in Animal Breeding Experiments. 1981. Green EL. New York: Oxford University Press.

Gnotobiology and breeding techniques. 2004. Hardy P. In: The Laboratory Mouse, Hedrich H, ed. London: Elsevier. p 409-433.

Species-Specific References – Environment, Housing and Management

Agricultural Animals

Behavior of Domestic Animals. 1985. Hart BL. New York: WH Freeman.

Cattle: Good Practice for Housing and Care, 1st ed. 2008. RSPCA, Research Animals Department. Available at: http://content.www.rspca.org.uk/cmsprd

Responsiveness, behavioural arousal and awareness in fetal and newborn lambs: Experimental, practical and therapeutic implications. 2003. Mellor DJ, Gregory NG. NZ Vet J 51:2-13.

Restraint of Domestic Animals. 1991. Sonnshagen TF. American Veterinary Publications.

Ruminants: Cattle, Sheep, and Goats. 1974. Guidelines for the Breeding, Care and Management of Laboratory Animals. National Research Council. Washington: National Academy of Sciences.

Sheep: Good Practice for Housing and Care, 2nd ed. 2008. RSPCA, Research Animals Department. Available at: http://content.www.rspca.org.uk/cmsprd

Current issues in fish welfare. 2006. Huntingford FA, Adams C, Braithwaite VA, Kadri S, Pottinger TG, Sandøe P, Turnbull JF. J Fish Biol 68:332-372.

Enrichment for a captive environment: The *Xenopus laevis* 2004. Brown MJ, Nixon RM. Anim Technol Welf 3:87-95.

Fish, Amphibians, and Reptiles. 1995. ILAR J 37(4).

Guidelines for the care and use of fish in research. 1995. Dettlaff LJ, Srinivas S, Whitaker BR, Andrews C, Hecker B, Kane AS, Reimschuessel R. ILAR J 37:159-173.

Fish Models in Biomedical Research. 2001. ILAR J 42(4).

A fish model of renal regeneration and development. 2001. Reimschuessel R. ILAR J 42:285-291, 305-308.

Development of sensory systems in zebrafish (*Danio rerio*). 2001. Moorman SJ. ILAR J 42:292-298.

Mechanistic considerations in small fish carcinogenicity testing. 2001. Law JM. ILAR J 42:274-284.

Transgenic fish as models in environmental toxicology. 2001. Winn RN. ILAR J 42:322-329.

Fish Pathology, 2nd ed. 1989. Roberts RJ, ed. London: Saunders.

Frogs and toads as experimental animals. 1999. Tyler MJ. ANZCCART News 12(1) Insert.

The male red-sided garter snake (Thamnophis sirtalis parietalis): Reproductive pattern and behavior. 2004. Krohmer RW. ILAR J 45:65-74.

Tracing the evolution of brain and behavio r using two related species of whiptail lizards: Cnemidophorus uniparens and Cnemidophorus inornatus. 2004. Woolley SC, Sakata JT, Crews D. ILAR J 45:46-53.

Safeguarding the many guises of farmed fish welfare. 2007. Turnbull JF, Kadri S. Dis Aquat Org 75:173-182.

Stress and the welfare of cultured fish. 2004. Conte FS. Appl Anim Behav Sci 86:205-223.

Best practice in the accommodation and care of primates used in scientific procedures. 2004. MRC Ethics Guide. London: Medical Research Council.

Cage sizes for tamarins in the laboratory. 2004. Prescott MJ, Buchanan-Smith HM. Anim Welf 13:151-157.

Captivity and Behavior: Primates in Breeding Colonies, Laboratories and Zoos. 1979. Erwin J, Maple TL, Mitchell G, eds. New York: Van Nostrand.

Care and Management of Chimpanzees (Pan troglodytes) in Captive Environments. 1992. Fulk R, Garland C, eds. Asheboro: North Carolina Zoological Society.

Comfortable quarters for nonhuman primates in research institutions. 2002. Reinhardt V. In: Comfortable Quarters for Laboratory Animals, 9th ed. Washington: Animal Welfare Institute. p 65-77.

