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14. ABSTRACT The National Academies continue the activities of the Institute for Laboratory Animal Research (ILAR), the recognized leader in developing and disseminating guidelines for laboratory animal care, breeding, and use, (including the internationally accepted standard Guide for the Care and Use of Laboratory Animals); resources for identifying animal models for human diseases and physiological processes; and reports on the humane and scientific use of laboratory animals (including education and training of scientists and technicians in the care and use of laboratory animals; reduction of pain and distress in research animals; occupational safety and health of employees; and nomenclature of inbred, transgenic, and other genetically defined animals). The program goal is to improve the humane and scientifically valid use of laboratory animals as well as the availability, quality and care of laboratory animals. ILAR accomplishes this goal through a core program, carried out by staff, and a special-project program, carried out by National Academies-appointed experts. Both programs are guided by a 16-member advisory council (the Council). The Council meets three times a year to provide program direction and strategic planning; to oversee the communication and information programs (consisting of the ILAR web site and the ILAR Journal); to oversee special projects; and to direct ILAR's internation						
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Table of Contents

	Page
Introduction.....	4
ILAR's Goals	4
The Core Program	5
Special Projects.....	10
References.....	11
Appendix.....	12

INTRODUCTION

For many years the Army has provided partial core support to the Institute for Laboratory Animal Research (ILAR), a component of the National Research Council (NRC). Formerly contained within the Commission on Life Sciences, ILAR is now part of a larger division of the NRC, called the Division on Earth and Life Studies. The NRC is the operating arm of the National Academy of Sciences, a private, nonprofit organization that was created in 1863 by congressional charter to serve as an official advisor to the federal government on questions of science and technology.

Founded in 1952, ILAR is both a national and international leader in developing guidelines for animal care, breeding, and use; descriptions of animal models for human diseases and physiological processes; and reports on specific issues of scientific and humane use of laboratory animals. ILAR disseminates this information to the biomedical and laboratory animal science communities by wide distribution of its reports as well as through presentations and exhibits at national meetings. These guidelines from the National Academy of Sciences serve as important indications to members of the U.S. Congress and other government officials, the press, and the public of the high quality of care provided to laboratory animals. ILAR's mission is to help improve the availability, quality, care, and humane and scientifically valid use of laboratory animals.

Recognized experts in fields appropriate to the required tasks carry out ILAR's studies, like all those of the NRC. These experts serve on a volunteer basis, without compensation. As a part of the NRC, ILAR has access to this country's most knowledgeable and distinguished laboratory animal and biomedical scientists, who provide objective counsel on laboratory animal issues. Many of the experts used by ILAR are also members of the National Academy of Sciences or the Institute of Medicine. In some cases, ILAR utilizes scientists from other countries.

Independent NRC-appointed experts in the subject area extensively review reports of NRC studies before they are released. They are prepared in sufficient quantity to ensure distribution to the sponsor, experts, and other relevant parties in accordance with Academy policy. Reports are usually made available to the public without restriction.

ILAR'S GOALS

Since its founding, ILAR has provided guidance and information on laboratory animal matters to the federal government, the biomedical and laboratory animal science communities, and the public. In keeping with its mission, ILAR continually seeks to strengthen and refine its existing programs and to initiate new programs that will assist government officials; scientists who use animals in research, testing, and education; and the institutional animal care and use committees that monitor animal use. ILAR's goals are as follows:

- to provide a forum within the National Academy of Sciences for the Department of Defense to discuss issues and develop guidance for laboratory animal-related matters;
- to continue to serve on behalf of biomedical science and education as an authoritative voice within the U.S., and on behalf of the U.S. scientists internationally;
- to promote humane and appropriate care and use of laboratory animals;

- to provide scientific guidance on laboratory animal-related issues to agencies of the federal government and others on request;
- to provide information on laboratory animal matters to government officials, laboratory animal and other biomedical scientists, institutional animal care and use committees, and the public;
- to promote the use of standardized nomenclature for accurately defining and identifying genetic stocks of animals;
- to assist developing countries in attaining quality laboratory animal science programs through dissemination of information including the translation of ILAR reports;
- to promote cost-effective ways to preserve valuable animal models;
- to sponsor workshops in areas of importance to the laboratory animal community; and
- to increase access to information about appropriate biological models and methods through ILAR's home page, databases, publications, and resources of the ILAR Associates program, including the quarterly *ILAR Journal*.

