Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research

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SCIENTIFIC AND HUMANE ISSUES IN THE USE OF RANDOM SOURCE DOGS AND CATS IN RESEARCH

Committee on Scientific and Humane Issues in the Use of
Random Source Dogs and Cats in Research

Institute for Laboratory Animal Research

Division on Earth and Life Studies

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Preface

The ancient Indian fable of the Blind Men and the Elephant describes a group of blind men who each touch a different part of an elephant and, when they compare their individual impressions of the animal before them, discover that they are in complete disagreement. While assorted versions of this fable vary about the contentiousness of the debate and how it is resolved, the primary lesson is that opinions can differ among individuals. The secondary message is that differences must be resolved in order to reach consensus. Such were the challenges of this committee.

The National Academies endeavor to appoint committees that represent a broad range of perspectives and expertise in order to accomplish a fair and balanced study, and this committee was no exception. But what seemed to be a relatively straightforward task in determining the desirability and necessity of random source dogs and cats from Class B dealers for National Institutes of Health (NIH) research turned out to be far more complex than the committee initially realized. The complexity goes back to the very origins of medical research and the animal protectionist movement, and is steeped in the American public's emotional ties to dogs and cats (which Frank Loew[1] termed "America's Sacred Cows") and changing trends in public attitudes toward research using these familiar animals. The American public has insisted that their pets be protected, resulting in pas-

[1] Personal communication from the late Franklin Loew, DVM, PhD, Diplomate of the American College of Laboratory Animal Medicine, member of the Institute of Medicine, former Dean of Tufts School of Veterinary Medicine and Cornell School of Veterinary Medicine, past President of Becker College, research scientist, and advocate for research animal welfare.

sage of the original Animal Welfare Act in 1966, with several subsequent revisions. The enforcement arm of the Act, the U.S. Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS), has also repeatedly amended its Animal Welfare Regulations to better enforce the Act. Despite these efforts, infractions continue, including recent egregious ones that sparked renewed concern by the public and Congress, which was the impetus for convening this committee.

In contrast to the emotion and conviction that pervade public sentiment toward dogs and cats, the scientific community views the "elephant" rationally. The U.S. dog and cat population, with its many breeds and numbers, represents a rich resource for advancing medical knowledge through discovery and use of models with homology to many human diseases.

The panel of experts on this committee represented a broad spectrum of perspectives, and endeavored to approach its task without bias, despite strong and admittedly emotional personal opinions. As Chairman of this committee, I was impressed that its members set aside their individual differences in order to reach consensus, and as a result were able to factually describe the entire elephant, with all of its complexity.

The committee acknowledges with appreciation a number of individuals who provided input and testimony from their varied perspectives for the committee's deliberations. At the first meeting, in Washington, DC, on October 7, 2008, the following individuals presented information to the committee:

Kimberley Cohen, Covance
W. Ron DeHaven, American Veterinary Medical Association (AVMA)
Jerry DePoyster, USDA/APHIS
David A. Kass, Johns Hopkins University
Cathy Liss, Animal Welfare Institute
Stacey Pritt, Covance
Margaret Snyder, NIH sponsor and contact person
Bill Yates, University of Pittsburgh

The following additional individuals presented information to the committee during its January 12, 2009, meeting in Washington, DC:

Stephen O'Brien, National Cancer Institute, NIH
Robert Willems, USDA/APHIS

Others who provided invaluable assistance to the committee include:

Chester Gipson, USDA/APHIS
Jodie Kulpa-Eddy, USDA/APHIS

The committee also received written material submitted for consideration by the American Physiological Society, the Humane Society of the United States, and individuals with business or personal interests in the subject of the committee's deliberations. In addition, the committee received information from several Class B dealers in response to specific questions posed by the committee.

The draft of this report was reviewed by individuals chosen for their diverse perspectives and expertise, in accordance with procedures approved by the Report Review Committee of the National Research Council (NRC). 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:

B. Taylor Bennett, Management Consultant
Larry Carbone, University of California—San Francisco
Jerry Collins, Yale University
Linda Cork, Stanford University
W. Ron DeHaven, American Veterinary Medical Association
Betty Goldentyer, U.S. Department of Agriculture
David A. Kass, Johns Hopkins University
Hilton Klein, Taconic
Kathy E. Laber-Laird, University of South Carolina
Scott Marshall, Marshall BioResources
Howard G. Rush, The University of Michigan
Marty Stephens, The Humane Society of the United States
Victoria Voith, Western University
Craig L. Wardrip, The University of Chicago
Bill Yates, University of Pittsburgh

The review of the report was overseen by:

Peter Ward, University of Michigan
Peter Raven, Missouri Botanical Garden

Appointed by the NRC, these individuals 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.

I extend my sincere appreciation to the members of this Committee, who invested considerable time, effort, and interest in this report. Although we had our distinct perspectives on "the elephant," the individual members always remained respectful of one other and worked as a team with a unified concern for animal welfare. In addition, I acknowledge the assistance of Christine Henderson. This was her first effort at assisting with an Academy report, and I trust not her last.

Stephen W. Barthold, *Chair*
Committee on Scientific and Humane
Issues in the Use of Random Source
Dogs and Cats in Research

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Summary

BACKGROUND

Biomedical research uses various types of laboratory animals, known as animal models, to advance both human and veterinary medical knowledge. Most laboratory animals used in research today are rodents; a relatively small number are dogs and cats, most of which are either "purpose-bred" specifically for research by licensed commercial breeders (known as Class A dealers), or bred and raised in research colonies. Another smaller percentage of research dogs and cats, and the focus of this study, are commonly referred to as "random source" animals. Most, but not all, of these are provided by licensed dealers, known as Class B dealers (see below for a definition of the type of Class B dealer relevant to this report), which acquire dogs and cats from random sources, such as individual owners, small hobby breeders, and pounds and shelters.

Random source dogs and cats may possess a variety of desirable characteristics for research, including anatomic features, age, genetic diversity, and naturally occurring infectious disease, among others. However, they may also have undesirable features, such as unverifiable health status, zoonotic diseases, and inconsistent research qualities (such as temperament). In Chapter 3, this report provides detailed overviews of the characteristics of random source animals as they relate to the suitability of such animals for biomedical research.

Class A and Class B dealers are subject to federal regulation under the Animal Welfare Act (AWA) and are licensed by the United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA/

APHIS). The AWA has been revised, amended, and increasingly refined since its original passage in 1966. Enforcement of the AWA is the responsibility of the USDA/APHIS, which has also repeatedly revised its Animal Welfare Regulations (AWR).

In general, the American public is supportive of the use of animals in research. However, the public is also concerned about the humane treatment of these animals. This concern has contributed to the evolution of federal laws, principles, and policies that guide the use of animals in biomedical research; for example, concern over lost or stolen pets was a major impetus that shaped the AWA when it first passed in 1966. Despite increasingly effective (but still incomplete) enforcement of the law, public concern continues, especially with respect to the use in biomedical research of random source dogs and cats that are obtained from pounds and shelters and may have come from the general pet population. Recent failure of the AWA and USDA/APHIS to prevent abuses by some, but not all, Class B dealers who buy and sell random source dogs and cats for research have re-stimulated public concerns, particularly in regards to lost or stolen pets.

In response to a request of Congress, the National Institutes of Health (NIH) charged the National Academies to critically examine the general desirability and necessity of using random source dogs and cats in NIH-funded research, and the specific necessity of using dogs and cats from Class B dealers for such research.

MANDATE AND STATEMENT OF TASK FOR THE REPORT

As a result of the Fiscal Year 2008 House Appropriations Committee Report 110-231 and Fiscal Year 2008 Senate Appropriations Committee Report 110-107 regarding appropriations to the Department of Health and Human Services, with the Pet Safety and Protection Act of 2007 as an additional impetus, Congress charged the NIH with determining the humane and scientific issues associated with the use of random source[1] dogs and cats in research. NIH in turn asked the National Academies to assemble a committee of experts to prepare a report that addresses the following statement of task:

> The National Academies will form an expert committee (entitled "**Scientific and Humane Issues in the Use of Random Source Dogs and Cats for Research**") to address the use of Class B dogs and cats in research funded by the National Institutes of Health (NIH). Specifically, the committee will:

[1] Research animals that come from the general population, rather than from commercial breeders, are "random source" animals. See **Characteristics of Random Source Animals for NIH-Funded Research,** below.

1. 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).
2. Describe the specific characteristics, such as physiological, anatomical, or genetic characteristics, of the animals that make them particularly well-suited for the types of research described under Task #1.
3. 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.

The NIH, as the sponsor of this report, negotiated the Statement of Task with the National Academies, which, through its Institute for Laboratory Animal Research (ILAR), appointed an authoritative committee of experts in biomedical research, animal behavior, animal welfare, and veterinary medicine.

This is a highly nuanced report, since its deliberations and recommendations pertain only to the desirability/necessity of random source dogs and cats, and specifically random source dogs and cats from Class B dealers for NIH-funded research (not for other purposes, such as teaching, veterinary research, or research by industry). The animals that fall under these narrow definitions are relatively few in number, but may have potentially high value for advancing medical knowledge. They also profoundly impact public perceptions about humane treatment of all research animals, protection of pets from theft or loss, and public attitudes toward animal-related research funded by NIH.

CHARACTERISTICS OF RANDOM SOURCE ANIMALS FOR NIH-FUNDED RESEARCH

Random source animals (those that come from the general population rather than from Class A dealers) represent potentially important models for research on naturally occurring diseases such as cancer, infectious diseases, and age-related diseases because they may provide research scientists with a genetically diverse study group. They may also exhibit characteristics not available in purpose-bred animals; for example, random source dogs may be larger (especially useful for the study of heart disease) and/or older (desirable for research on the processes of aging).

Most random source animals come from Class B dealers who are exclusively licensed to buy and sell animals for research (Class A dealers breed animals, called purpose-bred, on their own premises and sell them to various entities, including research institutions; they do not buy animals

except to replenish their breeding stock). However, random source animals can also be obtained directly by research institutions through the same sources from which Class B dealers obtain them (e.g., pounds, shelters, and individual owners).

Because random source animals come from various sources, they are more likely to be associated with undesirable aspects such as infectious disease, occupational health (zoonotic) hazards, and inconsistent health and welfare standards. These undesirable aspects may limit their value for research purposes and place additional burden on institutions resulting from increased health and welfare surveillance.

Cost may be a factor in the decision to use random source animals for research, as they are less expensive than most purpose-bred dogs and cats. However, there are often additional costs associated with conditioning the animals to make them suitable for research, including quarantine, treatment for parasites, vaccination, de-worming, and other procedures. These costs for research institutions, as well as those incurred by the federal government (USDA) related to inspection and enforcement of Class B dealers, tend to equalize the costs compared to purpose-bred animals. Furthermore, cost alone should not be the sole determinant of the appropriateness of a particular animal model used in research.

TRENDS AND STATUS OF CLASS B ANIMALS AND DEALERS

There are more than 1,000 Class B dealers operating in different USDA-designated capacities such as distributors of animals for the pet industry, animals for exhibit purposes, and animals used in laboratory research. The specific group of interest for this study is the latter, which buys and sells live random source dogs and cats for biomedical research.

It is important to emphasize that this report addresses only those few Class B dealers—11 of them at last count—that acquire and sell live random source dogs and cats for research and teaching. Not all of these 11 dealers provide animals for NIH-funded research; and one has a suspended license and is not likely to resume activity. Furthermore, the demand for and use of random source as well as purpose-bred dogs and cats in research has fallen significantly over the last 30 years, as has the number of Class B dealers. These developments suggest that for a variety of reasons (research trends, alternate animal models, institutional policies, animal welfare, public opinion, animal rights pressure, regulatory and financial burden), the Class B dealer system may eventually become unavailable.

Although these facts narrow the focus of this report, the necessity of Class B dealer-derived dogs and cats must be assessed both (1) from the perspective of the general desirability and necessity of random source dogs and cats for biomedical research and (2) in the broader context of all of the

following factors: U.S. law (AWA); USDA/APHIS interpretation of the law (AWR); *U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*; *Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals*; the National Academies' *Guide for the Care and Use of Laboratory Animals*; and widely accepted voluntary assurance mechanisms for compliance of high standards of laboratory animal care through the *Association for Assessment and Accreditation of Laboratory Animal Care* (AAALAC) *International*.[2] These various laws, regulations, principles, policies, guidelines, and compliance mechanisms are inextricably intertwined and had a significant impact upon the Committee's deliberations.

GENERAL CONCLUSIONS

The Committee determined that although the number of random source dogs and cats used in research is small and declining, they represent an important but relatively small asset to biomedical research (in 2007 to 2008 approximately 4 percent of dogs and 1 percent of cats used in research were acquired from Class B dealers with a smaller percentage of those being random source animals from pounds and shelters). The principal question posed to the Committee was not whether such animals should be used in research but whether dogs and cats from Class B dealers are necessary. Animals with similar qualities are available from such alternate sources as direct acquisition from pounds and shelters, Class A dealers of purpose-bred dogs and cats, existing research colonies, and owner-donated animals. The Committee therefore determined dogs and cats from Class B dealers are not necessary for NIH-funded research. Regardless of the source however, if NIH deems animals with random source qualities to be important, proactive mechanisms to assure continued access to alternative sources, as well as consideration of additional options, are essential for the advancement of both human and animal research. One argument for the use of random source dogs and cats is that they come from a genetically diverse base within the general dog and cat populations and comprise many highly valuable genetic models of human disease. Class B dealers do not play a significant role in discovering and acquiring these models; rather, they have largely been discovered and acquired through NIH-funded programs that foster cooperation between the animal breeder community, private owners, the veterinary community, and NIH. Furthermore, as access to random source animals from pounds and shelters becomes increasingly limited, Class B animals are becoming more and more similar to those provided by Class A breeders because Class B dealers increasingly acquire animals from

[2] These guidelines and regulations also apply to Class A dealers.

hobby breeders. The Committee recognizes, however, that Class B dealers may still provide a benefit in acquiring dogs and cats from diverse sources and conditioning them before resale for research.

The Class B dealer system, as originally intended by federal law, would be desirable for the reasons stated above. But the Committee found that, despite over 40 years of regulations resulting from the AWA, the Class B dealer system does not operate consistently as intended. The USDA invests increasing efforts in enforcing the AWR with Class B dealers, primarily in tracebacks (the process of verifying the origins and, to a lesser extent, the standards of care of these animals). Standards of care for the animals at the remaining 11 Class B dealers appear to vary greatly. Some Class B dealers subscribe to the full intent of the law while others jeopardize the industry. Furthermore, the Committee noted that although dogs and cats acquired by Class B dealers are destined for research, including NIH-related research, the standards of care for these animals at some dealers are discordant with the standards set forth in the *U.S. Government Principles*, *PHS Policy*, and the *Guide*. Class B dealers and their facilities however, are governed only by the AWR. Although in principle these various standards are similar, in practice they are not. The AWR are difficult to enforce outside the PHS circle of influence: standards at a PHS-assured institution tend to be scrutinized more carefully because that institution's assurance is periodically reviewed and the institution's NIH funding is in jeopardy if the assurance is violated (including violations of the AWR), whereas non-PHS-assured entities are not subject to the same kinds of scrutiny or penalties. Moreover, some institutions that accept PHS funds also have AAALAC International accreditation adding another layer of animal welfare guidance. This dichotomy of standards colors public perceptions of the NIH and USDA, and brings into question the welfare of these animals.

CONCLUSIONS AND RECOMMENDATIONS

The Committee concluded that under some circumstances, dogs and cats with qualities of random source animals may be desirable and necessary for NIH-funded research. The Committee was unable to specifically identify research projects that used Class B animals, since NIH does not maintain records of the specific sources or numbers of research animals nor of grants that use Class B animals, and individual grants and publications do not identify sources of animals. However, the Committee found that it is not necessary to obtain random source dogs and cats for NIH research from Class B dealers, provided that alternative sources of animals with similar characteristics can continue to be assured.

The Committee concluded that alternative options are currently available to fill the majority of NIH needs for various types of research dogs and cats:

- **Direct Acquisition from Pounds and Shelters.** Albeit in diminishing numbers, animals can still be obtained directly from the few states that mandate pound seizure and from some municipal shelters in states that have no formal policy prohibiting such acquisition.
- **Donation Programs.** Direct acquisition of animals from small breeders, hobby clubs, and individual owners is a practice already in use by research institutions and accounts for a significant percentage of animals currently being acquired by Class B dealers.
- **Cooperative Pre-clinical Consortia.** The current use of pet animals with owner consent for NIH-supported comparative pre-clinical investigations for cancer research is a viable model for advancing both human and veterinary medical research. Cooperative efforts can capitalize on the rich genetic diversity and variety of cancers that arise in the canine population as well as on anatomic and disease characteristics that are more accurately reflective of the human condition than those of rodents. In addition, they ensure outstanding clinical care of the animals, and they are not constrained by human phase I, II, and III clinical trial designs. Such consortia could be readily developed for virtually any comparative disease research of interest to categorical institutes of NIH.
- **Class A Dealers.** Class A dealers of purpose-bred dogs and cats can accommodate many research needs, including, for example, larger animals, genetically diverse animals, and older animals. If a greater number of these animals are needed, Class A vendors could provide them, albeit at a greater cost. Moreover, the number of cats provided by Class B dealers is so small that they are likely to be available through other mechanisms such as Class A dealers.
- **NIH-Supported Resource and Research Development.** Programs such as the *Referral Center for Animal Models of Human Genetic Diseases* at the University of Pennsylvania School of Veterinary Medicine (Chapter 4) directly address the needs of NIH for discovery, accurate characterization, and access to these incalculably valuable dog and cat models of human disease that arise in the general dog and cat population. This program serves as an example in which the public willingly contributes animals for research in order to advance both animal and human health, and fosters a positive public image for NIH.

In order to assure continued availability of various types of dogs and cats in the absence of Class B dealers, the Committee recommends that NIH undertake an effort to explore new potential sources of random source dogs and cats to meet important biomedical research needs, including the following options:

- **NIH Request for Proposal.** Various NIH categorical institutes commonly use the Request for Proposal (RFP) mechanism to acquire needed items (including research animals) or to perform research and development on a contractual basis, including through contracts to provide or develop specific animal models. A variety of laboratory animals, ranging from rodents to nonhuman primates, are the subject of RFPs, and since the RFPs are NIH-supported, all such animals fall under the *PHS Policy*. Thus, the RFP mechanism is already in place and is quite suitable for fulfilling this need.
- **Coordination and Support of Private Research Animal Colonies.** Several academic and commercial entities maintain purpose-bred colonies of research dogs and cats, supported by NIH or private funding. These colonies already provide some animals to other research institutions, and with additional RFP-type cooperative agreements that provide NIH support, this source of animals could be assured and better coordinated.

IMPACT OF RECOMMENDATIONS

The numbers of dogs and cats used in research are very small, and justification for use of dogs and cats from Class B dealers is largely (but not entirely) based on anatomic features (e.g., size) that can also be provided by Class A dealers, or other sources. However, the discontinuation of Class B dealers may affect not only NIH but also other research and teaching activities that may use such animals, such as veterinary medicine and private industry. Furthermore, it is important to emphasize that the Committee's recommendations pertain only to Class B dealers of live random source dogs and cats for NIH-funded research, and not the other types of Class B dealers or animals, which may or may not be desirable or necessary.

CONCLUDING STATEMENT

Although the statement of task for this Committee initially appeared straightforward, the Committee soon realized that its task is deeply entwined with perceptions of both the public and scientific communities, increasing but as yet not completely effective efforts by USDA to assure the public trust, declining trends in the use of dogs and cats in research, and declining trends in the numbers of Class B dealers. Although random source dogs and cats represent a very small percentage of animals used in biomedical research, this small number is not commensurate with their potential value, and it is desirable to assure continued access to animals with random source qualities. This access can be accomplished with existing alternative mechanisms other than Class B dealers and can be assured with additional effort.