Creating housing to meet the behavioral needs of long-tailed macaques. 2008. Waitt CD, Honess PE, Bushmitz M. Laboratory Primate Newsletter 47(4): 1-5. Available at: www.brown.edu/Research/Primate/lpn47-4.html; accessed January 24, 2010.

Handbook of Primate Husbandry and Welfare. 2005. Wolfensohn S, Honess P. Ames IA: Blackwell Publishing.

Handbook of Squirrel Monkey Research. 1985. Rosenblum LA, Coe CL, eds. New York: Plenum Press.

Housing and care of monkeys and apes in laboratories: Adaptations allowing essential

Comfortable quarters for hamsters in research institutions. 2002. Kuhnen G. In: Comfortable Quarters for Laboratory Animals, 9th ed. Washington: Animal Welfare Institute. p 33-37.

Comfortable quarters for mice in research institutions. 2002. Sherwin CM. In: Comfortable Quarters for Laboratory Animals, 9th ed. Washington: Animal Welfare Institute. p 6-17.

Comfortable quarters for rabbits in research institutions. 2002. Boers K, Gray G, Love J, Mahmutovic Z, McCormick S, Turcotte N, Zhang Y. In: Comfortable Quarters for Laboratory Animals, 9th ed. Washington: Animal Welfare Institute. p 43-49.

Comfortable quarters for rats in research institutions. 2002. Lawlor M. In: Comfortable Quarters for Laboratory Animals, 9th ed. Washington: Animal Welfare Institute. p 26-32.

Definition, Nomenclature, and Conservation of Rat Strains. 1992. Committee on Rat Nomenclature. ILAR News 34(4):S1-S24.

Effect of ambient temperature on cardiovascular parameters in rats and mice: A comparative approach. 2004. Swoap SJ, Overton JM, Garber G. Am J Physiol 287:R391-R396.

Effect of cage bedding on temperature regulation and metabolism of group-housed female mice. 2004. Gordon CJ. Comp Med 54:63-68.

Effects of caging type and animal source on the development of foot lesions in Sprague Dawley rats (Rattus norvegicus) 2001. Peace TA, Singer, Niemuth NA, Shaw ME. Contemp Top Lab Anim Sci 40:17-21.

Effect of temperature on the behavioural activities of male mice. 2003. Ajarem J, Ahmad M. Dirasat Pure Sci 30:59-65.

Estimates of appropriate number of rats: Interaction with housing environment. 2001. Mering S, Kaliste Korhonen E, Nevalainen T. Lab Anim 35:80-90.

From house mouse to mouse house: The behavioural biology of free-living Mus musculus