Accomplishing the Goals

ILAR accomplishes its goals through its core program, which is carried out by the staff, and its special-project program. The number of studies and size of the staff are dependent on the number of special projects and available funding. Both programs are directed by a 16-member ILAR Council composed of experts in laboratory animal medicine, virology, zoology, genetics, medicine, ethics, and related biomedical sciences.

CORE PROGRAM

The Core Program of ILAR supports the activities of ILAR Council, ILAR's international activities, ILAR's information and communication programs (including the Animal Models and Strains Search Engine), the ILAR web site, and exhibits at major scientific and veterinary meetings. The production of the peer-reviewed *ILAR Journal* is also supported by core funds. Core funds support staff time devoted to these activities as well as development of new projects.

ILAR Council

The ILAR Council serves four principal functions: 1) to provide program direction and strategic planning; 2) to oversee the information and communication programs, which consist of the Animal Models and Strains Search Engine, the ILAR web site, and the quarterly *ILAR Journal*; 3) to oversee special projects; and 4) to direct ILAR's international programs and its participation as the U.S. national member in the International Council of Laboratory Animal Sciences (ICLAS). The international program is discussed in the Special Projects section below. Periodically, the Council meets with other scientists and funding agency administrators to discuss areas in which ILAR might provide guidance. The Council uses these discussions in strategic planning. The Council occasionally employs core funds to undertake specific, NRC-approved projects. The current members of ILAR Council are listed at the end of this document.

ILAR Council meets for two days, three times per year at one of the National Academies' facilities. In the past year, meetings were held on July 19-20, 2007 (Woods Hole, MA)

November 8-9, 2007 (Washington, DC), March 13-14, 2008 (Irvine, CA) and July 10-11 (Woods Hole, MA). During each of these meetings, ILAR Council's three subcommittees held separate half-day meetings to discuss subcommittee projects. The three subcommittees are: 1) ILAR Outreach Subcommittee, 2) International Subcommittee, and 3) the *ILAR Journal* Editorial Board.

Staff

ILAR is staffed by the director, a managing editor of the *ILAR Journal*, a project assistant who maintains the web page and various databases, an administrative assistant and secretary to the director, and a project director. A part-time web master provides support for online resources. Under the special projects program, staff works closely with experts to engage in studies, develops working papers, assists in the production of cohesive reports, and conducts literature reviews. ILAR staff members are listed at the end of this document.

International Activities Subcommittee

ILAR has had a long history of interest in international laboratory animal science. Historically, this interest has sought to assist young investigators in developing countries through dissemination of reports (some translated into foreign languages to increase their usefulness) and participation in international meetings that support young investigators. In 1988, ILAR became the U.S. national member of the International Council for Laboratory Animal Science (ICLAS), with support from member agencies of the Interagency Research Animal Committee (IRAC). This membership affords a conduit for U.S. investigators to develop and conduct an active international program in laboratory animal science. One goal of the U.S. membership in ICLAS was to streamline ICLAS management and programs to better represent U.S. scientists in the international community. Following are the major international efforts of ILAR.

Report Translations

ILAR's most longstanding international effort has been to have our seminal publication the *Guide for the Care and Use of Laboratory Animals* (the *Guide*) translated into as many languages as possible. The *Guide* is used as the standard for laboratory animal care by the Public Health Service in the U.S., and by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International in their certification of animal facilities throughout the world. The *Guide* has been translated into French, Spanish, German, Portuguese, Thai, Japanese, Korean, Arabic, Russian, and two versions of Chinese. An Indonesian version is being reviewed and will be published soon.