The Committee thus determined that Class B dealers are not necessary for supplying dogs and cats for NIH-funded research.

GLOSSARY OF ABBREVIATIONS USED IN THIS REPORT

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care (International)
APHIS	Animal and Plant Health Inspection Service, a division of USDA
APS	American Physiological Society
ASPCA	American Society for the Prevention of Cruelty to Animals
AVMA	American Veterinary Medical Association
AWA	Animal Welfare Act
AWI	Animal Welfare Institute
AWR	Animal Welfare Regulations
HSUS	Humane Society of the United States
IACUC	Institutional Animal Care and Use Committee
ILAR	Institute for Laboratory Animal Research (National Academies)
MISMR	Michigan Society for Medical Research
NABR	National Association for Biomedical Research
NIH	National Institutes of Health
OLAW	Office of Laboratory Animal Welfare/NIH
PHS	Public Health Service
SOP	Standard Operating Procedure
USDA	United States Department of Agriculture
WHO	World Health Organization
3R's	Overarching principles of animal-based research: replacement, refinement, and reduction

1

Introduction

CONGRESSIONAL MANDATE FOR THIS STUDY

Congress has been active since the late 19th century in pursuing legislation to protect the welfare of animals used in research (Chapter 2 provides a historical review of federal and state regulatory efforts in this area). Most recently, Senator Daniel Akaka (D-HI), and Representatives Mike Doyle (D-PA) and Phil English (R-PA), responding to public concerns that pet animals were being obtained from owners under fraudulent circumstances introduced in 2007 the **Pet Safety and Protection Act** (Senate Bill 714 and House of Representatives Bill 1280), "To amend the Animal Welfare Act to ensure that all dogs and cats used by research facilities are obtained legally." The bill was intended to ensure that dogs and cats used in research and education are not pets brokered through Class B dealers of random source animals, and would also establish monetary penalties for violations. However, this bill would not have affected the availability of purpose-bred and random source dogs and cats, young and old, genetically uniform and genetically diverse from a variety of other sources, such as Class A dealers, shelters, pounds, research facilities with breeding programs, and individuals.

In early 2007 S. 714 was referred to the Committee on Agriculture, Nutrition, and Forestry; H.R. 1280 was referred to the Subcommittee on Livestock, Dairy, and Poultry. However, both the Senate and House bills have received no action and are considered "dead." Nearly identical Class B dealer legislation was approved as part of both the House and Senate Farm Bills, but it was dropped in conference and the language calling for this study was substituted (Box 1-1). The Senate Fiscal Year 2008 Departments

BOX 1-1

"Class B Animal Dealers—While the Committee recognizes that the use of animals in research, under certain circumstances, has been beneficial to the advancement of biomedical research, the Committee would like assurances that such research is conducted as humanely as possible. In the case of the use of dogs and cats used in research and obtained from Class B dealers, the Committee is concerned that such dealers have the potential to provide animals that have not been treated in accord with USDA regulations for use in federally supported research. The Committee asks the NIH to seek an independent review by a nationally recognized panel of experts of the use of Class B dogs and cats in federally supported research to determine how frequently such animals are used in NIH research and to propose recommendations outlining the parameters of such use, if determined to be necessary."

of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill (S. 1710) report requested a study on this issue.

TIMELINE FOR THIS NRC STUDY

Based on the Fiscal Year (FY) 2008 Senate and House Appropriations Committee Reports,[1] with the Pet Safety and Protection Act of 2007 as an additional impetus, Congress charged the National Institutes of Health (NIH) to determine the humane and scientific issues associated with the use of random source dogs and cats in research. In turn, NIH asked the National Academies to assemble a committee of experts to prepare a report that addresses the topic as defined in its statement of task (Box 1-2). In August 2008 the National Academies' Institute for Laboratory Animal Research (ILAR) formed the Committee on Scientific and Humane Issues in the Use of Random Source Dogs and Cats (see Appendix A for biographies).

ANIMAL WELFARE ACT AND USDA DEFINITIONS

The following terms and definitions are used throughout this report. Where appropriate, the source of the definition is provided. The USDA Animal and Plant Health Inspection Service (APHIS) Animal Welfare Regulations (AWR) 9 CFR Ch. 1 (January 2006 Edition) contain the following definitions:

[1] House Appropriations Committee Report 110-231 and Senate Appropriations Committee Report 110-107 regarding FY 2008 appropriations to the Department of Health and Human Services

BOX 1-2
NIH Statement of Task for the Committee on Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research

The National Academies will form an expert committee to address the use of Class B dogs and cats in research funded by the National Institutes of Health (NIH). Specifically, the committee will:

1. 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).
2. Describe the specific characteristics, such as physiological, anatomical, or genetic characteristics, of the animals that make them particularly well-suited for the types of research described under Task #1.
3. 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.

- **Dealer** (Sec 1.1)**:** means any person who, in commerce, for compensation or profit, delivers for transportation, or transports, except as a carrier, buys, or sells, or negotiates the purchase or sale of: Any dog or other animal whether alive or dead (including unborn animals, organs, limbs, blood, serum or other parts), for research, teaching, testing, experimentation, exhibition, or for use as a pet; or any dog at the wholesale level for hunting, security, or breeding purposes. This term does not include: A retail pet store, as defined in this section, unless such store sells any animal to a research facility, an exhibitor, or a dealer (wholesale); any retail outlet where dogs are sold for hunting, breeding, or security purposes; or any person who does not sell or negotiate the purchase or sale of any wild or exotic animal, dog, or cat and who derives no more than $500 gross income from the sale of animals other than wild or exotic animals, dogs, or cats during any calendar year.
- **Random source** (Sec 1.1)**:** dog or cat is one obtained from an animal pound or shelter, auction, or from any person who did not breed and raise them on his or her premises.
- **Pet animal** (Sec 1.1)**:** means any animal that has commonly been kept as a pet in family households in the United States, such as

dogs, cats, guinea pigs, rabbits, and hamsters. This term excludes exotic animals and wild animals.

- **Pound** or **shelter** (Sec 1.1)**:** means a facility that accepts and/or seizes animals for the purpose of caring for them, placing them through adoption, or carrying out law enforcement, whether or not the facility is operated for profit. These terms are used interchangeably in this report.
- **Animal** (Sec 1.1)**:** means any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes birds, rats of the genus *Rattus*, and mice of the genus *Mus*, bred for use in research; horses not used for research purposes; and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs, including those used for hunting, security, or breeding purposes.

The Committee used the following as working definitions:

- **Lost pets:** pet animals that are missing but not stolen, and the owner would like to reacquire.
- **Stolen pets:** animals that have been illegally removed from the owner's possession.
- **Abandoned pets:** animals that have been left or discarded by their owners.
- **Relinquished pets:** animals that have been voluntarily released by their owners to shelters and pounds.
- **Feral animals:** animals that have escaped from domestication and returned, partly or wholly, to their wild states.

The following definitions were provided directly from the USDA upon questioning by the Committee (January 2009):

- **Purpose-bred:** a dog or cat bred and raised specifically for research purposes; however, this term is not defined in the AWR.
- **Non-random source:** was used to describe animals that were obtained from persons who bred and raised them on their premises, such as hobby breeders. An example of a non-random source animal would be a hobby breeder of purebred working, hunting, or

security dogs. This term was deleted from the AWR as a result of a rule change in 2004.

- **Buncher:** a person who collects dogs, cats, or other regulated animals from random sources and supplies these animals to laboratory animal dealers. Bunchers are now required to be licensed as Class B dealers. This term is not defined in the AWR, but it is defined in the USDA/APHIS Animal Care Resource Dealer Inspection Guide.[2]
- **Mongrel:** a random or non-random source dog of mixed or indeterminate breed.
- **Inspection manuals:** internal USDA documents which provide specific instructions and definitions for USDA inspectors to use during their inspections. Currently, there are 3 different manuals (USDA 1999, 2001, 2004), one each for dealers, research facilities, and exhibitors. These manuals allow for the application of different standards for each of these groups (e.g., oversight committees [see below regarding institutional animal care and use committees] apply to research facilities but not to dealers).
- **Contract pound:** a private pound or shelter established for the purpose of caring for animals, such as a humane society, or other organization that is under contract with a state, county, or city, that operates as a pound or shelter, and that releases animals on a voluntary basis.
- **Pound seizure:** the legally mandated sale or release of cats and dogs from a pound or shelter to a research, testing or educational facility.

It is important for the readers of this report to understand the specific characteristics of the following types of dealers (based on AWR 9 CFR Ch. 1, January 2006 Edition):

- **USDA Class A Licensee:** a USDA-licensed dealer that breeds animals (i.e., purpose-bred animals) which may include dogs and cats on their own premises, and which are sold to various sources, including research facilities (USDA Sec. 1.1).
- **USDA Class B Licensee:** a USDA-licensed dealer that purchases and resells animals, which may include dogs and cats. These animals may be random source, or non-random source animals. Regardless of the source of purchase, once the Class B dealer obtains ownership of an animal, it is considered a random source animal. As USDA licensees, Class B dealers may broker different types of

[2] http://www.aphis.usda.gov/animal_welfare/downloads/manuals/dealer/definitions.pdf

animals, including pets for the pet trade, exhibitor animals and laboratory animals for research. Some Class B Laboratory Animal Dealers deal with live animals other than dogs or cats, and some Class B Laboratory Animal Dealers do not deal with live animals (USDA Sec. 1.1).

USDA Class B Laboratory Animal Dealer of Live Random Source and Non-Random Source Dogs and Cats: a specific group of USDA-licensed Laboratory Animal Dealer that buys and sells live random and non-random source dogs and cats for research. Only a Class B dealer is permitted to acquire random source dogs and cats for resale.

The statement of task specifically involves **USDA Class B Laboratory Animal Dealers of Live Random Source and Non-Random Source Dogs and Cats**. Because the Committee's deliberations and recommendations do not pertain to other types of Class B dealers or animals, this designation is important to define as the specific category of dealers under consideration in this report.

OVERVIEW OF EXISTING ANIMAL WELFARE REGULATIONS AND GUIDELINES

In addition to the Congressional efforts cited above, a number of well-established and widely accepted regulations and guidelines inform the research use of laboratory animals. An abiding principle in biomedical research is that reproducible and valid scientific data require healthy[3] and well-cared-for laboratory animals. The biomedical research community is very much aware of this principle, and subscribes to a number of laws, regulations, guidelines, and voluntary compliance measures, summarized below, that ensure humane animal care, but also good science.

3Rs: All laws, guidelines and policies involving sentient research animals incorporate the principles originally put forth in Russell and Burch (1959) and updated in the *Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research* (NRC 2003):

- **Reduction*:*** Alternatives as methods for obtaining comparable levels of information from the use of fewer animals in scientific procedures, or for obtaining more information from the same number of animals.
- **Refinement:** Alternatives as methods which alleviate or minimize

[3] See Chapter 3 for discussion on rare exceptions.

potential pain, suffering, and distress, which enhance animal well-being.

- **Replacement:** Alternatives as methods which permit a given purpose to be achieved without conducting experiments or other scientific procedures on animals.

Although these principles apply to all animal-related research, they do not apply to either Class A or Class B dealers or their animals until the animals are acquired for research.

U.S. Animal Welfare Act (AWA): Originally enacted in 1966, with a number of revisions over the ensuing years, the AWA[4] names the USDA as the responsible federal agency for its implementation and enforcement through the USDA Animal and Plant Health Inspection Service (APHIS). The AWA Animal Welfare Regulations (AWR)[5] define standards and requirements for animal care and use programs, including research facility registration, establishment and responsibilities of institutional animal care and use committees (IACUCs), requirements for attending veterinarians and veterinary care, record keeping, reporting, and procurement, handling, care, treatment, and transportation of research animals. In addition, APHIS has established Animal Care Policies (AC Policies) that further clarify the intent of the AWA. The AWA specifically applies to any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or other warm-blooded animal used or intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes birds, rats of the genus *Rattus*, and mice of the genus *Mus*, bred for use in research; horses not used for research purposes; and other farm animals, such as, but not limited to, livestock or poultry used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. The term *dog*, means all dogs, including those used for hunting, security, or breeding purposes. Licensure and compliance of Class B dealers is covered by the AWA through the USDA/APHIS.

Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals: The *PHS Policy* originally drafted in 1973, and revised in 1979 and 1986 (NIH/OLAW 2002), applies to all institutions that use live vertebrate animals in research supported by any component of the PHS, including the Agency for Health Care Research and Quality, the Centers for Disease Control and Prevention, the Food and Drug Administration, the

[4] http://www.aphis.usda.gov/animal_welfare/downloads/awa/awa.doc
[5] http://www.aphis.usda.gov/animal_welfare/downloads/awr/awr.doc

Health Resources and Service Administration, the Indian Health Service, the National Institutes of Health, and the Substance Abuse and Mental Health Services Administration. Since 1985 *PHS Policy* has the force of law, requires research institutions that receive federal funds to establish and maintain appropriate programs for the care and use of animals involved in research, research training, and biologic testing. It requires institutions to comply with the AWA and AWR, and requires institutions to follow the National Research Council's *Guide for the Care and Use of Laboratory Animals* (NRC 1996). Oversight of *PHS Policy* is the responsibility of the NIH Office of Laboratory Animal Welfare (OLAW). All covered institutions must register an animal welfare assurance statement with OLAW, assuring compliance with *PHS Policy*. The *PHS Policy* also requires and defines the functions of the IACUC, mandates IACUC review of all animal-related research projects that involve federal funds, defines the information required in PHS proposals for research, and stipulates record keeping and reporting requirements. PHS research proposals must include a description and justification of animal use and are subject to review by scientific peers and funding agencies.

***Guide for the Care and Use of Laboratory Animals* (*Guide*):** This NRC report was first published in 1963, under the title *Guide for Laboratory Animal Facilities and Care*, by the Animal Care Panel,[6] a group of professionals with interest in laboratory animal care, in collaboration with the NRC Institute for Laboratory Animal Resources.[7] The *Guide* was revised in 1965, 1968, 1972, 1978, and 1985. These editions were supported by NIH and published by the Government Printing Office. The most recent edition of the *Guide* was updated in 1996 by ILAR (which is responsible for execution of this study) of the National Research Council (NRC 1996), and was supported by NIH, the USDA, and the Department of Veterans Affairs, and was published by the National Academies Press. The *Guide* is currently being updated (in progress). The *Guide* promotes the humane care of animals used in biomedical research, teaching, and testing. It provides guidelines on institutional policies and responsibilities, and performance-based standards for animal environment, housing, management, veterinary care, and physical plant. As noted above, *PHS Policy* requires research institutions to base their programs of animal care and use on the *Guide*.

[6] Precursor to the American Association for Laboratory Animal Science, AALAS; http://www.aalas.org

[7] Renamed the Institute for Laboratory Animal Research in 1998; http://www.dels.nas.edu/ilar

***U.S. Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (U.S. Government Principles)*:** The *U.S. Government Principles* (NIH/OLAW 2002) were published in 1985 by the Interagency Research Animal Committee, which consisted of representatives from federal agencies that use or require the use of animals for research and testing. The *U.S. Government Principles* ensure that the use of animals in research is justified and humane, and mandates compliance with the AWA and other applicable federal laws, guidelines, and policies (including the AWR, *PHS Policy* and the *Guide*). In turn, compliance with the *U.S. Government Principles* is mandated by the *PHS Policy* and recommended by the *Guide*.

Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International): AAALAC International[8] is a private, non-profit organization that promotes the humane treatment of animals in science through a program of voluntary inspection, compliance and accreditation. AAALAC International utilizes the *Guide* as its primary reference document, augmented by current research and professional standards of care. Since the *Guide*, AWA, AWR and *PHS Policy* are closely inter-related, AAALAC International also assesses compliance with these regulations and policies through its accreditation process. Certification of compliance with AAALAC International standards is awarded for a 3-year term, and is based on review of a detailed description of the institution's program of animal care and use, followed by on-site evaluation by a team of experts.

Laws, Policies, Principles, and Guidelines Pertaining to Class B Dealers: All Class A and Class B dealers are covered by the AWA, but since they do not receive federal funds directly, they are not required to follow *PHS Policy* or the *U.S. Government Principles*. They may voluntarily elect to follow the *Guide* and opt for AAALAC accreditation, but none of the existing Class B dealers are AAALAC International accredited. In contrast, some, but not all, Class A dealers are AAALAC International accredited. Therefore, compliance and enforcement of humane treatment of dogs and cats from Class A and Class B falls under the AWA only until the animals enter a research institution.

[8] Founded in 1965 as the American Association for Accreditation of Laboratory Animal Care; http://www.aaalac.org

ANIMAL WELFARE ACT PROVISIONS IN REGARD TO DOGS AND CATS

USDA Licensing

Any person operating or planning to operate as a dealer must have a valid USDA license. There are three classes of license holder (AWR Sec 2.1), Class A and Class B licensees who are referred to as dealers, and Class C licensees who are referred to as exhibitors. In general, Class A dealers breed animals, Class B dealers purchase and resell animals, and Class C exhibitors display animals. A review of the Animal Care Annual Report of Activities for Fiscal Year 2007 (USDA, APHIS 41-35-075) revealed that, of the over 1,000 Class B dealers licensed in the U.S., only 11 operate as random source Class B dealers that purchase dogs and cats for resale (USDA 2007).

Class A dealers breed and raise on their own premises, animals that are then sold to various sources, including research facilities. The animals they breed are referred to as purpose-bred animals. Purpose-bred animals from the same vendor have similar environmental backgrounds and are usually of the same breed-type and temperament. They are typically under an established program of veterinary care including vaccination and de-worming programs. Such factors help to minimize physiological and behavioral research variables (Fox et al. 2002). Purpose-bred dogs are the most common type of dogs and cats used in research. USDA was unable to provide the current number of Class A dealers of dogs and cats (as of April 2009 there are over 4,000 Class A dealers of all animals based on the USDA licensee information), but according to the Lab Animal Buyers Guide of 2008, there were 6 such dealers breeding beagles, hounds and mongrel dogs.

Class B dealers purchase animals from various sources and then resell them. Only a Class B dealer may acquire random source dogs and cats for resale. Animals from Class B dealers may be sold to research institutions or to other licensees. According to the AWR, Sec 2.132 (a) Class B dealers may obtain live random source dogs and cats only from (1) Another licensed dealer (this includes auction houses, see below); (2) State, county, or city-owned and operated pounds and shelters; and (3) Contract pounds or shelters. The animals these dealers buy and sell may be random source or non-random source dogs and cats (among other species) and regardless of source once these dogs and cats enter the Class B system, they are collectively referred to as random source animals, or Class B animals.

Class A or Class B dealers whose business involves dead animals may sell cadavers or tissues including organs, blood, or other body parts for use in various research, teaching, medical, or training institutions. Typically, dogs and cats used as blood donors for privately held blood banks are

maintained by Class B dealers, but not necessarily Class B dealers of live random source dogs and cats. Sellers of such blood products also require a Class B license as they deal in parts of animals that have otherwise not been tested.

The USDA established the annual license renewal fee for a Class B dealer by calculating the total amount received from the sale of animals to research facilities, dealers, exhibitors, retail pet stores and persons for use as pets, either directly or through an auction sale, during the preceding business year (calendar or fiscal) less the amount paid for the animals by the dealer or applicant.[9]

Class B dealers include brokers and operators of auctions, since these individuals negotiate or arrange for the purchase, sale, or transport of animals in commerce (see definition of dealer). An auction may not take physical possession or control of the animals, nor hold animals in any facilities. Auction houses are licensed as Class B dealers, but they are not considered random source Class B dealers because they do not take possession of the animals.

Typically, dogs and cats from Class B dealers are of various breed-types and ages, and have variable environmental and microbial backgrounds, and have variable vaccination and medical treatment histories. The health status of these animals may be the same quality as purpose-bred animals, or it may be unknown. Random source animals that have been treated and vaccinated in preparation for use in research are termed "conditioned" animals. Non-conditioned random source animals are useful in only a limited number of research studies, such as non-survival training preparations (Fox et al. 2002).