The Hamster: Reproduction and Behavior. 1985.Siegel HI, ed. New York: Plenum Press.
Handbook on the Laboratory Mouse. 1975. Crispens CG Jr. Springfield IL: Charles C Thomas.
Histological Atlas of the Laboratory Mouse. 1982. Gude WD, Cosgrove GE, Hirsch GP. New York: Plenum.
Individually ventilated cages: Beneficial for mice and men? 2002. Baumans V, Schlingmann F, Vonck M, van Lith HA. Contemp Top Lab Anim Sci 41:13-19.
Individually ventilated microisolation cages. 1997. Novak G. Lab Anim 26:54-57.
Inventory of the behaviour of New Zealand white rabbits in laboratory cages. 1995. Gunn D. Appl Anim Behav Sci 45 (3/4):277-292.
Joint Working Group on Refinement: Husbandry refinements for rats, mice, dogs and non-human primates used in telemetry procedures. 2004. Seventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement, Part B. Hawkins P, Morton DB, Beyan R, Heath K, Kirkwood J, Pearce P, Scott L, Whelan G, Webb A. Lab Anim 38:1-10. Available at: www.rspca.org.uk/ImageLocator/LocateAsset?asset=documentandassetId=1232712323251andmode=prd; accessed January 24, 2010.
Laboratory Anatomy of the Rabbit, 3rd ed. 1990. McLaughlin CA, Chiasson RB. New York: McGraw-Hill.
Laboratory Animal Management: Rodents. 1996. National Research Council. Washington: National Academy Press.
Laboratory Hamsters. 1987. van Hoosier GL, McPherson CW, eds. New York: Academic Press.
Modulation of aggression in male mice: Influence of cage cleaning regime and scent marks. 2000. van Loo PLP, Kruitwagen CLJJ, van Zutphen LFM, Koolhaas JM, Baumans V. Anim Welf 9:281-295.
Observations on the prevalence of nest-building in non-breeding TO strain mice and their use of two nesting materials. 1997. Sherwin CM. Lab Anim 31:125-132.
Origins of Inbred Mice. 1979. Morse HC III, ed. New York: Academic Press.
Period length of the light-dark cycle influences the growth rate and food intake in mice. 1999. Campuzano A, Cambras T, Vilaplana J, Canal M, Carulla M, Diez Noguera A. Physiol Behav 67:791-797.
Preference of guinea pigs for bedding materials: Wood shavings versus paper cutting sheet. 2003. Kawakami K, Takeuchi T, Yamaguchi S, Ago A, Nomura M, Gonda T, Komemushi S. Exper Anim (Japanese Assoc Lab Anim Sci) 52:11-15.
Preferences of laboratory mice for characteristics of soiling sites. 1996. Sherwin CM. Anim Welf 5:283-288.
Preferences for nesting material as environmental enrichment for laboratory mice. 1997. VandeWeerd HA, van Loo PL, van Zutphen LF, Koolhaas JM, Baumans V. Lab Anim 31:133-143.
Proceedings of the Third International Workshop on Nude Mice. 1982. Reed ND, ed. vol 1: Invited Lectures/Infection/Immunology; vol 2: Oncology. New York: Gustav Fischer.
Rabbits: Good Practice for Housing and Care, 2nd ed. 2008. RSPCA, Research Animals Department. Available at: http://content.www.rspca.org.uk/cmsprd

goBlobsandblobwhere=1232988745180andssbinary=true; accessed January 24, 2010.

Rat: Good Practice for Housing and Care, 2nd ed. 2008. RSPCA, Research Animals Department. Available at: http://content.www.rspca.org.uk/cmsprd /Satellite?blobcol=urldataandblobheader=application%2Fpdfandblobkey=idandblobnocache=falseandblobtable=MungoBlobsandblobwhere=1232988745061andssbinary=true; accessed January 24, 2010.

Report of the 2002 RSPCA/UFAW rodent welfare group meeting: Individually ventilated cages and rodent welfare. 2003. Hawkins P, Anderson D, Applebee K, Key D, Wallace J, Milite G, MacArthur Clark J, Hubrecht R, Jennings M. Anim Technol Welf 2:23-24.

Refinements in rabbit husbandry. 1993. Morton DB, Jennings M, Batchelor GR, Bell D, Birke L, Davies K, Eveleigh JR, Gunn D, Heath M, Howard B, Koder P, Phillips J, Poole T, Sainsbury AW, Sales GD, Smith DJA , Stauffacher M, Turner RJ. Lab Anim 27:301-329.

Refining Rabbit Care: A Resource for those Working with Rabbits in Research. 2008. Hawkins P, Hubrecht R, Bucknell A, Cubitt S, Howard B, Jackson A, Poirier GM. RSPCA. Available at: www.rspca.org.uk/ImageLocator/LocateAsset?asset=documentandassetId=1232712644330andmode=prd; accessed January 24, 2010.

Refining rodent husbandry: The mouse. 1998. Jennings M, Batchelor GR, Brain PF, Dick A, Elliott H, Francis RJ, Hubrecht RC, Hurst JL, Morton DB, Peters AG, Raymond R, Sales GD, Sherwin CM, West C. Lab Anim 32:233-259.

Research Techniques in the Rat. 1982. Irby C. Springfield IL: Charles C Thomas.

Rodents and Rabbits: Current Research Issues. 1994. Niemi SM, Venable JS, Guttman JN, eds. Bethesda MD: Scientists Center for Animal Welfare.

Short-term effects of a disturbed light-dark cycle and environmental enrichment on aggression and stress-related parameters in male mice. 2004. Van der Meer E, van Loo PL, Baumans V. Lab Anim 38:376-383.