International Council for Laboratory Animal Science (ICLAS)

ILAR supports the activities of ICLAS through its participation as the US representative. ICLAS is an international scientific organization dedicated to advancing human and animal health by promoting the ethical care and use of laboratory animals in research worldwide. ICLAS was established in 1956 under the auspices of UNESCO, and interacts in an official capacity with the World Health Organization (WHO), the International Council of Scientific Unions (ICSU), the Council for International Organizations of Medical Sciences (CIOMS), and the World Veterinary Association (WVA). ICLAS sponsors meetings throughout the world, but focuses particularly on third world countries, where animal care conditions are in need of improvement. Through ICLAS, ILAR provides guidance in the field of laboratory animal science

to scientists in developing countries. Dr. Steven Pakes, former chair of ILAR Council, was the President of ICLAS until October 2003. Dr. Harry Rozmiarek is now the US representative to ICLAS and provides reports to ILAR Council. ICLAS co-sponsored a meeting with the OIE, the World Animal Health Organization, at the AALAS meeting in Salt Lake City in October 2006 and is working with many international organizations to prepare guidance documents for use around the world.

International Workshops

As part of ILAR core activities, ILAR has sponsored meetings first with scientists from the U.S. and Japan, and more recently on a more comprehensive international basis. In 2003, ILAR hosted another International Workshop on the Development of Science-based Guidelines for Laboratory Animal Care, which focused on issues of international harmonization and on the need for more research in order to develop scientifically sound regulations. The proceedings for this workshop were published in 2004 and a follow-up meeting occurred in August 2005 in Berlin in association with the World Congress on Animals and Alternatives in the Life Sciences. A second follow-up meeting was held in conjunction with the National AALAS meeting in Salt Lake City. A second international workshop is being planned for 2008.

Observer Status at the Council of Europe

In 1999, ILAR was granted observer status to the Council of Europe in the preparation of guidelines for the protection of live animals used for experimental and other scientific purposes. The goal of the Council of Europe is to harmonize guidelines throughout Europe and it is desirable to have these guidelines harmonized with regulations and guidelines in the U.S. Since the *Guide* provides the basis for many of the current U.S. guidelines, it was useful and efficient for ILAR to be an observer to this process and have the opportunity to comment. The convention has now been ratified and was implemented in June 2007.

Foreign Participation in ILAR Activities

ILAR actively seeks foreign participation in its Council and ad hoc committees. Currently, one Council member is from the European Union, Dr. Timo Nevalainen from Finland, replacing Dr. Coenraad Hendriksen who recently completed his six year term. Dr. Nevalainen is intimately involved with the current and developing policies in Europe that will affect the U.S. He provides valuable insights and guidance for ILAR's international activities. ILAR has also included international representatives on the ongoing project to update the *Guide for the Care and Use of Laboratory Animals*.

Future Activities

ILAR will continue to become more involved in international activities in the future. The need for greater international involvement arises from a common desire to harmonize guidelines and standards for laboratory animal care across the world with the goals of improving animal welfare, conserving animal resources, and improving scientific interchange through detailed characterization of the animals used in research. ILAR has the international recognition and credibility to foster dialogue among individuals from across the globe and will serve to facilitate these interactions. To this end, ILAR is hosting an international conference titled "Animal Research in a Global Environment – Meeting the Challenges" in Washington, DC on September 23-26, 2008. The conference will focus on conducting animal research across borders and how to

address differences in animal welfare guidelines, training of animal care personnel, veterinary care and quality of animals.