There are a number of exemptions to the Class B licensing requirement including:

- Retail pet stores (unless they sell for research, exhibition, or sell wild or exotic animals);
- Any person who derives no more than $500 gross income from the annual sale to exhibitors, dealers, or pet stores of animals other than wild or exotic animals, dogs or cats, and dogs or cats sold to research;
- Any person who maintains three or fewer breeding females of dogs, cats, and/or small exotic or wild mammals sold as pets or for exhibition;
- Any person who sells fewer than 25 dogs and/or cats that were bred and raised on their premises per year;

[9] Title 9 – Animals and Animal Products. Chapter 1 – APHIS USDA Subchapter A – Animal Welfare Part 2 – Regulations, Subpart a – Licensing. 2.6 – Annual license fee.

- Any person who transports animals for breeding, exhibition in purebred shows, participation in competitions, and the like;
- Any person who buys, sells, or transports animals used only for the purposes of food or fiber;
- Any person who breeds and raises domestic animals for direct retail sales to another person for the buyer's personal use and;
- Any person who buys animals solely for their own use or enjoyment.

Prior to 2004, these exemptions allowed individuals (bunchers) to traffic in dogs and cats for profit and without a license. Bunchers provided a mechanism for animals not bred and raised on an individual's premises to enter the Class B system. Bunchers were a difficult entity to regulate. Changes were proposed in 1987 to the AWR with a final rule issued in 1989, to prohibit the purchase, sale, use or transportation of stolen animals (Section 2.60); added a requirement that dealers record the driver's license number and state for every individual from whom a dog or cat is purchased (Sec 2.75); and a requirement that all operators of auction sales be licensed as Class B dealers. To further strengthen oversight of bunchers, the USDA issued the "Animal Welfare; Inspection, Licensing and Procurement of Animals" docket, which was proposed in 2000 and finalized in 2004. This policy prohibits Class B dealers from acquiring animals through bunchers who are operating as unlicensed dealers. Currently, anyone who sells "any dogs and cats not born and raised on the premises for research purposes requires a license" (AWA Subpart A, 2.1 (3) (iv)). Furthermore, the USDA fact sheet *Animal Welfare Act (AWA) Provisions Regarding Animal Dealers*[10] states that "Anyone importing, buying, selling, or trading laboratory animals, either directly to research institutions or through other dealers, **must be licensed**. This licensing requirement includes "bunchers," who supply dealers with dogs, cats, and other regulated animals collected from random sources . . ." (emphasis added). Random source dogs and cats by definition may come from individual entities that did not breed or raise the dog or cat on their own premises. A Class B dealer may not obtain dogs and cats from an unlicensed individual who did not breed and raise the animal on his/her premises or by use of false pretenses, misrepresentations, or deception (9 CFR 2.132(b) and (d)).

Research facilities may obtain dogs and cats from Class A or Class B dealers, directly from pounds or shelters, or from persons who have bred and raised the animals on their premises and fall within the exemption requirements (listed above) (Letter to the Committee, from Chester Gipson, USDA/APHIS, January 2009). An institution that sells or exchanges dogs or

[10] http://www.aphis.usda.gov/animal_welfare/downloads/aw/awlicreg.pdf

cats that it no longer needs, may be acting as a Class B dealer and needs to be licensed as such. However, the AWR do allow for some *de minimis* exceptions in this area upon consultation with the USDA for a specific determination. This provides a mechanism that allows academic institutions to trade with each other in unwanted or unused dogs and cats without obtaining a license.

Specific AWR Provisions

Holding periods: Holding periods for Class B dealers were established to ensure that lost or potentially stolen dogs and cats had adequate time to be reunited with their owners. Holding periods range from 24 hours to 10 days, depending on the source (pound versus private individual versus other USDA licensee) and age of the animal (9 CFR 2.101). If the dog or cat came from another USDA licensed individual or from a private individual who bred and raised the dog or cat on his/her premises, and it is less than or equal to 120 days of age, the holding period is 24 hours. If the dog or cat came from a government-operated pound or shelter or a hobby breeder, and is 120 days of age or older, it must be held for 5 days. If it came from a private or contract pound, it must be held by the Class B dealer for 10 days. According to the AWR Sec. 2.133, the sources from which Class B dealers may obtain random source dogs and cats from (another licensed dealer, pound or shelter; Sec. 2.132 (a) (1) – (3)) must hold and care for the animal for a period of not less than 5 full days (including one Saturday). And a Class B dealer who obtains a random source dog or cat from a private or contract pound or shelter, must hold and care for the animal for a period of at least 10 full days (AWR Sec. 2.101 (a) (1)).

Certification requirements (AWR Sec. 2.133 (b) (1)-(6))**:** Upon selling a random source dog or cat to any person or institution, the Class B dealer must provide the recipient with certification that contains the following information:

- The name, address, USDA license number, and signature of the Class B dealer;
- The name, address, USDA license or registration number (as applicable), and signature of the recipient;
- A description of each dog or cat sold that includes the breed-type, sex, date of birth or approximate age, color and/or distinctive markings, and any official USDA approved identification number;
- The name and address of the person, pound, or shelter from which the dog or cat was acquired by the Class B dealer and an assurance

that this source was notified that the dog or cat might be used for research;
- The date the dealer acquired the dog or cat; and
- If acquired from a pound or shelter, a signed assurance that it met all of the holding requirements.

Traceback Investigations: The source of animals sold by Class B dealers, specifically random source animals, has been the subject of continuing public concern and scrutiny. Although the regulations clearly state the sources from which Class B dealers may obtain animals, there remains a public perception that Class B dealers obtain lost, stolen, or fraudulently acquired pets. Given the public concern regarding random source dogs and cats sold to research facilities, the USDA has maintained a heightened awareness of these particular licensees (Letter to the Committee from Chester Gipson, October 2008).

Although the AWA and USDA AWR and Animal Care Policies provisions cover both Class A and Class B dealers, the USDA inspects Class B dealers with more scrutiny and more frequency than other dealers (internal USDA Standard Operating Procedure (SOP) for Conducting Tracebacks from Random Source B Dealers; implemented in October, 2008) and at considerable cost. Whereas the AWA mandates annual inspections for research facilities, the frequency of Class A and Class B dealer inspections are determined by the USDA/APHIS risk-based inspection system (personal communication, USDA/APHIS) which currently suggests annual inspections for Class A dealers and quarterly for Class B dealers. The visits are unannounced and therefore may require more than one attempt to gain access to the facility.

A major focus of these inspections is tracing the acquisition of random and non-random source animals (tracebacks). The traceback process is designed to determine where an animal came from and who sold it, to ensure regulatory compliance. The number of tracebacks conducted depends on the number of dogs or cats acquired since the previous inspection, but at a minimum of 4 dogs and/or cats and up to 10 percent of those acquired since the last inspection are traced back. The legality of acquisition is evaluated by conducting tracebacks on a representative sampling of animals. All dogs and cats whose acquisition appears suspicious will be traced back. Because the number of Class B dealers is small, the USDA is currently performing a 100 percent traceback on a rotational basis; that is, once a year each dealer will have 100 percent of its acquisitions since the previous quarterly inspection traced back. However, due to turnover, not all animals that pass through a dealer's facility will be the subject of a traceback.

As part of the traceback, inspectors are encouraged to visit the original seller's place of business when practical. Telephone tracebacks are permis-

sible only under specific circumstances when, for example, the seller is a licensed dealer, a pound, or a person or broker recognizable to the inspector. Sellers identified outside a particular area will be inspected by other USDA inspectors and the results provided to the originating inspector. If the last seller is determined to be another Class B dealer, a second traceback is performed for the previous seller to that dealer. Once contact with a seller is made, the individual is questioned by the inspector to ensure that the individual listed on the records did actually sell the dog or cat and bred and raised the animal. If the seller did not breed or raise the dog or cat, they are questioned about the source of the animal. During the early 1990s tracebacks were 40-50 percent successful at correctly identifying the seller; by 2000-2001, this estimate was 95 percent (personal communication, Ron DeHaven, formerly of the USDA, October 2008). However, the traceback for dogs and cats acquired from an auction ends at the auction house; these animals are not traced back to the person who sold them.

During an inspection of a Class B dealer, the inspector will determine whether the acquisition and disposition records meet all of the requirements set forth in AWR Sec. 2.75(a). The required records must include:

- The name and address of the person from whom the dog or cat was purchased by the dealer;
- The USDA license or registration number of the seller if he/she is USDA licensed or registered;
- The vehicle license number and state, and the driver's license number and state of the seller, if he/she is not licensed;
- The name and address of the person to whom a dog or cat was sold or given by the dealer and that person's USDA license;
- The date the dog or cat was acquired or disposed of;
- The USDA tag number or tattoo assigned to the dog or cat;
- A description of each dog or cat; and
- The method(s) of transportation, including the name(s) of the initial and intermediate handlers.

All records must be held and made available for inspection for 1 year after an animal is disposed of or euthanized. Records may be kept longer if required to comply with federal, state, or local law or if APHIS requests. If a review of traceback records shows that an unlicensed person does not meet the exemptions listed under Section 2.1 the name and address of this person is forwarded to the USDA Regional Office for further investigation. The inspection also includes an evaluation of the animals (e.g., for malnutrition or dehydration), husbandry conditions, and medical records.

Animal Care Policies

Since the early 1990s USDA has supplemented the AWR with Animal Care (AC) Policies to enhance Class B dealer accountability under the regulations and to guide APHIS officers in reducing the number of unlicensed dealers. The AWR broadly defines those business entities or relations that may be affected in order to have a wide impact.

AC Policy #1 (April 14, 1997): *Denial of AWA License Applications* strengthens the regulations that entitle APHIS to deny licensure if an applicant does not comply with AWR Section 2.11(a)(3): "Applicant has been fined or sentenced to jail under state or local animal cruelty laws as specified in Section 2.11(a)(4)," or "Applicant is under investigation by state or local authorities for animal cruelty." These provide additional tools by which a license could be revoked if a fine has been issued or the business entity was under investigation.

AC Policy #8 (May 8, 2001): *Guidelines for the Confiscation of Animals* provides guidance to APHIS officers for the confiscation of regulated animals if they are suffering. This policy states who defines suffering and how suffering is defined, and establishes the authority to require proper care and relief "as soon as possible, but typically not to exceed 24 hours." In the event of confiscation, APHIS has the power to immediately suspend an agent's license.

COMMITTEE APPROACH TO ITS CHARGE

To address the charge set forth in the Statement of Task, the Committee assessed the use of dogs and cats in research based on reporting data from the USDA. Then, using information from the NIH, the USDA, and the scientific literature, the Committee attempted to relate the use of animals from Class B dealers with particular areas of research. In reviewing this information, the Committee struggled in much the same way as the rest of society with the issues related to the perceived care and well-being of animals in the hands of Class B dealers. The emotionality of the topic and the polarization of opinion and information presented a challenge to the Committee in the objective evaluation of the data and testimony (both oral and written). Each member of the Committee dealt with mental images and writings spanning more than 40 years on this topic and considered the information in the context of American culture, laws, regulations, practices, and science related to the care and use of laboratory animals. The Committee was further challenged in its efforts to understand the process of animal acquisition and sale by Class B dealers. The relationship of these small businesses to local pounds, shelters, and small volume breeders as sources of animals for research is a complicated tangle of trade. Finally, the short

timeline for the Committee to wrestle with these difficult issues and scarce data compounded the challenge.

In the end, it was impossible to identify specific research projects that used animals from Class B dealers, since NIH does not maintain records of specific sources or numbers of animals nor of grants that use animals from Class B dealers, and individual grants and publications do not identify sources of animals. Nevertheless, the Committee used available data provided by the USDA and NIH to assess overall dog and cat use, areas of research using dogs and cats, and numbers of animals sold to research institutions by Class B dealers. The Committee was able to partially ascertain "the important … questions and common research topics … where Class B dogs and cats are desirable/necessary" and to estimate "the frequency of these various research topics." Through the testimony provided by the scientific community, the Committee was able to "describe the specific characteristics, such as physiological, anatomical, or genetic characteristics" of random source animals "that make them particularly well-suited for the types of research." Those characteristics are reflected in dogs and cats that represent a resource of significant morphological and physiological diversity. This diversity has been used in the development of animal models for the study of both human and animal diseases.

The Committee found that dogs and cats represent only 8.7 percent[11] of the total number of research animals covered by the AWA (non-covered species include mice, rats, and birds). Table 1-1 summarizes the numbers of each species covered by the AWA that were used in research from 2001-2007. For dogs and cats used in research in 2002, 20 percent came from Class B dealers, 70 percent were purpose-bred animals from Class A dealers, and 10 percent were random source animals obtained directly from shelters or pounds (Federal Register 69 (134), July 14, 2004 page 42098/National Association for Biomedical Research[12]).

FOCUS AND ORGANIZATION OF THIS REPORT

It is important to point out that there are over a thousand Class B dealers licensed with the USDA, but there are currently only 11 Class B dealers that sell live random source dogs and cats for research. USDA Class B licensed dealers may operate in different capacities such as dealing in animals destined for the pet industry or for exhibition, or brokering animals for laboratory research. Furthermore, some Class B dealers do not deal with live animals, and some Class B Laboratory Animal Dealers broker live

[11] Percentages are estimates based on USDA data both in references cited and provided to the committee.

[12] http://bulk.resource.org/gpo.gov/register/2004/2004_42098.pdf

TABLE 1-1 Numbers of Animals Used in Research, by Type and Year, 2001-2007

	2001	2002	2003	2004	2005	2006	2007
Cats	22,755	24,222	25,997	23,640	22,921	21,637	22,687
Dogs	70,082	68,253	67,875	64,932	66,610	66,314	72,037
Guinea pigs	256,193	245,576	260,809	244,104	221,286	204,809	207,257
Hamsters	167,231	180,000	177,991	175,721	176,988	167,571	172,498
Rabbits	267,351	243,838	236,250	261,573	245,786	239,720	236,511
Nonhuman Primates	49,382	52,279	53,586	54,998	57,531	62,315	69,990
Farm Animals	161,658	143,061	166,135	105,678	155,004	105,780	109,961
All Other Covered Species[a]	242,251	180,351	199,826	171,312	231,440	144,567	136,509
Total	1,236,903	1,137,718	1,188,469	1,101,958	1,177,566	1,012,713	1,027,450

[a] Any live or dead warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes birds, rats of the genus *Rattus*, and mice of the genus *Mus*, bred for use in research; horses not used for research purposes; and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management or production efficiency, or for improving the quality of food or fiber. Source: (AWR) 9 CFR Ch. 1 (January 2006 Edition) Section 1.1.

Source: *Animal Care Annual Report of Activities, Fiscal Year 2007, United States Department of Agriculture Animal and Plant Health Inspection Service APHIS 41–35–075 (2001-2007).* http://www.aphis.usda.gov/animal_welfare/publications_and_reports.shtml

animals other than dogs and cats. This report focuses on the small number of *USDA Class B Licensed Laboratory Animal Dealers* that supply *live* dogs and cats for *NIH-funded research*. The Committee emphasizes the narrow focus of this perspective, which does not address the role of random source animals for industry, education, training, or veterinary medical and other basic research.

In an effort to place these issues into their proper perspective, this report provides specific definitions of dealers of dogs and cats, summarizes the various laws, principles and guidelines that pertain to the use of dogs and cats in research and which are crucial to understanding the nuances of the USDA regulations (Chapter 1); surveys the history of U.S. animal welfare regulations and their intent (Chapter 2); examines the characteristics of random source animals for research (Chapter 3); assesses Class B dealers and animals from Class B specifically (Chapter 4); and provides recommendations in regard to Class B dealers for supplying random source dogs and cats for NIH-based research (Chapter 5).

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2

Use of Dogs and Cats in Research: Public Perception and Evolution of Laws and Guidelines

Dogs and cats occupy a particularly important place in American society in their roles as companion, work, and hobby animals. In addition, they serve as important animal models for research that has advanced both human and animal health. This multifaceted relationship with humans has fostered an uneasy tension between general society and the scientific community, and this tension has intensified as the stature of pet dogs and cats has risen in many households to that of family member. The specter of lost or stolen pets being used for research has evolved from a galvanizing concern into increasing resistance to the use of any former pet for research. Over the years the public's concern about the welfare of research animals, and dogs and cats in particular, has been instrumental in the development of laws, guidelines, and policies that affect research with all types of animals.

It is thus not possible to accurately assess the desirability and necessity of using random source dogs and cats, and in particular those from Class B dealers, for research without taking into account public perceptions, the impact of the animal protection movement both on public attitudes and on the availability of these animals for research, changing trends in the use of animal models for research, and responses of the scientific community to all of these factors. The evolution of laws, policies, and guidelines regarding the use of dogs and cats in research has been an accurate barometer of these changing trends.

In particular, in 2007 the Senate considered the Pet Safety and Protection Act, which became the impetus for Congress to charge the National Institutes of Health (NIH) to determine the humane and scientific issues

associated with the use of random source dogs and cats in research. Consequently, NIH asked the National Academies to assemble a committee of experts to address the statement of task shown in Chapter 1. This chapter provides a review of these issues to set the context for subsequent chapters that focus on the use of random source animals, and animals from Class B dealers in NIH-funded research.

PUBLIC PERCEPTIONS OF DOGS AND CATS AND OF THEIR USE IN RESEARCH

The public's perception of their pets, and of animals in general, has been one of the main driving forces behind the legislation that created and refined the Animal Welfare Act (AWA). It is estimated that nearly half of all U.S. households have at least one dog or cat, with a total population of 72 million dogs and nearly 82 million cats (American Veterinary Medical Association [AVMA] 2007[1,2]). In a survey conducted by the American Animal Hospital Association (2004[3]), approximately 94% of owners attributed human personality traits to their pets and said they would risk their lives for their pet. Indeed, in urban disasters, pet owners risk their lives (and those of rescue workers) when they fail to evacuate or attempt to reenter an unsafe building or area to save a pet (Heath et al. 1998). In addition, pet owners spend over $11 billion per year on veterinary care (American Pet Products Association 2008 survey[4]), and the pet products industry contributes over $50 billion to the U.S. economy, with the exponential growth of pet superstores, play parks, day care centers, and training centers.

Assessments of pet ownership and the state of affairs of dogs and cats in the U.S. must take into account the plight of homeless animals. However, it is impossible to provide a current or accurate estimate of the numbers of animals that enter shelters or are euthanized because there is no federal requirement to gather or release such data, shelters may obscure or refuse to release data to avoid negative publicity, and there is no reliable public list of shelters. Furthermore, although "shelter" or "pound" is defined in this report as a "facility that operates as a pound or shelter (e.g., a humane society or other organization established for the purpose of caring for animals), under contract with a state, county, or city, and that releases animals on a voluntary basis" the shelter data provided in this chapter may include statistics from other facilities commonly referred to as shelters. In the absence of

[1] http://www.hsus.org/pets/animal_shelters/common_questions_about_animal_shelters_and_animal_control.html#Why_are_there_so_many_animals_in_animal_

[2] http://www.petpopulation.org/index.htm

[3] American Animal Hospital Association 2004 Pet Owner Survey; http://www.aahanet.org/media/graphics/petownersurvey2004.pdf

[4] http://www.americanpetproducts.org/press_industrytrends.asp

accurate statistics, the estimated number of animals euthanized in shelters was 4.5 and 4.6 million in 1999 and 2000, respectively (Clifton 2002).

The inflow of animals into shelters varies considerably by area of the country and even among shelters within an area (Scarlett 2004). Several sources have suggested that 6–12% of the dog population entered shelters in the 1990s and that approximately 50–55% were euthanized (representing 4% of the total dog population) (Patronek and Glickman 1994; Wenstrup and Dowidchuk 1999), and that 5–8% of the estimated population of owned cats entered shelters and 65–80% of those (or roughly 3–6% of the total population of owned cats) were euthanized (Arkow 1994; Wenstrup and Dowidchuk 1999).