The Biology of the Guinea Pig. 1976. Wagner JE, Manning PJ, eds. New York: Academic Press.

The Biology of the Laboratory Rabbit, 2nd ed. 1994. Manning PJ, Ringler DH, Newcomer CE, eds. San Diego: Academic Press.

The Brattleboro rat. 1982. Sokol HW, Valtin H, eds. Ann NY Acad Sci 394:1-828.

The cage preferences of laboratory rats. 2001. Patterson Kane EG, Harper DN, Hunt M. Lab Anim 35:74-79.

The effects of different rack systems on the breeding performance of DBA/2 mice. 2003. Tsai PP, Oppermann D, Stelzer HD, Mahler M, Hackbarth H. Lab Anim 37:44-53.

The effects of feeding and housing on the behaviour of the laboratory rabbit. 1999. Krohn TC. Lab Anim 33:101-107.

The effects of group housing on the researchuse of the laboratory rabbit. 1993. Whary M, Peper R, Borkowski G, Lawrence W, Ferguson F. Lab Anim 27:330.

The effects of intracage ventilation on microenvironmental conditions in filter-top cages. 1992. Lipman NS, Corning BF, Coiro MA Sr. Lab Anim 26:206-210.

The impact of cage ventilation on rats housed in IVC systems. 2003. Krohn TC, Hansen AK, Dragsted N. Lab Anim 37:85-93.

Anesthesia, Pain and Surgery

Anaesthesia in ferrets, rabbits, and guinea pigs. 1998. Alderton B. In: Internal Medicine: Small Companion Animals. The T G Hungerford course for veterinarians, Proceedings 306, Stephen Roberts Lecture Theatre, University of Sydney, Australia, June 15-19. Bryden D, ed. University of Sydney Post Graduate Foundation in Veterinary Science. p 241-268

Anaesthetic and Sedative Techniques for Aquatic Animals, 3rd ed. 2008. Ross L, Ross B. Somerset NJ: Wiley-Blackwell.

Anesthesia and analgesia. 1997. Schaeffer D. In: Nontraditional Laboratory Animal Species in Anesthesia and Analgesia in Laboratory Animals. Kohn DF, ed. San Diego: Academic Press.

Anesthesia and Analgesia in Laboratory Animals, 2nd ed. 2008. Fish R, Danneman PJ, Brown M, Karas A, eds. 2008. San Diego: Academic Press.

Anesthesia for Veterinary Technicians. 2010. Bryant S, ed. Somerset NJ: Wiley-Blackwell.

Anesthesia and Analgesia in Laboratory Animals. 1997. Kohn DF, Wixson SK, White WJ, Benson GJ, eds. San Diego: Academic Press.

Animal Physiologic Surgery, 2nd ed. 1982. Lang CM, ed. New York: Springer Verlag.

AVMA Guidelines on Euthanasia. 2007. Schaumburg IL: American Veterinary Medical Association.

Challenges of pain assessment in domestic animals. 2002. Anil SS, Anil L, Deen J. JAVMA 220:313-319.

Definition of Pain and Distress and Reporting Requirements for Laboratory Animals. 2000. National Research Council. Washington: National Academy Press.

Handbook of Veterinary Anesthesia, 4th ed. 2007. Muir WW III, Hubbell JAE. Maryland Heights MO: Mosby.

Handbook of Veterinary Pain Management. 2002. Gaynor JS, Muir W. St. Louis: Mosby.

Laboratory animal analgesia, anesthesia, and euthanasia. 2003. Hedenqvist P, Hellebrekers LJ. In: J. Hau J, Van Hoosier GL, eds. Handbook of Laboratory Animal Science: Essential Principles and Practices, 2nd ed. Boca Raton FL: CRC Press.

Laboratory Animal Anesthesia, 3rd ed. 2009. Flecknell PA. London: Academic Press.

Lumb and Jones' Veterinary Anesthesia and Analgesia, 4th ed. 2007. Tranquilli WJ, Thurman JC, Grimm KA, eds. San Francisco: Wiley-Blackwell.