ILAR Journal Subcommittee

Work Statement

ILAR Journal is produced quarterly and provides a unique repository of timely, high quality information on new developments in biomedical research that involve the use of laboratory animals. It seeks to be the premier U.S. periodical resource for investigators, institutional animal care and use committee (IACUC) members, and veterinarians involved in writing and/or reviewing protocols for laboratory animal research that must comply with national, and sometimes international, regulations and policies. Individuals and institutions who subscribe to the Journal help defray the cost of publication. In the last year, the following issues were published:

Volume 48 (4) Animal Models Used in the Study of Movement Disorders, 2007.

Volume 49 (1) Noninvasive Bioimaging of Laboratory Animals, 2008.

Volume 49 (2) Microbial Quality Control for Nonhuman Primates, 2008.

Volume 49 (3) Detection and Management of Microbial Contamination in Laboratory Rodents, 2008.

Volume 49 (4) Animal Use Oversight: Balancing Risk Management with Burden, 2008.

The *ILAR Journal* is produced by a full-time Managing Editor, who is a member of ILAR staff, with oversight by the *ILAR Journal* Editorial Board. The Editorial Board is made up of 5 Council members, one of whom is the Editor-in-Chief. This group meets three times per year in conjunction with the full Council meeting to plan the structure and authorship of future issues.

ILAR Associates Program

In an effort to increase ILAR's information resources and to better leverage funding from core and project sponsors to support other activities, ILAR initiated an Associates program in 1997. Individuals and institutions that subscribe to the Associates program help defray the cost of publishing the *Journal*. ILAR Associates receive the *ILAR Journal* (number of copies varies with level of Associate membership) and a 20% discount on all ILAR and other National Academy Press publications. ILAR Associates represent the best of US biomedical and laboratory animal scientists and serve as an important audience to receive, critique, and provide guidance to ILAR's programs. Institutional and Supporting Institutional members receive free online access for all members of their institution immediately after publication. ILAR's core sponsors are valuable members of the Institutional Associates program.

Future Issues of ILAR Journal

The Editorial Board must identify topics for future issues of ILAR Journal well in advance. The following issues (with anticipated publication date) are in some stage of planning or production:

Neural Regulation of Social Behavior (2009).

Gene Therapy in Large Animal Models of Human Genetic Diseases (2009).

Regenerative Medicine: Role of Animal Models from Stem to Cure (2009).

Pain and Distress in Fish (2009).

ILAR Outreach Subcommittee

Work Statement and Recent Accomplishments

For more than 40 years, ILAR has provided assistance to biomedical researchers, veterinarians, and Institutional Animal Care and Use Committees (IACUCs) in interpreting guidelines for the humane care and use of animals, and fulfilling requirements of the Animal Welfare Act and PHS policy regarding reduction of pain and distress and identification of alternative methodologies. The main outlet for this information is our newly launched website, which is now more user-friendly and contains components for different constituencies. ILAR has recently been working to develop a web-based search engine that would enable investigators to search through all available sources of animal strains and models. The current search engine has the capability of searching all of the commercial and private animal breeders, lab animal repositories, and animal resource databases that are linked to ILAR's site, as well as the ILAR website. Current activities are focused on expanding this list of linked websites and partnering with these organizations to provide high level search capabilities. The ILAR website also hosts registry of codes used with standardized nomenclature of rodents and rabbits to identify institutions that maintain breeding colonies. We continually monitor traffic to the site utilizing the web statistical package Web Trends, and we also monitor the number of downloads of ILAR Journal articles.

Other aspects of ILAR's information program are focused on the ability to interact with scientists and veterinarians at national meetings. ILAR exhibits and/or lectures at these national meetings to enhance our outreach programs and increase the visibility of ILAR's programs and publications. ILAR has routinely traveled to the national meetings of the Society for Neuroscience, Experimental Biology, the American Association for Laboratory Animal Science, the Society of Toxicology, the Scientists Center for Animal Welfare, and Public Responsibility in Medicine and Research.