Although those percentages have likely changed since the 1990s, one might be able to make a rough estimate of the shelter intake numbers for any given year by taking AVMA demographic numbers of owned dogs and cats and multiplying them by the percentages above. According to the 2007 AVMA *U.S. Pet Ownership and Demographics Sourcebook*, the population of owned dogs in 2006 in the U.S. was 72 million (page 15, Table 1.8) and the number of owned cats was 81.7 million (page 24, Table 1.13). Those figures suggest that 4.3 to 8.6 million dogs and 4.1 to 6.5 million cats may have entered shelters, and as many as 7 million animals may have been euthanized.

Consideration of public perceptions was important to the Committee's analysis, and such information is generally derived from surveys and other sources. Although there is a risk of bias in polls and surveys (see Box 2-1), it

BOX 2-1
Using Caution with Survey Results

Information on public perceptions is generally derived from a variety of sources, most of which may be subject to bias. Polls and surveys conducted by special interest groups (which in the case of this report are likely to be either animal protectionist groups or scientific organizations), in particular, may be biased in the wording of the questions, the selection of the group to be polled, the numbers of respondents, the types of questions, the conditions under which they are answered, and the analysis of the data (Crespi 1989; Herzog et al. 2001). In addition, the decision to release the results of a poll or survey conducted by a special interest group may be influenced by whether the results support the group's position on the issue in question (Crespi 1989). For all of these reasons, the results of public opinion surveys on the use of animals in research should be interpreted with caution, and polls conducted by third-party organizations (e.g., media research and consulting firms, academic institutions)—especially when they formulate the questions—should be considered more objective (Crespi 1989).

appears that a majority of the American public is generally supportive of the use of animals in biomedical research but that the proportion has declined significantly over the last several decades, from about 85% in 1950 to 50–60% in the late 1990s and early 2000s (Herzog et al. 2001; Moore 2003; Rowan and Loew 2001). The reasons for this decline are unknown, although they appear to reflect changes in public attitudes to a wide variety of animal-related issues over the same period (Herzog et al. 2001). In 2008 the Foundation for Biomedical Research (FBR) commissioned Zogby International to conduct a nationwide telephone survey. The survey revealed that although a majority of those polled supported the use of animals for medical and scientific research, they were much less supportive than those polled in 2004 (personal communication, FBR). Other survey findings suggest that public support for animal research is influenced by the perceived importance of the medical problem being researched and the type of animal used. The use of animals (of any type) to study relatively serious medical problems (e.g., cancer, heart disease, diabetes) tends to garner more support than their use for studying relatively minor problems (e.g., allergies), while research involving the use of dogs and cats receives considerably less support than that involving the use of rodents (Herzog et al. 2001). These findings illustrate the higher value that the American public places on dogs, cats, and other companion animals (Kellert 1989).

THE ANIMAL PROTECTION MOVEMENT

The animal protection movement has had a profound impact on public attitudes toward the use of animals in research and on the evolution of laws, policies, and voluntary compliance by the scientific community (as discussed in the section below on the history of U.S. laws and guidelines; also see Rudacille 2000).

Jasper and Nelkin (1992) defined three types of animal protectionists: welfarists, pragmatists, and fundamentalists. Welfarists accept most current uses of animals, but seek to minimize their suffering. Pragmatists and fundamentalists are motivated to invoke fundamental changes in the use of animals by humans, but pragmatists seek to reduce animal use through legal actions, political protests, and negotiation whereas fundamentalists demand the abolition of all exploitation of animals, on the grounds that animals have inherent, inviolable rights. Clearly, it is impossible to classify every individual into one of these categories but this system may be a useful way to understand individual motivations.

Since the beginning of the animal protection movement in Europe in the early 1800s up through the present, the iconic species that continue to capture public sympathy are the dog, cat, horse, and nonhuman primate. The U.S. animal protection community is large and varied—in 1994, there

were over 400 animal advocacy groups, with a combined membership of more than 10 million (Blum 1994), and these figures have likely grown substantially since then. These groups include organizations such as the Animal Welfare Institute (AWI[5]), which focuses on the welfare of research animals and has published graphic documentation of animal dealer abuse (AWI 2007, which was provided to the committee); the Humane Society of the United States (HSUS[6]), which seeks to eliminate animal-based research that is harmful to animals; and People for the Ethical Treatment of Animals (PETA[7]), which seeks to eliminate all exploitive uses (research, food, fiber, and entertainment) of animals by humans. At the extreme end of the spectrum of the animal rights organizations is the Animal Liberation Front (ALF[8]), which uses acts of intimidation, terrorism, and violence to disrupt the scientific enterprise as well as to "liberate" animals from use in sports, textiles, research, and agriculture. The actions of organizations such as the ALF have been designated as terrorism[9] and resulted in passage of the Animal Enterprise Terrorism Act (S. 3880), introduced by Congressman Thomas Petri (R-WI) and signed into law on November 27, 2006.

EVOLUTION OF ANIMAL CARE OVERSIGHT WITHIN THE SCIENTIFIC COMMUNITY

The scientific community has had a long and contentious relationship with animal protection groups since the 1800s (reviewed in Rudacille 2000). In the past, the research community could be described as maintaining a somewhat imperious attitude toward the public, with overconfidence that what it was doing was right. Over the years, however, the scientific community has evolved the view that healthy and well-maintained animals are beneficial to and necessary for quality research and, indeed, has promulgated voluntary compliance beyond that which is mandated by law.

Since the early 1950s—well before the 1966 Laboratory Animal Welfare Act and the 1985 Research Animals Congressional Mandate[10]—the biomedical research community has engaged in organized efforts to improve and ensure the humane care and use of animals in research. Prominent nongovernmental scientific organizations include the National Research

[5] http://www.awionline.org

[6] http://www.hsus.org

[7] http://www.peta.org

[8] http://www.animalliberationfront.com

[9] John E. Lewis, Deputy Director of the FBI's Counterterrorism Division, testified before the Senate Committee on Environment and Public Works on May 18, 2005, "One of today's most serious domestic terrorism threats comes from special interest extremist movements such as the Animal Liberation Front (ALF)…."

[10] Public Law 99-158, Health Research Extension Act of 1985, Sec. 495.

Council's Institute for Laboratory Animal Research (ILAR); the American College of Laboratory Animal Medicine (ACLAM[11]), established in 1957 to advance the humane care and responsible use of laboratory animals through certification of veterinary specialists, professional development, education, and research; and the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International).

Since its creation in 1953, ILAR has played a critical role in developing and publishing numerous science-based guidelines on issues involving animals in research settings. The most important of the ILAR reports is the *Guide for the Care and Use of Laboratory Animals,* published under the 1963 title 3 years before the Laboratory Animal Welfare Act became law and is periodically updated (see Chapter 1). Since 1965, compliance with the *Guide* has been the AAALAC International standard for institutions seeking accreditation (in 2009, 770 institutions in 31 countries reported having been accredited[12]), and, as discussed below, the *Guide* has been incorporated by reference in federal guidelines for government-funded research.

The National Institutes of Health has also been at the forefront of efforts to improve both scientific research and laboratory animal care. In 1961 NIH funded a contract to the Animal Care Panel (now AALAS) to "determine and establish a professional standard for laboratory animal care and facilities." The Panel appointed a Committee on Ethical Considerations in the Care of Laboratory Animals and a Professional Standards Committee to evaluate laboratory animal care and use, and their efforts, in collaboration with ILAR, resulted in the 1963 publication of the *Guide for Laboratory Animal Facilities and Care* (precursor to the ILAR *Guide*; reviewed in NRC 1996). NIH also led the way in development of the *Public Health Service (PHS) Policy* that applies to most federally funded animal research (more on this below). The *PHS Policy* requires that institutions eligible for PHS funding use the *Guide* "as a basis for the development and implementation of an institutional program for activities involving animals," and the *U.S. Government Principles* (see below) similarly refer to the *Guide*.

Although the scientific community has come to embrace changes leading to the improved health and welfare of animal research subjects, at the same time the perception within the research community is that it has been under siege (Conn and Parker 2008). Attacks on and intimidation of scientists by extremist organizations have increased dramatically in recent years (FBR[13] Illegal Incidents Map[14]). Furthermore, as animal protection groups

[11] http://www.aclam.org

[12] http://www.aaalac.org/accreditation/index.cfm

[13] http://www.fbresearch.org

[14] http://www.fbresearch.org/Media/MediaRoom/Backgrounder/IllegalIncidentsMap/tabid/960/Default.aspx

have pushed for greater regulation of animal research, the cost of regulatory compliance in terms of dollars and time has become an increasing burden on biomedical research, even though it is not clear that the increased regulatory oversight directly benefits the health and welfare of the animals (Decker et al. 2007; Haywood and Greene 2008; Goldman et al. 2000). When regulations do not improve animal health and well-being, they are no more than regulatory burden. An earlier report (NRC 1988) noted the diminishing availability of random source animals nearly 20 years ago. The research community has attempted to push back against these trends through national science advocacy groups such as the FBR, the National Association for Biomedical Research (NABR[15]), and Americans for Medical Progress (AMP[16]), all of which work to educate the public about the importance of animals in research.

EFFECTS OF ANIMAL PROTECTION ACTIVITIES ON CLASS B DEALERS AND ON SCIENTIFIC ACCESS TO RANDOM SOURCE DOGS AND CATS

Despite improvements in the biomedical research community, the use of random source dogs and cats, and animals from Class B dealers, remains a divisive and publicly visible issue. The consequences of the animal protection movement and public opinion are (1) reduced access to random source dogs and cats from pounds and shelters, (2) increased USDA efforts to inspect and enforce the AWA in regards to Class B dealers, and (3) pressure on research institutions to use purpose-bred animals from Class A dealers, to explore alternative sources of animals (e.g., donation programs, direct acquisition), to use non-animal models, and to use less iconic species (e.g., pigs, small ruminants, in addition to rats, mice, and other rodents).[17] Other causes of the declining use of dogs and cats in research include reduced research funding, changing NIH program priorities, increased regulatory burden, and greater availability of other models. Animal protection activity is one of several factors that have contributed to these trends.

HISTORY OF U.S. LAWS AND GUIDELINES REGARDING THE USE OF DOGS AND CATS IN RESEARCH

Many of the changes in societal thinking that eventually led to the U.S. Animal Welfare Act of 1966 (P.L. 89-544) emerged in tandem in

[15] http://www.nabr.org

[16] http://www.amp.org

[17] In addition, although difficult to prove, there is a perception that some members of the scientific community resist termination of the use of Class B dealers as a source of research animals because they regard it as another step by the animal rights movement toward eliminating animal-based research altogether.

England and the United States over the past two centuries. In the 1820s, the English Parliament outlawed cruelty to cattle, horses, and other beasts of burden. At about the same time, the precursor to the Royal Society for the Prevention of Cruelty to Animals (RSPCA) was founded. But it was not until some 40 years later (1863–1876) that policies were developed that related to animal experimentation and the RSPCA adopted a policy against painful animal experiments. Shortly thereafter, the British Association for the Advancement of Science produced guidelines calling for the minimization of animal suffering and discouraging noncompliant experimentation (P.L. 89-544). Thomas Huxley and Charles Darwin composed a bill to regulate painful animal experiments and require the licensing of experimenters. Finally, in 1876 the Cruelty to Animals Act required experimenters to obtain yearly licenses and restricted potentially unnecessary experimental duplication.

In the colonies that formed the nucleus of what became the United States, concerns about the treatment of animals emerged early and evolved gradually over the next several centuries. The Massachusetts colony enacted the first humane law in 1641, forbidding cruelty to domestic animals. The history of this state's actions regarding the prevention of cruelty to animals serves as an example of the changes in thinking about animals in society. In 1829 the state of New York prohibited "misuse" of horses, cows, and sheep, and in 1867 it was the site of pivotal legislation that prohibited animal baiting and fighting and required the humane treatment and transportation of impounded animals. Henry Bergh, founder of the American Society for the Prevention of Cruelty to Animals (ASPCA[18]), was instrumental in persuading New York lawmakers to support this bill. It was not until 1921, however, that all states had animal protection laws.

In the 1940s, the National Society for Medical Research helped various states formulate "pound release laws," requiring states and local municipalities to have their animal shelters relinquish unclaimed cats and dogs to biomedical research institutions for experimentation and teaching. Minnesota passed such a law in 1949; other states soon followed. Conflicts over the humane treatment of research dogs and cats arose immediately between animal welfare advocates and those supporting medical research, and these conflicts became more overt in the ensuing years.

Federal Legislation 1877–1966

The first federal law prohibiting cruelty to animals took effect in 1877. Known as the "28-hour Law," it regulated the amount of time and the conditions of confinement for animals transported by the meat packing

[18] http://www.aspca.org

industry (the law required the unloading of such animals for food, water, and rest after no more than 28 hours in transit). The USDA was subsequently tasked with inspection and enforcement in this industry as well as in other instances of animal transportation, use, and processing.

During the late 1950s and early 1960s, groups concerned about the humane treatment of animals called for federal regulation of their use in research. These calls were brought into the public spotlight by two highly publicized events, both involving dogs. In 1965, a pet Dalmatian named Pepper was reported missing and was subsequently identified, by her owner, in a newspaper photograph of dogs being unloaded from a dog dealer's truck; Pepper was never located but may have been used in a medical experiment and euthanized before she could be recovered.[19] A bill (H.R. 9743) sponsored that year by Congressman Joseph Resnick (D-NY) to regulate the use of dogs in medical research was, in part, a response to the owner's plight. Later that same year, Coles Phinizy of *Sports Illustrated* wrote "The Lost Pets That Stray to Labs," chronicling the story of Pepper, and on February 4, 1966, "Concentration Camps for Dogs" was published in *Life* magazine. The text of the *Life* article was written by Michel Silva, but it was largely a photographic essay by award-winning photographer Stan Wayman, documenting the poor conditions of dogs at the White Hall (Maryland) property of Lester Brown, a Class B dealer, revealed during an investigation by HSUS Chief Investigator Frank McMahon.

Heightened public awareness following these exposés catalyzed landmark legislation in 1966. Congressman W.R. Poage (D-TX) and Senators Warren Magnuson (D-WA) and Joseph Clark (D-PA) shepherded what would become the Laboratory Animal Welfare Act, signed by President Lyndon B. Johnson on August 24 of that year. The Act established standards for the care, housing, sale, and transportation of dogs, cats, and other animals kept by animal dealers and laboratories (it defined "animal" to include only dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits, which were thus the so-called "covered species"). It also required the licensing of dog and cat dealers and set standards for the identification of dogs and cats by dealers and research facilities in order to prevent the acquisition of animals that had been obtained inappropriately. Authority was delegated to the Secretary of Agriculture to promulgate regulations for the appropriate treatment of animals intended for research or other purposes such as exhibition and use in teaching.

[19] Animal Welfare Act: Historical perspectives and future directions: Symposium Proceedings, September 1996, p. 19, http://www.nal.usda.gov/awic/pubs/96symp/awasymp.htm#pet

The Animal Welfare Act and Related Legislation since 1970

The Animal Welfare Act (AWA) of 1970 (P.L. 91-579)[20] was essentially a revision of the Laboratory Animal Welfare Act of 1966, expanded to include all species of warm-blooded animals intended for or used in research or exhibition, under the purview of the Secretary of Agriculture, as well as the sale of pet animals other than in stores. The Act also requires the licensing of all animal dealers and the humane treatment of animals in all phases of experimentation (i.e., transportation, purchase, sale, housing, care, handling, and treatment). The AWA excludes horses not used in research and farm animals used for improving animal nutrition, breeding, management, production efficiency, and the quality of food and fiber.

In 1976 amendments to the AWA categorized research institutions, exhibitors, and dealers similarly in determining fines for violations. The amendments also held government research facilities to the same standards as private institutions. Amendments to the AWA in 2002 excluded mice, rats, and birds as well as some farm animals from regulation by the Secretary of Agriculture. These species had not been regulated because they were not defined previously as "animals" and with the 2002 AWA amendments they were specifically excluded for regulatory purposes. The AWR was amended in 2004 to reflect the 2002 AWA changes.

The Food Security Act of 1985 (Subtitle F, Animal Welfare, P.L. 99-198;[21] also known as the Improved Standards for Laboratory Animals Act) defines humane care to include specific criteria such as sanitation, ventilation, and housing. It directs the Secretary of Agriculture to establish, and the USDA to enforce, regulations covering, for example, exercise for dogs and a physical environment that promotes the psychological well-being of nonhuman primates. The Act notably establishes the requirement for an institutional animal care and use committee (IACUC). Details of the current requirements are incorporated in the AWA Regulations (AWR; 9 CFR Part 1, Subpart C, 2.31[22]), which charge those involved in animal care and use to minimize pain and distress in animals by using appropriate veterinary care, anesthesia, analgesia, tranquilizers, and euthanasia. The regulations also require principal investigators to consider alternatives to any procedure likely to cause pain or distress. In commenting on the Act, Senator Robert Dole observed that "the farm bill contains legislation dealing with the humane treatment of animals. The main thrust of the bill is to minimize pain and distress suffered by animals used for experiments and tests. In so doing, biomedical research will gain in accuracy and humanity. We owe much to laboratory animals and that debt can best be repaid by good treatment

[20] http://awic.nal.usda.gov/
[21] http://awic.nal.usda.gov/
[22] http://www.nal.usda.gov/awic/pubs/Legislat/awafin.shtml

and keeping painful experiments to a minimum" (Congressional Record, December 17, 1985, U.S. Government Printing Office, Washington, DC).

In 1985, an Interagency Research Animal Committee representing the Department of Health and Human Services (with PHS components including the Alcohol, Drug Abuse, and Mental Health Administration, Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), NIH, and Office of International Health), USDA, Department of State, Department of the Interior, Environmental Protection Agency, National Aeronautics and Space Administration, National Science Foundation, and Veterans Administration formulated and published the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*.[23] These *U.S. Government Principles* were universally adopted by U.S. government agencies that either develop requirements for or sponsor procedures involving the use of all vertebrate animals.

Also that year, the Health Research Extension Act of 1985 (P.L. 99-158), Animals in Research, became law (November 20, 1985), mandating establishment by the PHS of an overarching *Policy on Humane Care and Use of Laboratory Animals* (*PHS Policy*).[24] The *U.S. Government Principles* were incorporated in the *PHS Policy* in 1986 and provide a framework for conducting research in accordance with the *PHS Policy*. *PHS Policy* requires institutions to establish and maintain proper measures to ensure the appropriate care and use of *all* vertebrate animals (including those excluded under the AWA) involved in research, research training, and biological testing activities conducted or supported by the PHS, whether performed at a PHS agency, an awardee institution, or any other institution (the PHS agencies include the CDC, NIH, and FDA). The NIH Office of Laboratory Animal Welfare (OLAW) is responsible for the administration and coordination of *PHS Policy*.