Pain alleviation in laboratory animals: Methods commonly used for perioperative pain-relief. 2002. Vainio O, Hellsten C, Voipio HM. Scand J Lab Anim Sci 29:1-21.

Pain and distress. 2006. Karas A, Silverman J. In: Suckow M, Silverman J, Murthy S, eds. The IACUC Handbook. Boca Raton FL: CRC Press.

Pain Management in Animals. 2000. Flecknell PA, Waterman-Pearson A, eds. Philadelphia: WB Saunders.

Paralytic agents. 1997. Hildebrand SV. In: Kohn DF, Wixson SK, White WJ, Benson GJ, eds. Anesthesia and Analgesia in Laboratory Animals. San Diego: Academic Press.

Position Statement on Recognition and Alleviation of Pain and Distress in Laboratory Animals. 2000. AALAS. Available at: www.aalas.org/pdf/Recognition_and_Alleviation_of_Pain_and_Distress_in_Laboratory_Animals.pdf; accessed January 24, 2010.

Recognition and Alleviation of Pain in Laboratory Animals. 2009. National Research Council. Washington: National Academies Press.
Recognizing pain and distress in laboratory animals. 2000. Carstens E, Moberg GP. ILAR J 41:62-71.
Recommendations for euthanasia of experimental animals. 1996. Close B, Baniste K, Baumans V, Bernoth EM, Bromage N, Bunyan J, Erhardt W, Flecknell P, Gregory N, Hackbarth H, Morton D, Warwick C. Lab Anim 30:293-316.
Small Animal Anesthesia and Analgesia. 2008. Carroll GL. Ames IA: Blackwell Publishing.
Small Animal Surgery Textbook, 3rd ed. 2007. Fossum T. Maryland Heights MO: Mosby.
Small Animal Surgical Nursing, 2nd ed. 1994. Mosby's Fundamentals of Animal Health Technology. Tracy DL, ed. St. Louis: CV Mosby.
Surgery: Basic Principles and Procedures. 2003. Waynforth HB, Swindle MM, Elliott H, Smith AC. In: Hau J, Van Hoosier GL, eds. Handbook of Laboratory Animal Science: Essential Principles and Practices, 2nd ed, vol 1. Boca Raton FL: CRC Press. p 487-520.
Textbook of Small Animal Surgery, 3rd ed. 2003. Slatter D. Philadelphia: WB Saunders.
The Biology of Animal Stress: Basic Principles and Implications for Animal Welfare. 2000. Moberg GP, Mench JA. Wallingford UK: CAB International.
The IACUC Handbook. 2006. Flecknell P, Silverman J, Suckow MA, Murthy S, eds. New York: CRC Press.
The importance of awareness for understanding fetal pain. 2005. Mellor DJ, Diesch TJ, Gunn AJ, Bennet L. Brain Res Rev 49:455-471.
When does stress become distress? 1999. Moberg GP. Lab Anim 28:422-426.

Disease Surveillance, Diagnosis and Treatment

Clinical Laboratory Animal Medicine. 2008. Hrapkiewicz K, Medina L, eds. San Francisco: Wiley-Blackwell.
Current strategies for controlling/eliminating opportunistic microorganisms. 1998. White WJ, Anderson LC, Geistfeld J, Martin D. ILAR J 39:391-305.
Drug Dosage in Laboratory Animals: A Handbook. 1989. Borchard RE, Barnes CD, Eltherington LG. West Caldwell NJ: Telford Press.
FELASA recommendations for the health monitoring of breeding colonies and experimental units of cats, dogs and pigs. 1998. Rehbinder C, Baneux P, Forbes D, van Herck H, Nicklas W, Rugaya Z, Winkler G. Report of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Animal Health. Lab Anim 32:1-17.
Ferrets, Rabbits and Rodents: Clinical Medicine and Surgery. 1997. Hillyer EV, Quesenberry KE. Philadelphia: WB Saunders.
Handbook of Veterinary Drugs: A Compendium for Research and Clinical Use. 1975. Rossoff IS. New York: Springer Publishing.
Invertebrate Medicine. 2006. Lewbart GA. Ames: Blackwell Publishing.
Kirk and Bistner's Handbook of Veterinary Procedures and Emergency Treatment, 8th ed. 2006. Ford RB, Mazzaferro E. Philadelphia: WB Saunders.
Laboratory Animal Medicine. 2002. Fox JG, Anderson LC, Loew FM, Quimby FW, eds. New York: Academic Press.