Core funds are used to pay staff time to develop and maintain the databases and web development, for software and other materials needed in web activities, and for travel of staff to national meetings. Core funds have also supported the development of a marketing plan for ILAR to increase its visibility throughout the scientific community. The marketing plan is also poised to help increase the visibility of the *ILAR Journal* and to increase the number of associates (subscribers). ILAR strives to provide information and scientifically-based guidelines that will benefit the research enterprise and to communicate the message that humane science is the best science.

SPECIAL PROJECTS

Projects are developed in response to specific requests from government agencies and private organizations or are initiated by ILAR staff or Council members. Although these projects are supported by contracts and grants from federal agencies, foundations, and private organizations, they are never completely separate from the core program as the ILAR Council is involved during each step of the project. The Council reviews each project extensively before it is undertaken, examines the qualifications of experts, and monitors the conduct of the project to ensure that it is accomplished in a timely manner. As such, core sponsorship (including funding provided by this grant) is recognized in each ILAR project report. In addition, some ILAR project reports are published as special inserts of the core-supported *ILAR Journal*. The following projects are under way or will begin when funding has been received.

Projects Recently Completed

Recognition and Alleviation of Distress in Laboratory Animals

A study committee has updated and supplemented the ILAR report *Recognition and Alleviation of Pain and Distress in Laboratory Animals* related to distress. This book aims to educate laboratory animal veterinarians; students, researchers, and investigators; animal care staff, as well as animal welfare officers on the current scientific and ethical issues associated with stress and distress in laboratory animals.

Projects in Progress

Update of Recognition and Alleviation of Pain in Laboratory Animals

This is the second part of the update of the 1992 report *Recognition and Alleviation of Pain and Distress in Laboratory Animals* that will focus on pain. This report will update information based on the current scientific literature on recognizing and alleviating pain in laboratory animals. The report will discuss the physiology of pain in commonly used laboratory species. Specific emphasis will be placed on the identification of humane endpoints, pharmacologic and non-pharmacologic principles to control pain, and principles to utilize in minimizing pain associated with experimental procedures. As with the first report, general guidelines and examples will be given to aid IACUC members, investigators and animal care staff in making decisions about protocols using laboratory animals under current federal regulations and policies.

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

A committee will update the 1996 version of the *Guide for the Care and Use of Laboratory Animals* (the Guide) to reflect new scientific information related to the issues already covered in the Guide, and to add discussion and guidance on new topics of laboratory animal care and use related to state-of-the-art animal research programs.

Upcoming Activities

Scientific and Humane Issues in the Use of Random-source Dogs and Cats for Research

A committee will determine the important biomedical research questions and common research topics in contemporary NIH-funded research where Class B dogs and cats are desirable/necessary as well as the frequency of these various research topics (i.e. number of grants where the potential exists or the source of the animal is identified as coming from a Class B source); describe the specific characteristics, such as physiological, anatomical, or genetic characteristics, of the animals that make them particularly well-suited for these types of research; and; make recommendations, if necessary, for new or revised scientific parameters to guide their use, if these Class B dogs and cats are deemed to be necessary for research.

REFERENCES

National Research Council (2008) *Recognition and Alleviation of Distress in Laboratory Animals*. Washington, DC, National Academies Press.

Institute for Laboratory Animal Research 2007. *ILAR J.* 48 (4) Animal Models Used in the Study of Movement Disorders.

Institute for Laboratory Animal Research 2008. *ILAR J.* 49 (1) Noninvasive Bioimaging of Laboratory Animals.

Institute for Laboratory Animal Research 2008. *ILAR J.* 49 (2) Microbial Quality Control for Nonhuman Primates.

Institute for Laboratory Animal Research 2008. *ILAR J.* 49 (3) Detection and Management of Microbial Contamination in Laboratory Rodents.

Institute for Laboratory Animal Research 2008. *ILAR J.* 49 (4) Animal Use Oversight: Balancing Risk Management with Burden.

Appendix: ILAR Council (with areas of expertise) and Staff (as of July 1, 2008)

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