In 1990 the AWA was amended by the Food, Agriculture, Conservation, and Trade Act to improve the humane handling, care, treatment, and transportation of dogs and cats. This amendment was in response to public attitudes (as determined through public comments) and APHIS' experience in administering and enforcing the regulations.[25] Specifically, the Act strengthened regulations to prohibit the use of stolen pets in research and to provide owners the opportunity to locate their animals.[26] These amend-

[23] http://grants.nih.gov/grants/olaw/references/phspol.htm#USGovPrinciples

[24] http://grants.nih.gov/grants/olaw/references/phspol.htm

[25] *Animal Welfare; Standards, Proposed Rule*. Federal Register Vol. 55, No. 158 [15 August 1990], 33448-33531; *Food, Agriculture, Conservation, and Trade Act of 1990* [P.L. 101-624], U.S. Statutes at Large, § 2503—Protection of Pets, Approved 28 November 1990, http://www.nal.usda.gov/awic/legislat/pl101624.htm

[26] *Random Source Dogs and Cats, Final Rule*. Federal Register Vol. 58, No. 139 22 July 1993, http://www.nal.usda.gov/awic/legislat/cat1.htm

ments established a minimum 5-day holding period (including one weekend day) before the sale to a USDA-licensed Class B dealer or research facility of dogs and cats acquired by (1) pounds and shelters owned and operated by states, counties, and cities, (2) private entities established for the purpose of caring for animals, such as humane societies or contract pounds or shelters, and (3) research facilities licensed by the USDA, before being sold to a [Class B] dealer. They also require Class B dealers to provide written certification of each animal's background to the recipient. (For additional information about the Pet Theft Act of 1988, Pet Protection Act of 1990, and public perception about pet theft, see *Animal Welfare Act: Historical perspectives and future directions (Symposium Proceedings),* September 1996, pp. 32-34.[27])

The Farm Bill of 2002 included an amendment by Senator Jesse Helms (R-NC) to legally redefine "animal" in the AWA to match the 1972 change in the AWR that excludes "birds, mice of the genus *Mus*, and rats of the genus *Rattus*, bred for use in research." This version of the Farm Bill was passed by Congress in May 2002. On June 4, 2004, USDA published the "Final Rule" in the Federal Register to include the language contained in the 2002 Farm Bill excluding mice, rats, and birds bred for use in research from regulation by USDA under the AWA.

Unsuccessful Legislative Efforts

In addition to these laws, there have been numerous unsuccessful attempts at legislation to further protect animals (Table 2-1). On February 28, 2007, Senator Daniel Akaka (D-HI) introduced a bill (S. 714) that proposed amendments to the AWA "to ensure that all dogs and cats used by research facilities are obtained legally." The proposed Pet Safety and Protection Act of 2007 (S. 714) was intended to modify the AWA (7 USC 2137) and was part of a series of legislative efforts to ensure that dogs and cats used in research are obtained by appropriate means. The bill never became law, although it received two readings and was referred to the Senate Committee on Agriculture, Nutrition, and Forestry.

The Pet Safety and Protection Act of 2007 became the impetus for Congress to charge the NIH to determine the humane and scientific issues associated with the use of random source dogs and cats in research. In turn, NIH asked the National Academies to assemble this committee of experts to compile a report that addresses the statement of task found in this document.

[27] http://www.nal.usda.gov/awic/pubs/96symp/awasymp.htm#pet

TABLE 2-1 Congressional Legislation Proposed (But Not Passed) to Amend Permissible Sources for Obtaining Dogs and Cats for Research, 1997–2007.*

Year	Congress	Number	Introduced	Sponsor	Number of Co-Sponsors
2007	110	H.R. 1280	1-Mar-07	Rep. Michael Doyle [D-PA]	130
2007	110	S. 714	28-Feb-07	Sen. Daniel Akaka [D-HI]	19
2005	109	S. 451	17-Feb-05	Sen. Daniel Akaka [D-HI]	2
2005	109	H.R. 5229	27-Apr-06	Rep. Philip English [R-PA]	61
2004	108	S. 2346	26-Apr-04	Sen. Daniel Akaka [D-HI]	0
2002	107	H.R. 4039	20-Mar-02	Rep. Michael Doyle [D-PA]	44
2001	107	S. 668	30-Mar-01	Sen. Daniel Akaka [D-HI]	3
1999	106	S. 1522	5-Aug-99	Sen. Daniel Akaka [D-HI]	1
1999	106	H.R. 453	2-Feb-99	Rep. Charles Canady [R-FL]	77
1998	105	S. 2202	23-Jun-98	Sen. Daniel Akaka [D-HI]	8
1997	105	H.R. 594	5-Feb-97	Rep. Charles Canady [R-FL]	71

*At the end of the 2-year session of Congress all proposed bills and resolutions that had not passed are cleared from the books and are eligible to be reintroduced for debate under a new number in the next session. *Source:* http://www.govtrack.us/congress.

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3

Use of Random Source Dogs and Cats for Research

The statement of task given to this Committee by NIH was specific to the use of animals from Class B dealers in scientific research, but this report addresses the use of random source dogs and cats in particular, per the intent of Congress (as discussed in the Summary and Chapter 1). The two types of animals, random source and Class B, are inextricably linked but also differ; Class B dealers acquire both random source and non–random source animals, as defined in Chapter 1. As detailed in Chapter 4, only 20 percent of dogs from Class B dealers are clearly identified as random source animals from pounds and shelters. Thus, most dogs from Class B dealers are non–random source and similar to those available through other sources. Because random source animals and specifically random source animals from pounds and shelters are the driving force for Congressional and public concern, and are the animals of interest to NIH, the Committee was compelled to discuss the specific attributes, both desirable and undesirable, of random source animals in this report.

Dogs and cats, regardless of source, have been used in American biomedical research for over a century, and random source dogs and cats have contributed to advances in both human and animal health. But the American public is divided in its opinions about the use of dogs and cats from shelters and pounds in research. Public attitudes are difficult to measure accurately, however, since opinion polls are often biased to serve the needs or perspective of the polling agency. For example, in a 1990s public opinion poll conducted by the Survey Research Center of the University of Michigan Institute for Social Research, 61 percent of respondents favored the use of unwanted animals from the pound for medical research and only

23 percent were against such use. Similarly, 75 percent would oppose a law to prevent unclaimed pound animals from being used in medical research for the public benefit (Michigan Society for Medical Research [MISMR]).[1] But the results of the Michigan poll must be balanced with the knowledge that it is a regional poll, limited in scope (see Box 2-1).

At the other end of the spectrum, the results of a national poll conducted by the American Humane Association in 1988 showed that many members of the public opposed pound seizure (discussed further in Chapter 4) because they viewed shelters as havens for homeless animals and not a resource for biomedical research (American Humane Shoptalk 1988). This perspective is shared by some academic institutions, exemplified by the Colorado State University College of Veterinary Medicine and Biological Sciences (CVMBS) policy on animal use: "College policy prohibits the acquisition of live animals from shelters, either directly or indirectly through third party vendors, for use in research or teaching. The College recognizes that many individuals in our society are opposed, on ethical and scientific grounds, to the release of animals from shelters (pound seizure) for use in research or teaching. This objection is founded in the understanding that pounds or animal shelters were not designed as facilities to supply animals for such activities. Rather, they were developed to be places where people may bring unwanted or stray animals in the hope of a new home being found. If not successfully adopted, the animals may be euthanized. The release of these animals for research or teaching may be interpreted as a breach of the public trust that could lead to loss of public support" (CVMBS 2006a). In addition to concern about the use of pound animals in research, the CVMBS policy also addresses the quality of care provided to the animals used by the College: "In selecting sources from which to purchase animals to be used in research and teaching, the CVMBS strives to patronize only those suppliers who maintain the highest standards of animal care. Examples of preferred animal sources for teaching and research include: Animals typically available through well-established, federally licensed and regulated sources of purpose-bred and raised animals for teaching and research are used exclusively for species such as dogs and cats" (CVMBS 2006b).

The tendency to view dogs and cats as family members has become stronger in the past 20 years, as evidenced not only by polls (according to a 2007 Harris poll, 88 percent of pet owners view their pets as family members) but also by increased spending on veterinary care, food, toys, clothing, and day care, and by the PETS Act passed by Congress in 2006 (Harris Poll 2007). After Hurricane Katrina, when scores of people either refused to evacuate and/or returned home early out of concern for their pets,

[1] http://www.mismr.org/educational/pound.html

the PETS Act mandated that disaster plans include provisions for companion animals (The White House 2006). The public has also become increasingly vocal in support of improved care for pound animals and in opposition to the euthanasia of adoptable shelter animals, as evidenced by the rise in the number of "no kill" pounds and shelters and by veterinary specialization in shelter medicine (Zawistowski 2008). It is unlikely that public opinion has shifted dramatically to now favor pound seizure.

The professional and scientific communities view the issue somewhat differently. The American Veterinary Medical Association, in its November 2007 official policy position statement, "believes there is ample justification for prudent and humane use of random source dogs and cats in research, testing and education."[2] The American Physiological Society (APS) supports the continued use of random source animals, recognizing that they have attributes that are important in the fields of study relevant to its members: "The American Physiological Society recognizes the importance of research that depends upon animals of large size, advanced age, and diverse genetic background. These are known as 'random source animals'. . ."[3]

THE "3RS" PRINCIPLE

The universal principle that guides biomedical research on animals is the **"3Rs"** doctrine of Russell and Burch (1959; see also NRC 2003) that promotes **reduction**, **refinement**, and **replacement** of research animals whenever scientifically feasible. As discussed in Chapter 2, the number of dogs and cats used in research has been dwindling for the past 20 years, and random source dogs and cats make up a very small percentage of those animals. Although many animals in shelters and pounds are elderly or terminally ill and brought to shelters by their owners for immediate euthanasia (Kass et al. 2001), substantial numbers are otherwise healthy and could in theory be used for biomedical research studies. In addition, if these animals are not accessible for research, additional purpose-bred animals must be generated to fill the need. Therefore, some might argue that failure to use unwanted pound and shelter animals for research runs counter to the "reduction" component of the 3Rs principle. In contrast, others would argue that use of random source animals does not address the "refinement" or "replacement" components, or the "reduction" of the overall number of animals used. Thus, even this issue is not straightforward.

[2] http://www.avma.org
[3] http://www.the-aps.org

DESIRABILITY OF RANDOM SOURCE DOGS AND CATS FOR RESEARCH

One of the challenges of animal-based research is identification of an optimal model for biomedical research endeavors. Well-chosen animal models provide reproducible insight into normal function, disease states, and effectiveness of drugs and devices for treatment. Animal models that are less than optimal decrease the quality of knowledge and increase the chance for adverse drug and device events. As a result, the search for the best animal model is essential for understanding diseases and developing treatments for them.

Random source dogs and cats represent a potentially important source of animals with unique anatomic and physiologic attributes as well as naturally occurring diseases such as cancer, genetic diseases, age-related diseases, and infectious diseases. The Committee emphasizes that its task was to identify "common research topics" for which these animals are "desirable" and to describe "specific characteristics" that make them "particularly well suited" for these studies. The Committee was *not* tasked with comparing attributes of random source animals to those of purpose-bred animals nor with identifying attributes *unique* to random source or Class B dogs and cats.

The supposedly greater tractability of random source dogs and cats is sometimes cited as an advantage for their use. For example, opinion provided to the Committee by some investigators through the APS (personal communication to the Committee from David Kass, October 2008) indicated that random source animals were often behaviorally more predisposed than purpose-bred animals to training such as resting quietly for conscious animal studies or running on a treadmill. While tractability is certainly an important trait for studies requiring measurement of blood pressure, heart rate, and circulating hormones in conscious animal models, it is important to emphasize that this trait is largely a function of prior socialization with humans and therefore not confined to random source animals. Poorly socialized dogs and cats, regardless of source, can be expected to be more fearful of, and resistant to, interactions with unfamiliar people including laboratory personnel (Serpell and Jagoe 1995; Turner 2000). Conversely, properly socialized purpose-bred animals can be as tractable as former pets. Therefore, generalizations regarding tractability cannot be made, and depend on individual animals and their socialization and history.

Furthermore, according to the AWA, *PHS Policy*, and the *Guide*, justification for the use of a particular species is required for approval of a scientific protocol, but justification of the source of such animals is not. Because there is no regulatory requirement to maintain records of the source(s) of research animals, documentation and justification for the use of dogs and

cats from random sources (such as Class B dealers, pounds, and shelters) are not available. Given this lack of information, the "necessity" of the use of these animals is nearly impossible to determine. Nonetheless, the Committee was able to identify fields (described in the next section) and "common research topics" where the potential exists to use random source animals, including in NIH-funded research, and describe the particular characteristics that may make these animals well suited for research in these areas. It is important to emphasize that these characteristics may not be unique to random source animals and that in many cases other animals, including Class A animals, may also have these particular characteristics.

RANDOM SOURCE DOGS: ANATOMIC AND PHYSIOLOGIC ATTRIBUTES

Scientific investigation may require the use of older, larger, or genetically diverse dogs, or dogs with naturally occurring disease, any of which may be available as random source animals. In contrast, purpose-bred dogs, such as those supplied by Class A dealers, tend to be young and healthy; they include beagles, "mini-mongrels," and hounds weighing 23-27 kg (50-60 pounds) with a defined genetic background and disease-free status suitable for many types of biomedical research.

A common argument for the use of random source dogs is the need for larger (27-37 kg, or 60-80 pounds) and older animals that are physically and physiologically similar to humans (Parsons et al. 1996; Sasajima et al. 1999). But demand for these larger and older animals is usually not great and maintaining even small numbers of larger animals for long periods may not be cost effective for vendors of purpose-bred dogs.

Cardiovascular

Large mixed-breed random source dogs have been used in the study of cardiac diseases, and in the development of procedures and devices to alleviate them, because of their size, depth of the chest cavity, and large heart and great vessels (aorta and pulmonary arteries). These features allow adequate working space to perform complex cardiac procedures and accommodate human commercially produced devices for testing.

The dog's cardiovascular system is similar to that of humans in both size and function. Anatomically, the dog's coronary artery system mimics chronic remodeling in humans following myocardial ischemia with extensive subepicardial collateral vessels and can serve as a model for regional and global myocardial ischemia (Swindle and Adams 1988). But there are differences in coronary artery anatomy and cardiac physiology between random source dogs and purpose-bred dogs, and these differences (or "con-

ditioning") can affect the animal's physiological status. Data presented on behalf of the American Physiological Society indicated that random source animals exhibited a greater increase in coronary blood flow and myocardial oxygen consumption (Tune et al. 2000; personal communication, Bill Yates, to Committee, October 2008). Furthermore, the incidence of idiopathic extramural coronary arteritis occurred less often in purpose-bred animals than in random source animals (Hartman 1989).

The dog's coronary sinus, or venous drainage of the heart, is also similar to human anatomy, allowing for investigation of chronic resynchronization therapy and development of devices and procedures to treat severe congestive heart failure (Reising et al. 1998; Williams et al. 1994). Physiologically, the cardiac electrical conduction system in the dog mimics that of humans, so dogs are used for studies of normal and abnormal cardiac conduction, including atrial fibrillation and other dysrhythmias (Lee et al. 2006).

Random source animals have also been used to study dilatative cardiomyopathy using an induced rapid pacing model. These dogs had cardiac myosin isoform shifts (myosin heavy chain (MHC)-b and ventricular light chain (VLC)-2) in the heart chambers similar to those observed in end-stage human heart failure (Fuller et al. 2007). Conditions have been identified in random source animals that specifically contributed to identification and treatment of mechanisms associated with cardiac arrhythmias—including Long QT syndrome, Brugada syndrome, and Timothy's syndrome—that are not present in purpose-bred dogs. For example, when purpose-bred beagles were used for research associated with Brugada syndrome, they were found to be unsuitable due to the lack of certain ion channel mutations, whereas random source dogs developed the characteristics of this arrhythmia (Antzelevitch 2008).

Pulmonary

Scientists investigating diseases in pulmonary medicine and using thoracic surgical procedures seek barrel-chested large breed dogs for several reasons. Pulmonary function studies use dog models because of physiologic aspects such as increasing microvascular pressure creating pulmonary edema (Swindle and Adams 1988), which has been used as a model for acute respiratory distress syndrome (Reising et al. 1998) and acute lung injury (Kaczka et al. 2005) in humans. Large dogs have a readily accessible single pulmonary artery and vein of the left lower lung lobes, allowing for ease of cannulation and analysis of pulmonary metabolism. Historically, lung transplant procedures were developed using large random source dogs because of the deep chest cavity, again allowing access for complex anastomoses of vascular and airway structures (Blumenstock et al. 1981).

Orthopedic

Random source dogs have been and continue to be integral to the development of prosthetic devices for hip and knee replacements and of fixation devices and techniques, as well as vertebral fusion models, tendon and ligament repair, and assessment of biomaterials for orthopedic procedures (Arnoczky et al. 1982; Greis 2001). In some circumstances, the larger animal's size accommodates human prosthetic devices, but many of these materials and devices eventually are designed for veterinary use in smaller animals. Thus medical advances with research dogs now afford companion dogs many of the same benefits as for humans, such as hip and knee replacement, arthroscopic ligament repair, meniscectomy, and other procedures associated with degenerative joint disease.

Older dogs have been used to study osteoarthritis, cervical disc degeneration, and vertebral fusion because the pathophysiology of the mature articular surfaces and vertebral disc is similar to that of aged humans (An and Friedman 1999; Hunter et al. 2004; Smith et al. 1998). Cervical disc degeneration occurs naturally in older large breed dogs and the cervical and lumbar disc spaces are large enough to support artificial disc prosthetics and materials used for fusion or replacement of this structure (Cook et al. 1994). Many orthopedic studies use older, skeletally mature animals to reflect an adult human population rather than younger (less than 1-year-old) dogs (Frick et al. 1994). In humans, intervertebral disc disease is preceded by the disappearance of notochordal cells in the nucleus pulposus (inner portion of the disc). Similarly, older (5-year-old) mixed-breed dogs have few notochordal cells in the nucleus pulposus and are considered to be an adequate model of the human clinical condition (Hunter et al. 2004). Therefore, older large breed random source dogs have been used and are desirable for these studies (Hasegawa et al. 1995; Katsuura and Hukuda 1994; Nguyen-minh et al. 1997).

Age-Related Disease

Rodent and primate studies indicate that older animals are physiologically different from younger animals (Ferrari et al. 2003). Advanced age is an attribute commonly found in random source animals and may make them desirable for research.

Random source dogs may have age-related chronic or persistent disease conditions such as congestive heart failure, arthritis, allergy, dementia, and neoplastic conditions that may make them desirable for investigations into similar human conditions. For example, canine osteosarcoma has a predictable metastatic rate and pattern that make it attractive for studies of antimetastatic approaches. Canine and feline malignant mammary tumors

have a similar metastatic pattern to that of mammary tumors in women, namely metastasis to the regional lymph nodes and lung (MacEwen 1990). More recently, random source animals have been used in NIH-funded studies of the ocular system, dementia, and cardiac function (Anyukhovsky et al. 2005; Dun et al. 2003; Goralska et al. 2007, 2009; Studzinski et al. 2006; Taylor et al. 2004).

Advanced age itself, independent of disease conditions, may be desirable for some studies. Several studies investigating veterinary and human pharmaceuticals have revealed varying efficacies and toxicological side effects related to the age of the animal subjects. For example, a COX-2 inhibitor intended to treat older, arthritic animals was recently developed and toxicologically tested using only young beagle dogs. Once on the market, it was discovered that older dogs metabolized the drug very differently, resulting in severe side effects that included gastric ulcers, liver and kidney damage, and death.[4,5]

Acquisition of aged dogs poses a logistical and financial challenge that can be addressed with random source animals. Representatives of one purpose-bred vendor testified that they could provide older animals (retired breeders) on a limited basis but that they are unavailable in substantial numbers; purpose-bred animals generally are sold as young as possible (usually 6-9 months) to minimize the expense of housing (personal communication with Class A vendors). In addition, the average duration of NIH grants usually prohibits an investigator from requesting animals years before they are required given the lack of certainty of funding beyond a single grant cycle. It would be reasonable to assume that the cost of maintaining dogs and cats for several years would be passed on to the users (personal communication with Class A vendors), as vendors of purpose-bred animals would be unlikely to sustain the costs of maintaining the animals for a long time unless they knew a customer base was available to purchase them at or beyond a certain age.

The challenge of funding is illustrated by an example of recent work on a canine model of dementia in the aged beagle. Approximately 20 animals from a single colony were used for these studies over a 2- to 3-year period. The multicenter investigative team was supported by up to four NIH individual investigator grants and by several other significant non-NIH sources, all of which represent a level of combined extramural support far beyond that typically attained by individual NIH-funded investigators (Opii et al. 2008; Siwak-Tapp et al. 2007, 2008). On the other hand, this work also exemplifies an alternative for access to aged animals through existing purpose-bred research colonies.