Mosby’s Fundamentals of Animal Health Te chnology: Principles of Pharmacology. 1983. Giovanni R, Warren RG, eds. St. Louis: CV Mosby.

Pathology of Laboratory Animals. 1978. Benirschke K, Garner FM, Jones TC. 1978. New York: Springer Verlag.
The Pathology of Laboratory Animals. 1965. Ribelin WE, McCoy JR, eds. Springfield IL: Charles C Thomas.
Veterinary Clinical Parasitology, 6th ed. 1994. Sloss MW, Kemp RL. 1994. Ames: Iowa State University Press.
Veterinary Pathology, 5th ed. 1983. Jones TC, Hunt RD. Philadelphia: Lea and Febiger.

Species-Specific References – Veterinary Care

Agricultural Animals

Basic Surgical Exercises Using Swine. 1983. Swindle MM. 1983. New York: Praeger.
Diseases of Poultry, 9th ed. 1991. Calnek BW, Barnes HJ, Beard CW, Reid WM, Yoder HW, eds. Ames: Iowa State University Press.
Diseases of Sheep. 1974. Jensen R. Philadelphia: Lea and Febiger.
Diseases of Swine, 7th ed. 1992. Leman AD, Straw BE, Mengeline WL, eds. Ames: Iowa State University Press.
FELASA recommendations for the health monitoring of breeding colonies and experimental units of cats, dogs and pigs. 1998. Rehbinder C, Baneux P, Forbes D, van Herck H, Nicklas W, Rugaya Z, Winkler G. Report of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Animal Health. Lab Anim 32:1-17.
Swine in the Laboratory: Surgery, Anesthesia, Imaging, and Experimental Techniques, 2nd ed. Swindle MM, ed. 2007. Boca Raton FL: CRC Press.
Techniques in Large Animal Surgery, 3rd ed. 2007. Hendrickson D, ed. 2007. Somerset NJ: Wiley-Blackwell Publishers.
Textbook of Large Animal Surgery, 2nd ed. 1987. Oehme FW, Prier JE. Baltimore: Williams and Wilkins.

Amphibians, Reptiles and Fish

An evaluation of current perspectives on consciousness and pain in fishes. 2004. Chandroo KP, Yue S, Moccia RD. Fish Fisher 5:281-295.
Anesthesia and analgesia in reptiles. Mosley CA. 2005. Semin Avian Exot Pet Medic 14:243-262.
Can fish suffer? Perspectives on sentience, pain, fear and stress. 2004. Chandroo KP, Duncan IJH, Moccia RD. App Anim Behav Sci 86:225-250.
Disease Diagnosis and Control in North American Marine Aquaculture, 2nd rev ed. 1988. Sindermann CJ, Lichtner DV. New York: Elsevier.
Diseases of Fishes. 1971. Bullock GL, Conroy DA, Snieszko SF. Neptune NJ: TFH Publications.
Diseases of Fishes. 1971. Bullock GL. Book 2B. Identification of Fish Pathogenic Bacteria. Neptune NJ: TFH Publications.
Diseases of Fishes. 1974. Anderson DP. Book 4: Fish Immunology. Neptune NJ: TFH Publications.
Diseases of Fishes. 1976. Wedemeyer GA, Meyer FP, Smith L. Book 5: Environmental Stress and Fish Diseases. Neptune NJ: TFH Publications.

Do fish have nociceptors? Evidence for theevolution of a vertebrate sensory system.

Cats and Dogs

FELASA recommendations for the health monitoring of breeding colonies and experimental units of cats, dogs and pigs. 1998. Rehbinder C, Baneux P, Forbes D, van Herck H, Nicklas W, Rugaya Z, Winkler G. Report of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Animal Health. Lab Anim 32:1-17.

Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat, 6th ed. 2005. Ettinger SJ, Feldman EC, eds. Philadelphia: WB Saunders.

Exotic, Wild and Zoo Animals

Biology, Medicine, and Surgery of South American Wild Animals. 2001. Fowler ME, Cubas ZS. Ames: Iowa State University Press.

CRC Handbook of Marine Mammal Medicine: Health, Disease, and Rehabilitation. 2001. Dierauf LA, Gulland FMD. Boca Raton FL: CRC Press.

Diseases of Exotic Animals: Medical and Surgical Management. 1983. Philadelphia: WB Saunders.

Essentials of Disease in Wild Animals. 2005. Wobeser GA. Wiley-Blackwell.

Exotic Animal Formulary, 3rd ed. 2004. Carpenter JW. Philadelphia: WB Saunders.

Infectious Diseases of Wild Mammals. 2000. Williams ES, Barker IK, eds. Wiley-Blackwell.

Pathology of Zoo Animals. 1983. Griner LA. San Diego: Zoological Society of San Diego.

Veterinary Clinics of North America: Exotic Animal Practice Series. Elsevier.

Zoo Animal and Wildlife Immobilization and Anesthesia. 2007. West G, Heard D, Caulkett N, eds. Wiley-Blackwell.

Zoo and Wild Animal Medicine: Current Therapy 4. Fowler ME, Miller RE, eds. 1999. Philadelphia: WB Saunders.

Zoo and Wild Animal Medicine, 5th ed. 2003. Fowler E, Miller RE, eds. Philadelphia: WB Saunders.

Zoo and Wild Animal Medicine Current Therapy, 6th ed. 2007. Fowler ME, Miller RE, eds. Philadelphia: WB Saunders.

Nonhuman Primates

Rodents and Rabbits

A Guide to Infectious Diseases of Guinea Pigs, Gerbils, Hamsters, and Rabbits. 1974. National Research Council. Washington: National Academy of Sciences.

Anesthesia and analgesia for laboratory rodents. 2008. Gaertner D, Hallman T, Hankenson F, Batchelder M. In: Anesthesia and Analgesia in Laboratory Animals. Fish R, Brown M, Danneman P, Karas A, eds. San Diego: Academic Press. p 239-298.

Aversion to gaseous euthanasia agents in rats and mice. 2002. Leach MC, Bowell VA, Allan TF, Morton DB. Comp Med 52:249-257.

Behavioural and cardiovascular responses of rats to euthanasia using carbon dioxide gas. 1997. Smith W, Harrap SB. Lab Anim 31:337-346.

http://oacu.od.nih.gov/ARAC/documents/Rodent_Euthanasia_Pup.pdf, Accessed January 24, 2010.

Helicobacter bilis-induced inflammatory bowel disease in SCID mice with defined flora. 1997. Shomer NH, Dangler CA, Schrenzel MD, Fox JG. Infect Immun 65:4858-4864.

Humane and practical implications of us ing carbon dioxide mixed with oxygen for anesthesia or euthanasia of rats. 1997. Danneman PJ, Stein S, Walshaw SO. Lab Anim Sci 47:376-385.

Improving murine health surveillance progra

Prenatal transmission and pathogenicity of endogenous ecotropic murine leukemia virus AKV. 1999. Hesse I, Luz A, Kohleisen B, Erfle V, Schmidt J. Lab Anim Sci

Design and Management of Research Facilites for Mice. Lipman NS. 2007. In: Fox JG, Barthold SW, Davisson M, Newcomer CE, Quimby FW, Smith AL, eds. The Mouse in Biomedical Research, vol III: Normative Biology, Immunology and Husbandry. Orlando: Academic Press. p 271-319.

Design and optimization of airflow patterns. 1994. Reynolds SD, Hughes H. Lab Anim 23:46-49.

Design of surgical suites and post surgical care units. 1997. White WJ, Blum JR. In:

APPENDIX B: U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible Institutional Official shall ensure that these principles are adhered to:

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

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

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

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

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

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

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

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

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

*For guidance throughout these Principles, the reader is referred to the Guide for the Care and Use of Laboratory Animals prepared by the Institute for Laboratory Animal Research, The National Academies.