[4] http://www.the-aps.org/pa/policy/animals/ pethealth.htm

[5] http://www.fda.gov/ohrms/DOCKETS/dockets/04n0559/04N-0559_emc-000003-01.pdf

Genetic Diversity

Genetic diversity may be an attribute necessary for some aspects of current and future biomedical research, and the genetic diversity represented among the many breeds in the general dog population cannot be reproduced in purpose-bred colonies. Furthermore, maintenance of maximal genetic diversity in a single colony of dogs would require more than 200 breeding pairs (personal communication from Stephen O'Brien to the Committee, January 2009). Nobel laureate Dr. E. Donnall Thomas, who received the award for his work in bone marrow transplantation, stated that "marrow grafting could not have reached a clinical application" (Thomas 1990, pp. 581-582) without the use of outbred dogs. Non-purpose-bred dogs have also been critical in the development of hematopoietic cell transplantation or bone marrow transplantation because of their genetic diversity, large size, long life, and the fact that, other than humans, they are the only mammals to possess these qualities (Ostrander and Wayne 2005). In addition, genetically diverse animals have also been instrumental in studies of total body irradiation, chemical and radioimmunological myeloablation, in vivo and in vitro graft manipulation, and graft-versus-host disease studies (Lupo and Storb 2007).

Naturally Occurring Infectious Diseases

Random source dogs exposed to outdoor environments and various vectors that may carry disease can be effective models of naturally occurring infectious diseases. Vector-borne diseases such as heartworm (*Dirofilaria immitus*), Lyme disease (*Borrelia burgdorferi*), Rocky Mountain spotted fever (*Rickettsia rickettsii*), babesiosis (*Babesia microti*), ehrlichiosis (*Ehrlichia canis*), and/or the antibodies to these organisms can be identified in random source dogs that have been exposed to outdoor environments (Scorpio et al. 2008). Random source animals may also have Sarcoptic mange (*Sarcoptes scabiei*), Demodectic mange (*Demodex canis*), or coccidiosis from natural exposure to parasites. To maintain the naturally occurring infection, standard conditioning or treatments for these parasitic diseases may be withheld from some random source animals so that they are available for studies involving these infections.

Research on naturally occurring infectious diseases of dogs is generally not supported by the NIH, but some members of the Committee believed that it was important to point out that the U.S. Department of Health and Human Services Food and Drug Administration (FDA) Center for Veterinary Medicine's (CVM) Guidance Document for New Animal Drug Applications[6]

[6] http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm123821.htm

(Guidance 61) states that for dose determination studies natural infections are ideal, whereas induced infections are acceptable. In addition, Guidance 90 "Guidance for Industry – Effectiveness of Anthelminthics: General Recommendations, Final Guidance" states that the use of natural or induced infections in effectiveness studies should be determined by the type of parasite and the claim proposed by the sponsor. Finally, according to the International Harmonization of Anthelminthic Efficacy Guidelines[7] (VICH GL#19, FDA/CVM Guidance #111), "Dose confirmation studies should be conducted using naturally or artificially infected animals; however, at least one study should be conducted in naturally infected animals for each parasite claimed on the label." Therefore, although studies on naturally infected dogs do not typically apply to NIH-funded research, random source animals may be important for other types of research.

Spontaneously Occurring Animal Models of Human Disease

The genetically diverse pet population has been the source of unique animal models that are not available from vendors of purpose-bred animals; for example, diseases have been identified in a mixed population of pet animals in Germany (Neumann and Bilzer 2005), and random source animals have served as controls for studies in comparison to purebred animals (Basso et al. 2004; Smucker et al. 1990).

Most often, spontaneously occurring diseases have been identified in a particular breed and a colony established using non-purpose-bred animals. For example, spontaneous genetic animal models for sleep apnea, muscular dystrophy, progressive retinal atrophy, hereditary nephropathy, and hemophilia A and B have been identified in non-purpose-bred dogs (Canine Inherited Disorders Database;[8] Wolfe 2009). There are no other large animal models for these diseases. In some circumstances, individual investigators have established breeding colonies to study these diseases. Examples of dog colonies maintained at research facilities as models of genetic disease include hemophilia A dogs derived from Irish setters, hemophilia B dogs derived from Lhasa Apsos, von Willebrand disease dogs derived from Scottish terriers, and Duchenne muscular dystrophy dogs derived from golden retrievers (Nichols et al. 2009; Wang et al. 2009).

In addition, other genetic diseases have been identified in breeds of dogs used for gene-based therapy. The Swedish Briard (RPE65) is the only dog

[7] http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TD7-42G0KJG-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_searchStrId=951858672&_rerunOrigin=google&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=cfaefa728a34a1786eb1f1b3d6ffbf66

[8] http://www.upei.ca/~cidd/intro.htm

breed that has responded successfully to gene therapy for retinal degeneration, opening the door for several human clinical trials. Alaskan Malamutes and German shorthaired pointers may also provide similar success in gene therapy for achromatopsia (Stieger et al. 2009). Finally, naturally occurring dog and cat models for human genetic heart diseases exist and are critical for the development of gene-based therapy; for example, Portuguese water dogs are maintained at the University of Pennsylvania as a model for dilatative cardiomyopathy (Sleeper et al. 2009).

These valuable models are examples of the desirability or necessity of access to random source animals as genetically diverse control animals, and of as yet undetermined animal models that may result from naturally occurring single nucleotide polymorphisms, epigenetic occurrences, or other genetic alterations (personal communication, Stephen O'Brien to the Committee, January 2009). Discovery of new models of human disease has not typically arisen through large-scale random screening of random source dogs from shelters, pounds, or Class B dealers. Instead, these animals are usually sought out as naturally occurring disease models based on knowledge of their availability from random sources. The development of novel dog models of human disease relies on a sophisticated process of referral by breeders or veterinarians aware of nuances in a certain breed, veterinary medical workup, scientific characterization, and validation as an animal model. Such programs are ongoing with NIH support for the discovery of novel models in dogs and cats (see Chapter 4).

RANDOM SOURCE CATS: ANATOMIC AND PHYSIOLOGIC ATTRIBUTES

Cats have long been a mainstay of NIH-funded studies of neurological, cardiovascular, and respiratory diseases and the immune system. The similarity of these physiological systems to those of humans as well as the size and tractability of cats make them ideal for many experimental models. As such, a large database exists based on studies using cats as models of human disease.

As with dogs, the genetic diversity of the general cat population (and of some purpose-bred cats) has provided several valuable genetically based models of human disease. For example, a colony of hypertrophic cardiomyopathy Maine Coon cats is maintained at the University of California, Davis, and cats with mucopolysaccharidosis are maintained and studied at the University of Pennsylvania (Haskin 2009).

There are over 200 hereditary human diseases with correlates in cats (O'Brien et al. 2008). Following are a few illustrative examples.

Feline Immunodeficiency Virus

Cats are naturally susceptible to infection by feline immunodeficiency virus (FIV), which induces an immune suppressive disorder very similar to human immunodeficiency virus (HIV) infection in humans (Willett and Hosie 2008). A number of studies are investigating the mechanisms of FIV infection in cats as a model for HIV infection, and the cat models are also important in efforts to understand HIV in order to develop novel and more effective therapies for this devastating disease.

While it is possible to experimentally infect purpose-bred cats with FIV, the clinical manifestations of experimental infections differ from naturally occurring FIV infection (English et al. 1994). Indeed, even after 4 years of FIV infection specific pathogen-free (purpose-bred) cats do not exhibit chronic clinical disease (Torten et al. 1991). The differences between naturally occurring and induced FIV may be due to infectious cofactors in the random source animals (English et al. 1994; Willett and Hosie 2008).

FIV is the only naturally occurring model of acquired immunodeficiency syndrome (AIDS) (Dias et al. 2006). An additional advantage of FIV models in the study of AIDS is that this virus does not infect humans. For all these reasons, random source animals naturally infected with FIV represent a critical resource for understanding FIV, its sequelae, and its transmission between hosts.

Feline Interstitial Cystitis

Human interstitial cystitis, a serious bladder disorder characterized by pain, urinary frequency, and nocturnal urination (Roppolo et al. 2005), occurs at frequencies as high as 1 in 4.5 women (March et al. 2001). The causes for this disorder are not well understood. Domestic cats develop feline interstitial cystitis, which is clinically indistinguishable from the human disorder (Westropp and Buffington 2002). Random source cats are the only known spontaneously occurring animal models of the disease (Westropp and Buffington 2002).

Feline Infectious Peritonitis

This disorder, associated with vascular inflammation in a variety of organs, is almost always fatal. It is caused by an infectious agent in the coronavirus family, feline infectious peritonitis virus (FIPV) (Olsen 1993; Takano et al. 2008), which is thought to mutate from the more commonly found feline enteric coronavirus (FECV) (Vennema et al. 1998). FECV is very common in random source animals, but does not induce life-threatening disease (Olsen 1993). The conditions responsible for the mutation of FECV

to FIPV are not well understood, but appear to be associated with significantly increased viral replication in immunosuppressed animals (Haijema et al. 2004). Replication of FECV also radically increases when infected random source animals are placed in close association, such as in shelters (Pedersen et al. 2004).

FIPV pathogenesis is dependent on a mechanism known as antibody-dependent enhancement, in which host antibodies bind to the virus and the antibody-virus complex infects macrophages (Takano et al. 2008). Because antibody-dependent enhancement may be important in human viral diseases such as Dengue fever and HIV infection (Olsen 1993), FIPV-infected animals represent important resources in efforts to understand the pathogenesis of such diseases. Purpose-bred animals can be infected with FIPV and the virus can be cultured in feline kidney cells (Takano et al. 2008), but random source animals are a valuable initial resource for FIPV and its multiple strains (Olsen 1993), and represent models for understanding the process of mutation that produces a highly pathogenic virus from a related but far less virulent one.

IACUC AND PRINCIPAL INVESTIGATOR CONSIDERATIONS REGARDING THE USE OF RANDOM SOURCE ANIMALS FOR RESEARCH

The use in biomedical research of species that society regards as companion animals poses several unique challenges to principal investigators (PIs) and to the institutional animal care and use committees (IACUCs) that evaluate protocols describing research involving dogs and cats. While both groups have several forms of guidance available to them as they navigate the scientific and ethical issues inherent in experimental species selection and justification, the appropriate course to resolving these issues is not always clear.

As stated earlier, the Health Research Extension Act of 1985 mandated the establishment of guidelines for proper animal care by individuals and institutions that conduct research with funds provided by NIH or other federal sponsors. IACUCs are responsible for institutional oversight of animal care and treatment and, together with the PIs at institutions receiving NIH and other federal funds to support research, must comply with guidance found in the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Teaching* (revised 2002). Although each of the nine Principles applies, several often receive special consideration when dogs and cats have been selected as research animals.

Principle III states, in part, "The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results." Research involving random source animals may

require more rigorous justification to satisfy the IACUC and the institutional community that these animal models are not only appropriate but also have scientific benefits that outweigh the use of purpose-bred animals. Thus, both PIs and IACUCs may need to consider strain, breed, and in some cases source when determining the appropriateness of animal models for particular studies.

The animal models may be defined as exploratory, explanatory, and/or predictive (Hau and Van Hoosier 2003); but cost alone has not routinely been a sufficient justification for the choice of an experimental model. The *Guide* (p. 12) and the AWR provide clear guidance related to cost and its inadequacy as the sole factor for determining the appropriateness of survival surgery models. Yet cost is a significant determinant; NIH grant budgets, for example, tend to favor the lower costs of random source animals over the higher costs of purpose-bred animals (see Chapter 4 for further discussion of the relative costs of animals from Class B dealers vs. purpose-bred animals).

As in all research involving animals, ethical and health concerns vary based on the condition of the animals when acquired and during their housing on the premises. Community concerns will vary based on the type of animal and its source. Although all animals used for research deserve humane treatment, additional training of IACUC members on the special challenges and opportunities associated with the use of random source animals may be warranted before the consideration and approval of any protocol involving animals of this type.

In particular, because random source animals have unknown health and care histories, potential health and animal welfare problems may be associated with their use, as discussed below. Not all IACUCs may have the collective experience to conduct a thorough risk-benefit analysis of the ramifications of using random source animals at their institution, so the use of random source animals requires teamwork, perhaps more so than in research involving purpose-bred animals whose health and care histories are known. PIs would be well advised to consult with institutional veterinarians, the IACUC, and the IACUC members who represent the concerns of the institutional community before, during, and after research involving random source animals.

IACUCs and PIs considering the use of random source animals may also face challenges related to Principle VII: "The living conditions of animals should 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 scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied." Institutions, and through them, veterinary staff and PI agree, in keeping with their PHS assurance, to uphold the high standards

of animal care and welfare. Thus, from the time of delivery of a research animal to the premises until the end of the research involving that animal, conditions of care and housing are subject to oversight by the IACUC and veterinarians periodically, and by the animal care and laboratory staff on a daily basis (9CFR 2.33(b)(3)). But institutions, IACUCs, and PIs are much less likely to oversee conditions at the sources from which they receive animals. There may be, either intentionally or unintentionally, different standards of care and animal housing at locations that provide animals compared with the research institutions that receive them. As with all other aspects of their animal programs, it would seem appropriate for institutions to periodically review their expectations about animal suppliers' premises before obtaining animals from them.

Principle IX reminds PIs and IACUCs of their shared responsibilities in experimental model selection: "Where exceptions are required in relation to the provisions of these Principles, the decision should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as the IACUC. Such exceptions should not be made solely for the purposes of teaching or demonstration." It is common practice for institutions to follow the *U.S. Government Principles* if PHS funds are received for research done on the premises. *PHS Policy* tends to be scrutinized more completely than the AWA. In addition, some institutions that accept PHS funding are more likely to be AAALAC accredited and therefore those institutions are subject to additional standards of oversight. Thus, if the use of animals of a given type or from a given source is considered (by the IACUC, the PI, or the institution itself) to differ from best veterinary and animal welfare practices, all of these groups should evaluate the possible justifications for exceptions to the *U.S. Government Principles*, *PHS Policy*, and perhaps the *Guide*.

In summary, IACUCs, PIs, and institutions face several challenges when studies are proposed and conducted that involve the use of random source companion animals, regardless of the sources of these animals. In such cases it is imperative that review committees evaluate the justification for animal use particularly carefully and thoroughly.

DELETERIOUS INFECTIOUS DISEASE ISSUES

Random source animals may be obtained from multiple sources, and the mingling of these animals may contribute to the spread of infectious disease. For example, 20 percent of dogs and 61 percent of cats acquired by Class B dealers come from shelters and pounds (USDA data submitted to the Committee, January 2009), and the health status of these animals is often unknown. Animals in shelters and pounds are more likely than purpose-bred animals to be exposed to outbreaks of infectious viral dis-

eases (e.g., canine distemper, canine parvovirus, canine parainfluenza virus, feline panleukopenia, feline calicivirus, and feline herpes virus). In addition, respiratory and intestinal diseases caused by viruses, bacteria, protozoa, and helminths are among the most common ailments that cause considerable morbidity and suffering for shelter animals.

The quality of care for shelter animals varies widely across the country. Shelters are not required to isolate, vaccinate, deworm, or provide treatment for illnesses in the animals (Miller and Zawistowski 2004) and, based on discussions with shelter experts (there is no published literature), the Committee found that many shelters do not have veterinarians on staff or even serving as advisors. Although some animals are very well cared for, they may be behaviorally abnormal, and they are almost certainly stressed. Furthermore, dogs and cats in shelters and pounds often have undocumented vaccination histories and frequently arrive at the shelter with compromised health—they may have heartworms, fleas, ticks, mites, lice, ringworm, or intestinal parasites, and/or a variety of disease agents that spread more readily than would normally be expected because the animals are mixed together. They may be placed into different types of group or communal housing, where unreliable sanitation practices contribute to disease spread. Research has shown that the longer animals stay in shelters and pounds, the more likely they are to develop respiratory disease (Edinboro et al. 2004). Even if vaccinated immediately upon entry, a stay of several days at a shelter puts animals at higher risk for respiratory disease because respiratory vaccines are not always effective in preventing infection. An additional consideration is that it is often not possible to detect animals that are incubating some infectious diseases because they appear clinically normal and diagnostic evaluation may be unavailable, incomplete, or misleading (as in instances of false negatives or positives).

To address these problems, the research institution or the Class B dealer (or both) conditions random source dogs and cats that enter research institutions (whether from shelters and pounds, Class B dealers, or other legal sources). The conditioning generally includes a period of quarantine, treatment for parasites, vaccination, deworming, and other health-related procedures that make the animal more suitable for research. Even so, the animals may still have health problems since not all infectious agents can be eliminated by antibiotics or deworming or prevented through vaccination. In contrast, purpose-bred animals are more likely to be microbiologically defined.

ZOONOTIC DISEASE HAZARDS AMONG RANDOM SOURCE ANIMALS

Some infectious disease agents associated with dogs and cats in the general pet population, and therefore among some random source animals,

pose a potential threat to humans. In the 2008 *Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel* (Appendix 1), the National Association of State Public Health Veterinarians lists 54 "zoonotic diseases of importance" in the United States; of these, 26 are associated with dogs and/or cats as the "most common species associated with transmission to humans" (2008). An earlier NRC report (1994, Table 2.1, p. 8) lists 27 "Selected Canine Zoonoses Causing Disease in Humans," beginning with "acariasis" (mange) and ending with "yersiniosis" (see also NRC 1997, p. 95). And the World Health Organization Collaborating Center for New and Emerging Zoonoses lists numerous zoonotic agents, both common and rare, in domestic dogs and cats.[9] Some common agents, such as *Pasteurella* spp., are present in the oral and nasal cavities of 12-92% of dogs and 52-99% of cats and are associated with infections from animal bites (Greene and Goldstein 2006). Other agents of concern include *Bartonella henselae*, the agent of "cat scratch disease" that is commonly carried by young cats; *Salmonella* and *Campylobacter* spp., which cause enteric disease; *Sarcoptes* spp., which causes scabies (in humans; called mange in animals); and *Microsporidium* (Microsporum) *canis,* which causes ringworm. Rabies represents a particularly serious zoonotic hazard among animals with unknown exposure and vaccination histories but is rare. Incidents of zoonoses in the research laboratory are fortunately rare, but recognition, control, and prevention of canine and feline zoonotic hazards are important aspects of institutional occupational safety programs (NRC 1997).

ADVERSE EFFECTS OF INFECTIOUS DISEASE ON RESEARCH

Exposure to infectious disease is a risk the research community can avoid. As discussed earlier, the use of random source animals for the study of naturally occurring infectious disease may be desirable, but in the other situations intercurrent infections may be deleterious to research. These considerations are generally taken into account by the individual investigator in concert with veterinary professionals at the research institution. Nonetheless, undetected (subclinical) infections can still compromise or confound research results. A recent study that documented canine exposure to three frequently reported tick-borne bacterial pathogens reported the results of molecular analysis and serology on 21 random source dogs from Class B dealers (Scorpio et al. 2008): the test results were positive in 17 dogs, but none showed any signs of clinical disease. The authors concluded that "Exposure to and potential for infection with these bacteria and other pathogens may contribute to blood and tissue alteration that

[9] http://faculty.vetmed.ucdavis.edu/Faculty/bbchomel/WHO_Zoonoses/zoonoses_species.htm

could confound experiments and lead to misinterpretation of data in canine models" (p. 23).

Heartworms (*Dirofilaria immitus*) are generally associated with dogs, but the incidence of infection in cats can be quite high in endemic areas—one study reported 76% prevalence in outdoor-housed cats in North Carolina (Atkins et al. 2005). Overt infection makes the animals unsuitable for most research, but even Dirofilaria-seropositive cats that lack adult worms in the heart and lung may have significant pulmonary disease, making them potentially unsuitable for cardiopulmonary studies (Browne et al. 2005).

ANIMAL WELFARE ISSUES

A basic understanding of the terms *animal welfare*, *stress*, and *distress* is essential to the discussion of humane issues and animal welfare in the context of this report and the Committee's statement of task.

"Animal welfare" generally refers to the state of an animal and the extent to which it is faring well or ill in a particular situation or at a particular point in its life. Different experts give priority to different aspects of an animal's state when assessing its welfare: some emphasize unpleasant or pleasant subjective feelings (Boissy et al. 2007; Dawkins 1980; Duncan 1993), while others focus on the animal's ability to express "natural" or species-typical behavior (Rollin 1995) or its capacity to adapt to, or cope with, the demands of its environment (Broom and Fraser 2007). One thing all agree on is that there is no single, reliable measure of an animal's welfare (Appleby 1999; Mason and Mendl 1993). Most animal welfare experts therefore advocate multiple measures of aspects that are likely to reflect an animal's welfare (e.g., behavioral responses, physiological indicators, immune function) while at the same time recognizing that the final determination inevitably involves a degree of subjectivity (Dawkins 1980; Fraser 1995; Mason and Mendl 1993).

A recent NRC report (2008, p. 2) defines "stress" as a "real or perceived perturbation to an organism's physiological homeostasis or psychological well-being." Animals respond to such perturbations by displaying a "stress response," characterized by behavioral and physiological efforts to restore homeostasis. Potential stressors may be physical or emotional and include overcrowding; changes in routine, diet, environment, temperature, or humidity; perceived threats to safety; sources of pain or discomfort; and malnutrition, illness, or physical restraint, among others.

A certain amount of stress is a normal part of any animal's life and should not necessarily be considered detrimental to welfare. Stress should be regarded as a welfare problem only when the degree of perturbation is sufficiently acute or prolonged, and an animal's capacity to restore homeostasis is exceeded. Many authorities now use the term "distress" to describe

the aversive negative state that arises when an animal is pushed to the limit of its ability to cope with, or adapt to, environmental stressors (NRC 2008), while the term "suffering" generally applies only to the *conscious experience* of highly aversive or unpleasant mental and emotional states, such as pain or fear (Dawkins 1998).

The question of whether random source dogs and cats experience a greater degree of stress and distress in the research laboratory setting than do purpose-bred animals cannot be answered directly as no published studies have addressed this question. Indirect evidence that the transition to life in laboratory housing may be stressful and distressing for former pets can, however, be derived from studies that have examined how pet dogs and cats respond to, and cope with, comparable transitions—for example, among pets relinquished to animal shelters, or those confined temporarily in boarding kennels, catteries, or veterinary hospital cages. Most such studies have found behavioral and physiological changes (e.g., elevated heart rate and glucocorticoid levels, reduced heart rate variability and white blood cell counts) consistent with the effects of moderate to severe stress. These responses may take 2 to 5 weeks to return to "normal" baseline levels, although some animals may remain in a distressed state for several months (Beerda et al. 1999a, b; Hennessy et al. 2001; Kessler and Turner 1997, 1999; McCobb et al. 2005; Rochlitz et al. 1998; Siracusa et al. 2008; Stephen and Ledger 2006; Väisänen et al. 2005).

Chronic stress is immunosuppressive and reduces both cell-mediated and humoral immunity, thus increasing susceptibility to infectious disease, vasodepressive syncope, blood clots, coronary vasoconstriction, and other effects (Gregory 2004). A variety of factors may contribute to these outcomes, including the stressful effects of physical confinement and lack of stimulation, loss of social companions, exposure to unfamiliar people or conspecifics, and lack of control over environmental stressors (Beerda et al. 1999a, b; Carlstead et al. 1993; Hubrecht 1995; McCrave 1991). Because some random source dogs and cats are former pets or strays and therefore not used to prolonged cage confinement, it is reasonable to infer that they may have more difficulty adjusting to laboratory conditions than purpose-bred animals (see British Veterinary Association Animal Welfare Foundation et al. 2004).

In summary, based on the limited available evidence, random source dogs and cats used for research probably endure greater degrees of stress and distress compared to purpose-bred animals. This conclusion has implications both for the welfare of random source animals and for their reliability as research models. Stress and distress are known to significantly alter animals' physiological and behavioral responses to experimental manipulations, and will therefore affect the quality of the scientific results obtained from such animals (NRC 2008; Reinhardt 2004).

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4

Class B Dealers and Animals

The previous chapters of this report have underscored factors that relate indirectly to determination of the desirability and necessity of animals from Class B dealers since use of such animals cannot be addressed without consideration of the broader context in which the Class B issue is embedded. The Committee was tasked to "determine the important biomedical research questions and common research topics in contemporary NIH-funded research where Class B dogs and cats are desirable/necessary. . . . " In addition, the statement of task given to the Committee requested data pertaining to "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). Because there is no requirement to include such information in research records and reports, the Committee considered references to the use of "mongrel" dogs to infer that a number of studies with NIH funding used random source dogs. The Committee was unable to determine whether such dogs came from Class B dealers because mongrel dogs are available from various sources, including Class A dealers. The Committee therefore relied on its own expertise, input from scientific organizations, the testimony of individual investigators and an NIH representative, and the biomedical research literature both for evidence of general areas of research and for specific examples of physiological, anatomical, and genetic research in which **random source** animals have been used and may be desirable. These accounts, provided in Chapter 3, did not identify any unique or irreplaceable features that made it necessary to obtain **random source** animals from Class B dealers.

This chapter provides information about trends in the numbers of dogs and cats from Class B dealers used in research, sources of such animals from Class B dealers, challenges in AWA enforcement with respect to Class B dealers, and alternatives to the use of Class B dealers.

TRENDS IN THE NUMBER OF CLASS B DOGS AND CATS USED IN RESEARCH

According to the USDA, the use of dogs and cats in research has declined significantly over the last 30 years. However, data in Tables 1-1 and 4-1 indicate an increase in the use of all dogs and cats in research between 2006 and 2007. The reasons for this recent increase after more than two decades of decline are not understood. The USDA was unable to provide corollary data of year-by-year numbers of animals from Class B dealers, or if the increase was due to random source animals, purpose-bred animals, or animals used for NIH-funded research. Ten-year averages show a decrease in the use of dogs from 187,464 between 1978 and 1987 to 109,353 between 1988 and 1997, and 69,223 between 1998 and 2007. This represents a reduction of 63.1 percent. A parallel 59.4 percent reduction was observed in the 10-year averages of cats with a decrease from 58,526 between 1978 and 1987 to 34,828 between 1988 and 1997, and 23,737 between 1998 and 2007 (Table 4-1). The use of guinea pigs, hamsters, and rabbits has fluctuated over this same time period. Only the use of nonhuman primates increased (from 2001 to 2007 by 29%). It is estimated that rats and mice also increased although numbers are not reported for these species (Table 1-1).

Statistics were not maintained by the USDA that discriminated between dogs and cats from Class A and Class B dealers for the last 30-year period; however, data were obtained from the USDA regarding animals from Class B dealers for November 2007 through November 2008 (Figures 4-1a-f). During Fiscal Year 2007 (FY 2008 was not available at the time this report was written), 72,037 dogs and 22,687 cats from all sources were used in research (Table 4-1). Combined dog and cat usage in research totaled 94,724 animals, roughly 9.2% of all species covered by the AWA that were used in research in 2007 (Table 1-1) and were reported to the USDA. For this reporting period, 2,863 Class B dogs (Figure 4-1b) and 276 Class B cats (Figure 4-1c) were sold for research representing only 4% of the dogs and 1.2% of the cats used in research. The combined total of dogs and cats from Class B dealers used in research represents only 3% of the total dogs and cats used in research and 0.3% of all animals reported to the USDA for research purposes.

Taking into account all animals used in research (assuming 90% of these are mice and rats), dogs and cats represent only 0.9% (Table 1-1)

TABLE 4-1 Total Numbers of Dogs and Cats Used in Teaching, Research, Experiments, and Tests, 1973–2007

Year	# Dogs	# Cats
1973	195,157	66,195
1974	199,204	74,259
1975	154,489	51,439
1976	210,330	70,468
1977	176,430	62,311
1978	197,010	65,929
1979	211,104	69,103
1980	188,783	68,482
1981	188,649	58,090
1982	161,396	49,923
1983	174,542	53,344
1984	201,936	56,910
1985	194,905	59,211
1986	176,141	54,125
1987	180,169	50,145
1988	140,471	42,271
1989	156,433	50,812
1990	109,992	33,700
1991	107,908	34,613
1992	124,161	38,592
1993	106,191	33,991
1994	101,090	32,610
1995	89,420	29,569
1996	82,454	26,035
1997	75,429	26,091
1998	76,071	24,712
1999	70,541	23,238
2000	69,516	25,560
2001	70,082	22,755
2002	68,253	24,222
2003	67,875	25,997
2004	64,932	23,640
2005	66,610	22,921
2006	66,314	21,637
2007	72,037	22,687

NOTE: Animals were counted once regardless of the number of protocols in which they were used. Animals used in multiyear studies were counted once each year regardless of when they were acquired. *Data source:* USDA in response to Committee request, 2008.

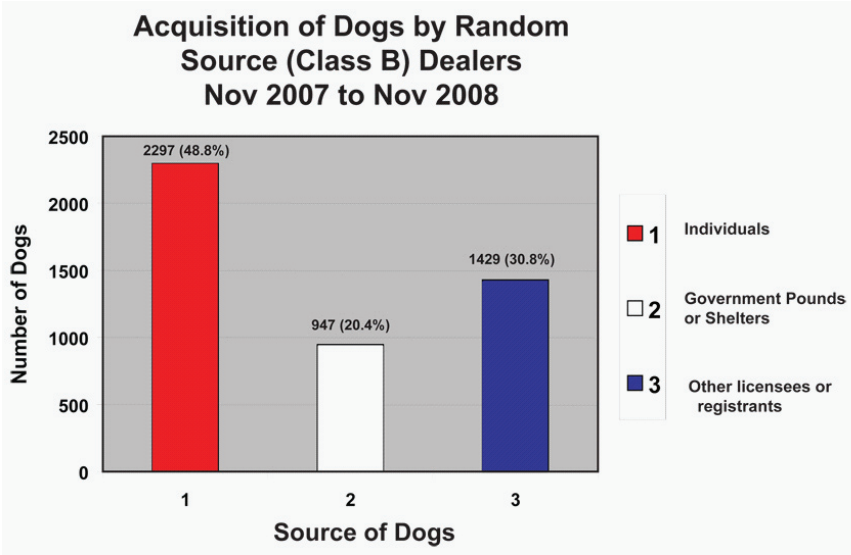

FIGURE 4-1a Acquisition of dogs by Class B dealers from eligible sources, November 2007–November 2008. *Data source 4-1 a-f:* USDA in response to Committee request, 2008.

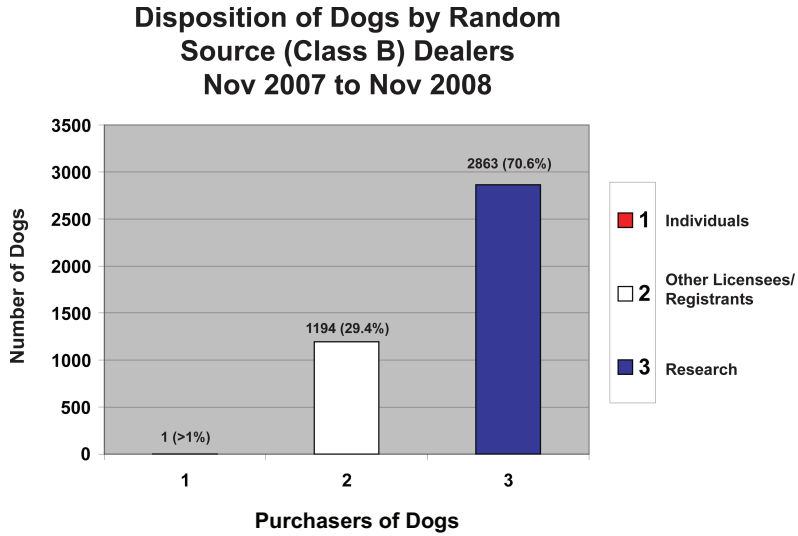

FIGURE 4-1b Disposition of dogs by Class B dealers, November 2007–November 2008. Disposition regulation (9 CFR 2.80) requires Class B dealers to maintain records for at least 1 year after an animal is disposed of, so the 12-month period represents the greatest amount of data USDA could access in response to a Committee request, 2008.

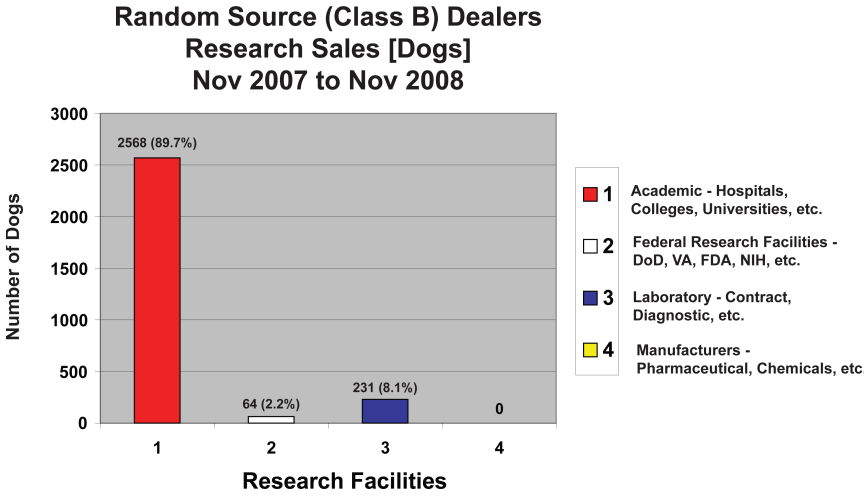

FIGURE 4-1c Disposition of dogs by Class B dealers to research facilities, November 2007–November 2008.

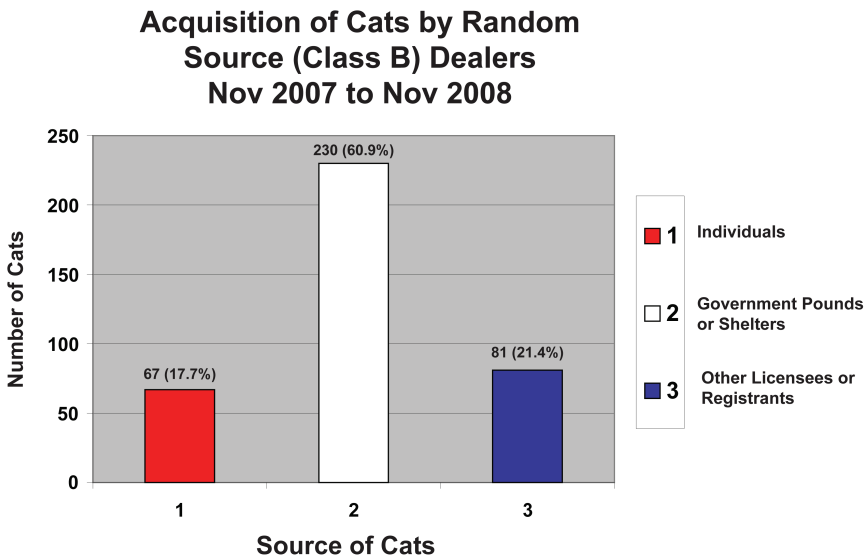

FIGURE 4-1d Acquisition of cats by Class B dealers from eligible sources, November 2007–November 2008.

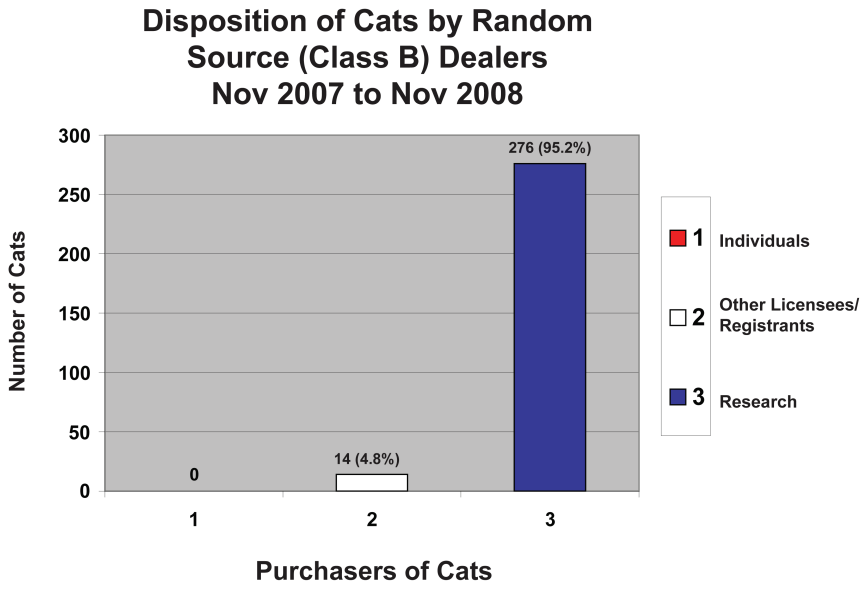

FIGURE 4-1e Disposition of cats by Class B dealers, November 2007–November 2008.

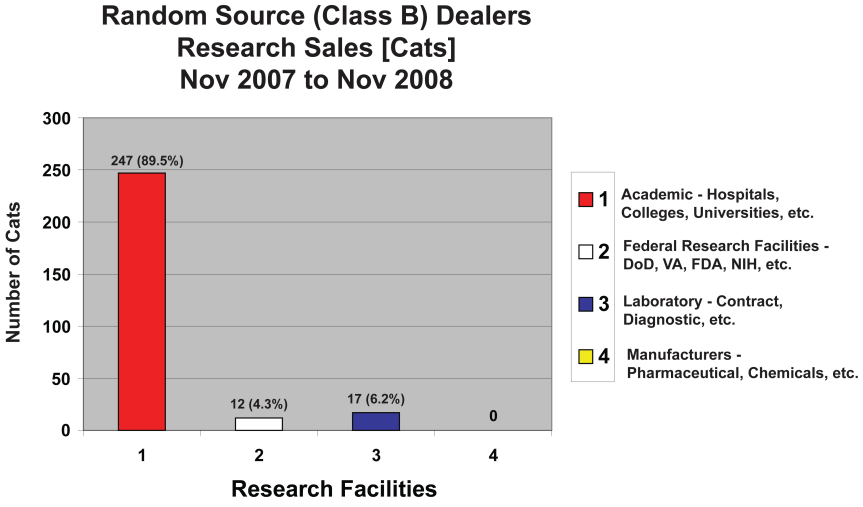

FIGURE 4-1f Disposition of cats by Class B dealers to research facilities, November 2007–November 2008.

and animals from Class B dealers only 0.03% of all animals studied (USDA 2007). Thus, while random source dogs and cats from Class B dealers, shelters, and pounds may supply some of the animals needed in research, a reasonable conclusion is that Class A dealers provide most of the dogs and cats used in research.

Furthermore, over the past two decades a trend has emerged among research institutions to move away from the use of dogs from Class B dealers or to require justification for their use. For example, Duke University's website states that "The Duke default for purchase of dogs for research is to use Class A dogs. The use of Class B dogs must be justified on a protocol-by-protocol basis [cost alone is insufficient justification]. The level of risk of using Class B dealers to the program or the research project is considered a level that generally outweighs the benefit."[1] The document lists the following reasons for this position: the animals' questionable health status, poor condition, and aggressive temperament, and the institution's inability to guarantee that an animal was not someone's pet. Iowa State University, the University of Illinois at Chicago, the University of Arizona, Yale University, the University of Texas at Houston, the University of California at Los Angeles, and Massachusetts Institute of Technology are just a few of the growing number of institutions to adopt similar policies.[2]

THE ROLE OF CLASS B DEALERS IN PROVIDING RANDOM SOURCE ANIMALS

Changing state and local laws have made it more difficult for research institutions to directly obtain random source dogs and cats, particularly in states that do not allow access to pound and shelter animals. Class B dealers, who obtain animals from other states, pounds, shelters, private breeders, bunchers, and other Class B dealers, provide access to animals that research institutions would otherwise have difficulty obtaining.