APPENDIX D: About the Authors

Janet C. Garber (Chair), DVM, PhD, received her Doctor of Veterinary Medicine degree from Iowa State University and her PhD in patho-physiology from the University of Wisconsin. Her experiences have included infectious disease research at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), primate medicine and research, GLP device and materials evaluation, and transplantation immunology. Her current interests are in the areas of laboratory animal facility management, infectious diseases, occupational health and safety and research program management. She most recently was Vice President, Safety Assessment, at Baxter Healthcare Corporation and is now a consultant with Garber Consulting, LLC in North Carolina. Dr. Garber is currently a member of the Council on Accreditation, AAALAC, International, and previously served as Chair of the Council. She served on the ILAR committee to revise the Guide for the Care and Use of Laboratory Animals and the committee on Occupational Health and Safety in the Care and Use of Research Animals.

R. Wayne Barbee, PhD, is Associate Professor and Associate Director of Research at the Department of Emergency Medicine, School of Medicine, Senior VCURES (Virginia Commonwealth University Reanimation Engineering Science Center) Fellow and chair of the IACUC at the Virginia Commonwealth University. Dr. Barbee holds a masters degree and doctorate in Physiology with three decades of research involving a wide variety of animals (bats, cats, crabs, dogs, rodents and swine) in a number of experimental settings. His research has focused on circulatory shock andresuscitation, acute and chronic rodent surgery, and analysis of rodent hemodynamics. He has been associated with IACUCs at small, medium and large institutions for over two decades, and is familiar with the oversight of animal care and use programs. He has served on multiple study sections for both the NIH and DOD. Dr. Barbee also served as an Oxford, UK 2006 fellow (recipient, VCU Harris-Manchester Award) where he examined policies, training, and security issues related to animal care and use within the UK.

Joseph T. Bielitzki, MS, DVM, is Research Manager, University of Central Florida. Dr. Bielitzki has worked with non human primates in the laboratory

environment for 20 years. Over this period he has worked with macaques (pig-tail, long tail, Japanese, rhesus, stump-tail), baboons (yellow, green and hybrids) squirrel monkeys, capuchin monkeys, mangabeys, gibbons, chimpanzees, orangutan, bonobos and gorillas. In the area of non human primates his area of expertise is in enteric diseases, nursery rearing, and colony management. He has also worked with mice and rats in a variety of international facilities. He was instrumental in the writing and acceptance of the NASA Bioethical Principles for the Use of Animals in Research (NPD 8910.1) He speaks frequently on IACUC function and the importance of ethics in the use of animals. His background includes experience in academia, industry and government in the role of attending veterinarian, program manager, and researcher.

Leigh Ann Clayton, DVM, is Director of Animal Health at the National Aquarium in Baltimore where she also chairs the Animal Welfare Committee. Dr. Leigh Clayton has worked in the zoo/aquarium field or the exotic pet medicine field exclusively since 2000. As she has worked with animals held in aquatics systems both in re-circulating fresh and salt water, she is experienced in managing disease and accomplishing preventive health programs for fishes, amphibians, and reptiles as well as birds and mammals. She is Diplomate of the American Board of Veterinary Practitioners (Avian). Dr. Clayton has routinely used her knowledge of nitrogen cycling and the basics of a variety of life support system designs to solve health issues in

Dennis F. Kohn , DVM, PhD, is Professor Emeritus of Clinical Comparative Pathology at Columbia University. He received his DVM from Ohio State University and a doctorate in Medical Microbiology from West Virginia University. He is board certified by th e American College of Laboratory Animal Medicine. He has directed laboratory animal resource/comparative medicine programs at West Virginia University Medical Center, University of Texas Medical School at Houston, and Health Sciences Division, Columbia University. His research interests have dealt primarily with the pathogenicity of Mycoplasma pulmonisin the respiratory tract of laboratory rats, and the experimental M. pulmonis. He is a past president of the American College of Laboratory Animal Medicine

broad experience with a wide assortment of laboratory animals including rodents, dogs, primates, livestock, poultry, and fish, and published on the

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