The potential desirability of random source animals for research (e.g., because of their size, age, genetic diversity and naturally occurring infectious disease) was described in Chapter 3. But the relatively small number of dogs (fewer than 1,000; Figure 4-1a) and cats (fewer than 300; Figure 4-1b) obtained by Class B dealers from pounds and shelters calls into question the genetic diversity of the animals provided by these dealers and to what extent they truly represent the general population of these species. In fact, most dogs (but not cats) sold by Class B dealers are not random source animals,

[1] http://vetmed.duhs.duke.edu/documents/iacuc/pdf/policy_on_source_of_canines.pdf

[2] Class B Dealers and Animals http://www.hsus.org/animals_in_research/class_b_dealers/does_your_university_buy.html

and are therefore similar to animals available from dealers of purpose-bred animals.

In addition, Class B dealers primarily buy and sell generic dogs (mongrels and hounds) and cats and are seldom involved in or skilled with the selection of specific diseases or models, and indeed are likely to cull diseased animals. However, at least one of the currently licensed Class B dealers acquired animals with parasitism that were suitable for veterinary research.

TRENDS IN THE NUMBER OF CLASS B DEALERS

The declining trends in the use of dogs and cats for NIH-based research are evident in a concomitant and more rapid decline in the number of Class B dealers that sell animals for biomedical research. When demands for random source dogs and cats were highest, in the 1970s and 1980s, approximately 200 Class B dealers sold research dogs and cats. In the 1990s, that number fell to approximately 100, and it declined further when, in 2005, the number of USDA inspections of Class B dealers selling research dogs and cats rose to a minimum of 4 times per year, with an emphasis on traceback verification. There are now only 11 Class B dealers, one of which has been suspended for 5 years because of AWA violations and is not likely to resume operation (personal communication, Robert Willems, USDA, to Committee, January 2009); five others are under "intense scrutiny" (personal communication, Jerry DePoyster, USDA, to Committee, October 2008). One Class B dealer deals with non–random source hounds only, and another deals principally in animals with naturally acquired parasitism for (non-NIH) veterinary product research.

SOURCES OF DOGS AND CATS FOR CLASS B DEALERS

A review of 2008 acquisition data provided by the USDA revealed the following numbers specific to Class B dealers (Figure 4-1; see Chapter 1 for the AWR definition of eligible sources):

4,643 dogs acquired by Class B dealers in 2008:
- 49% from individuals (e.g., hobby breeders)
- 31% from other licensees or registrants (e.g., other Class B dealers)
- 20% from government pounds or shelters

378 cats acquired by Class B dealers in 2008:
- 61% from government pounds or shelters
- 21% from other licensees or registrants (e.g., other Class B dealers)
- 18% from individuals (e.g., hobby breeders)

Pounds and Shelters as Sources of Animals from Class B Dealers

Pounds and shelters serve as points of acquisition of animals for research either directly or through Class B dealers. Usually, these are (government-sponsored) contract pounds or private shelters, but because the latter rely on donations and public support they may have ceased providing animals for research.

Pound seizure became common after World War II when biomedical research experienced an upsurge and shelters and pounds were seen as a readily available source of surplus animals (Zawistowski 2008). However, many members of the public and animal advocates were upset about the practice, which they considered a betrayal of trust since the mission of shelters is to provide care, adoption services, and law enforcement; modern-day shelters also provide spay/neuter services, pet behavior counseling, veterinary care, and humane education.

In Iowa, a 2003 statute (145B; repealed in 2008) explained licensed pound seizure:

> An institution so authorized by the Iowa Department of Public Health may request dogs from a pound. The pound may tender to such institution dogs in its custody seized or held by authority of the state, municipality, or other political subdivision. However, a dog shall not be tendered unless it has been held for redemption by its owner or for sale for a period of not less than three nor more than fifteen days. A dog lawfully licensed at the time of its seizure shall not be tendered unless its owner consents in writing. Unless a dog is sick or injured or lawfully licensed at the time of seizure, a pound shall not destroy a dog while a request of an authorized institution to that pound is pending. An institution obtaining dogs from a pound shall pay to the municipality or other political subdivision under whose authority each dog is held or was seized a reasonable fee not to exceed five dollars for each dog so obtained, and shall provide for the transportation of the dogs so obtained from the pound (Iowa 145B.4).

Thus the law allowed the acquisition of an animal by a research institution after only 3 days, a short time frame for the possible reunion of lost animals with their owners or for a new home to be found for relinquished animals. Once the minimum holding period expired, shelter operators seeking to find a home for an adoptable animal were in competition with research institutions or Class B dealers for those animals. A similar statute in Utah (UT26-26-4) states that "the authorized institution shall provide, at its own expense, for the transportation of such animals from the establishment to the institution and shall use them only in the conduct of scientific and educational activities and for no other purpose. The institution shall reimburse the establishment for animals received. The fee shall be, at a

minimum, $15 for cats and $20 for dogs. That fee shall be increased as determined by the department, based on fluctuations or changes in the Consumer Price Index."

According to the American Anti-Vivisection Society, 16 states[3] and the District of Columbia ban pound seizure, 3 states (Minnesota, Oklahoma, and Utah) mandate it, 9 states allow it,[4] and the rest leave the decision to the municipality.[5] These data may continue to change as states revisit these laws due to changing public attitudes and diminishing access to random source animals from pounds for research. In one instance, the state of California allows the release of unclaimed animals for research, but the individual counties have all enacted bans, in large part because of California Civil Code 1834.7, which requires any pound or shelter that provides living or dead animals to a biological supply company or research facility to post a publicly visible sign stating that "Animals turned in to this shelter may be used for research purposes or to supply blood, tissue, or other biological products." Given a choice, the public chooses not to allow the resale of pound or shelter animals to research. A 1988 American Humane Association survey involving 26 shelters found that respondents overwhelmingly would not bring a lost animal to a shelter that released unclaimed animals to research (of the 2,438 responses gathered, 2,273 said no, 165 yes). They would also be much less likely to report a stray dog or relinquish their own pet to the shelter if they knew it could end up in a research laboratory (American Humane Shoptalk 1988) (see also Box 2-1).

Alternative Sources of Animals for Class B Dealers

As an alternative to shelters and pounds, the AWA allows Class B dealers to purchase animals from private individuals who have bred and raised the animals on their premises, such as hobby breeders, who are exempt under the AWA (see Chapter 1 for definitions). Hounds are the most common type of hobby breeder–derived dogs bought and sold for research. Class B dealers can also obtain random source animals from other USDA-licensed dealers, including other Class B dealers and auction houses. Auction houses and bunchers are required to have Class B licenses, although they are not considered random source Class B dealers. A review of sourcing data by the USDA indicates that auction houses have not recently been a source of dogs and cats for research purposes (personal communication, Robert Willems,

[3] The 16 states are Connecticut, Delaware, Hawaii, Illinois, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, South Carolina, Vermont, Virginia, and West Virginia.

[4] The 9 states are Arizona, California, Colorado, Iowa, Michigan, Ohio, South Dakota, Tennessee, and Wisconsin.

[5] www.aavs.org (accessed September 2009)

USDA, to Committee, January 2009). Dog auctions are primarily involved with the pet trade; however, if auctions were to move into the research animal trade, the USDA would consider them random source Class B dealers and deal with them accordingly.

COST OF ANIMALS FROM CLASS B DEALERS

In an ideal world, cost would not be a factor in decisions about research, particularly those concerning animals. Realistically, however, resources are limited and researchers are constrained by financial concerns. Thus cost is a potential consideration for the continued use of animals from Class B dealers, which may cost less than animals from Class A dealers. Depending on circumstances, the financial incentives to use animals from Class B dealers may or may not be substantial.

According to information obtained from two Class B and three Class A dealers, the purchase price of a young, 20-25 kg (44-55 lbs) dog is $325-$350 for a random source animal and $600-$900 for a purpose-bred dog. However, oftentimes dogs and cats from Class B dealers are not free of disease and may require prolonged quarantine, socialization, treatment, or removal from the study altogether to avoid potential health threats to other animals or to people in the research facility. The hidden costs to address these conditions may substantially increase the actual final cost by hundreds of dollars per animal. Additionally, the price of USDA/APHIS oversight of Class B dealers (discussed below) represents a substantial cost to the U.S. government and ultimately the American public that is not borne by NIH, the research institution, or the research investigator.

In certain cases the difference in cost between dogs from Class A and Class B dealers may be prohibitive. For example, the cost of using unconditioned dogs from Class B dealers for an acute procedure would be substantially less than for dogs from Class A dealers; but much of the acute work in which an unconditioned dog from a Class B dealer would be an appropriate model, such as in a surgical training class, is beyond the scope of this report.

For studies that require older animals, the purchase price of animals from Class A dealers increases with the age of the animal; for example, one Class A vendor charges a base price of $730 for a 6-month old beagle and an additional $4.10/day after the animal's first 195 days. Thus, a skeletally mature beagle from a Class A dealer for orthopedic research would cost over $1400/dog, a purchase price that some would consider prohibitive (Class A vendor beagle price list provided to the Committee, January 2009).

One of the largest components to the cost of the animal, regardless of the source, is that of transporting the animal from the vendor to the research location. Surface transportation of groups of animals may cost thousands

of dollars depending on the location of the recipient. Air transportation is even more expensive, done less frequently, and, with new regulations on airlines, may not be an attractive or even viable mode of animal shipping in the future. Obviously, the closer the source of the animals, the lower the shipping costs. In fact, based on the locations of the current Class B dealers and the institutions that use these animals, transportation costs appear to be a factor in the use of animals from Class B dealers: (as of October 2009) the 10 remaining licensed Class B dealers are in Illinois, Indiana, Kentucky, Michigan, Minnesota, and Pennsylvania.

AWA ENFORCEMENT

It is the responsibility of the USDA/APHIS Animal Care agency to ensure that Class B dealers abide by the AWA statutes and the AWR. As explained in Chapter 2, the specter of lost or stolen pets being illegally or inadvertently used in research has been a driving force in the increasingly rigorous revisions of the AWA and USDA/APHIS interpretation and execution of the law. However, in the more than 40 years since passage of the AWA, the USDA/APHIS has been unable to completely enforce the Act with respect to the activities of Class B dealers and has thus been unable to ease the concerns of the American public (Box 4-1). The reasons for this failure are multiple, as discussed below, and underscore the necessity of carefully crafting and enforcing laws if they are to have their intended effect.

USDA veterinary officers who testified before the Committee were appropriately circumspect about their personal opinions, but described long-standing problems with regulation of the Class B dealer system. All stated that AWR enforcement was feasible, with emphasis on tracebacks during inspections. When the Committee queried Jerry DePoyster, a Senior Veterinary Medical Officer with APHIS, he acknowledged the USDA/APHIS could not guarantee that a C.C. Baird-type incident would not be repeated, and reaffirmed the disproportionate effort and difficulties APHIS experiences in regulating Class B dealers. Robert Willems, APHIS Assistant Director for the Eastern Region, testified that Class B dealers are regulated more heavily than any other USDA licensee and that, when he was involved in west coast operations, the office invested over 800 hours and 1½ years investigating the violations of a single dealer. W. Ron DeHaven discussed with the Committee regulatory changes proposed while he served as a USDA Regional Director for Animal Care and Use, including a possible 2-year phase-out of Class B dealers discussed at a Public Responsibility in Medicine and Research (PRIM&R) conference "Animal Care and Use: Hot Zones, Grey Zones and Go Slow Zones" (Rudacille 1996).

According to information that Dr. Willems provided to the Committee, APHIS has responded to these incidents and public pressure by increasing

BOX 4-1
Problems with AWA Enforcement: A Case Study

A notorious recent example is the case of the Class B dealer C.C. Baird.[a] For a number of years before 2003, USDA inspection reports indicated that Baird's Martin Creek Kennels and Pat's Pine Tree Farms operated within acceptable limits. Then a member of the organization Last Chance for Animals gained employment at Baird's facilities and obtained over 70 hours of video surveillance of sick, dead, and dying animals with little or no protection from wet and cold, grossly unsanitary conditions, inadequate veterinary care, and multiple instances of cruelty and animal abuse. This documentation was given to the U.S. Attorney's office, resulting in the largest multiagency (federal, state, and local) investigation of animal abuse in U.S. history. Included in the documentation was a conversation in which a buncher admitted to stealing animals that were probably people's pets.

A documentary film "*Dealing Dogs*" (HBO 2006) of these events was produced by Tom Simon and Sarah Tealer for Home Box Office. The Committee became familiar with the Baird case because of its importance to recent public perspectives (including congressional action) and decline in numbers of Class B dealers.

Baird avoided imprisonment (but paid a large fine) by agreeing to testify to USDA and others in regards to multiple other ongoing Class B dealer investigations. It is important to note that despite uncovering extensive evidence of gross mismanagement and animal suffering by an undercover investigator from the animal protectionist community rather than USDA/APHIS, it still required over a year of administrative procedure and due process for the government to investigate, prosecute, and close this case, not to mention years of USDA inspection and approval of this dealer to remain in operation before the situation became public. The USDA increased its oversight of other Class B dealers by requiring more frequent inspections of dealer premises and by requiring USDA inspectors to regularly trace back the ownership of animals held by Class B dealers to verify that animals were legally obtained. These changes, together with a decrease in demand, contributed to the number of Class B dealers selling dogs and cats to research facilities from nearly 200 to 11.

[a] http://www.lcanimal.org/invest/baird/baird_synopsis.htm

its regulatory oversight of Class B dealers by implementing in October of 2008 the new USDA internal SOP, *Conducting Tracebacks from Random Source B Dealers*. Whereas the regulations mandate annual inspections for research facilities and Class A dealers, Class B dealers now must undergo quarterly inspections with a major focus of these inspections on the acquisition of random and non-random source animals. This increased oversight is also now more feasible with the greatly reduced number of dealers. The legality of acquisition is evaluated by conducting tracebacks on a represen-

tative sampling of animals. For each dealer, tracebacks are performed on some animals at the facility at each inspection and on all animals present at the facility annually during one of the quarterly inspections. It must be made clear that due to the turnover of animals at a dealer facility, not all animals are traced back, only those on the premises at the time the inspection is conducted. In addition, during each quarter, approximately 25% of Class B dealers are now being subjected to 100% tracebacks of all acquisitions since the previous inspection and over the course of one year all Class B dealers will have undergone the process of 100% tracebacks. USDA inspectors are instructed to consider a traceback successful and complete when the origin of the animal has been traced to a legal source.

The USDA has expressed confidence that its increased scrutiny of Class B dealers is sufficient to address concerns about the Class B system and to keep pets out of the system. In 1998, Terry Medley, while serving as administrator of APHIS, stated in a letter to the House Committee on Agriculture, that the USDA was able to trace back original owners for more than 90% of the dogs brokered by Class B dealers (HSUS 2007; CBRA 2009), and Dr. DeHaven stated in testimony before this NRC Committee that in 2000 and 2001 the USDA was able to trace back original ownership for 95% of such dogs. This was well before the 2008 implementation of the new USDA SOP, *Conducting Tracebacks from Random Source B Dealers*, so it is likely that the current traceback figure is higher. But while such a success rate is admirable, it nonetheless suggests that the origins of 5-10% of animals in the Class B system are uncertain. Indeed, there remain loopholes in the system. For example, origination information is considered adequate if the sale of an animal is traced back to an auction. Thus, although there is no evidence that auction houses are currently used to sell animals to research institutions or Class B dealers, auction sales could serve as a mechanism to legitimize the sale of illegally acquired animals.

There is little evidence to prove that pets are stolen for research (HBO 2006) but the USDA could not offer assurances that pet theft does not occur, and agreed that such a crime is exceedingly difficult to prove, almost requiring an eyewitness. There are, however, descriptions of thefts provided by informants in prison (personal communication, Robert Willems, USDA, to Committee, January 2009) and documented accounts of lost pets that have ended up in research institutions through Class B dealers. For example, in June 2005, the University of Minnesota received from a Class B dealer a dog that was subsequently identified as a missing pet named Echo through microchip scanning by a veterinarian at the institution. Apparently Echo made his way to the university via a USDA-licensed Class B dealer from Michigan, who in turn reported buying Echo from another Class B dealer in Missouri (Fayetteville Free Weekly 2005).

The Committee requested FOIA access to USDA inspection reports over

the past three years of all licensed (as of October 2008) Class B dealers. Those reports revealed that one dealer purchased two cats from a private individual who during traceback investigation admitted that the animals were illegally acquired "strays." Other citations involved incomplete acquisition documentation. Thus, increased traceback oversight is working at discovering violations, but these ongoing events illustrate that the law continues to be violated.

No system of laws and regulations can absolutely assure protection against theft of pets or misplacement of lost pets, but even single incidents, however few, are a breach of the public trust. The reasons for these deficiencies are multifactorial. The most significant factor is that the acquisition and resale of animals by dealers, bunchers, and individuals is profit-driven, and thus may foster corrupt practices and less attention to animal welfare issues. The system therefore requires rigorous enforcement, but APHIS is understaffed for the task, even with the reduction in numbers of dealers. According to testimony by Dr. Willems, some tracebacks are dead ends, with suspicion of violation, but lack of evidence. Even if staffing were substantially increased, prosecution of AWA abuses requires a step-wise approach to enforcement of the AWR, with documentation to create a "paper trail" of evidence involving citations with correction dates, requests for investigation, warnings, stipulations, formal complaints, and finally a hearing, all before violators can be legally prosecuted. These steps are mandated by federal law in the *Administrative Procedures Act*, which requires due process and places time constraints on APHIS authorities for action. Regarding the humane issues this Committee was also charged to examine, there is a strong concern that animals can only be removed if they are in need of immediate veterinary care, leaving the potential for animals that are severely stressed or in need of less intensive care to be left unattended indefinitely.

The Committee considered the question of whether animals are still being stolen for research, but was not able to answer conclusively based on the evidence provided. The Committee recognizes, however, that lost animals may find their way into the system inadvertently. Shelter lost-and-found systems range from use of computerized programs to random tours through the shelter by poorly trained staff and distraught owners. Other reasons lost pets are not reunited with their owners are poor breed identification, and lack of resources.

Implanted microchips are a tool used to identify animals and are currently provided by three different companies. Yet, according to testimony provided by USDA staff, inspectors do not check for microchips when performing tracebacks. In order to be effective, recent research has shown that microchip scans should be performed at least 3 times, because such equipment as computers, fluorescent lights, and stainless steel exam tables

can interfere with a scan (Lord et al. 2008). The failure to take these factors into account when scanning could lead to false negatives. The use of microchips for reuniting lost animals with their owners is further complicated by the fact that an effective universal scanner that can detect the various types of microchips is not always available.

All of these factors mean that lost animals may escape detection despite efforts by their owners to recover them. While the individual owner is understandably upset when a lost animal is euthanized at a shelter, the public is outraged (as evidenced by repeated calls to strengthen the legislation to protect pets) when the lost or stolen animal turns up at a research facility.

INCONSISTENCIES IN QUALITY AMONG CLASS B DEALERS

Although it is legal under AWA provisions to obtain dogs and cats from licensed Class B dealers, it is apparent that there are significant differences in standards among dealers in regards to facilities, animal care, and sanitation. There is no set standard among Class B dealers for veterinary care; the required veterinary care plan is left to the discretion of the individual veterinarian employed by the dealer, which lends itself further to disparities in care. Furthermore, there is no requirement to maintain medical records unless an animal is receiving veterinary care. There is also concern that the inspection reports may not always reveal the true conditions at the facility, as the Baird facility also passed its inspections despite its numerous violations (Box 4-1). Inspections are random and unannounced and it may take more than one attempt to actually inspect a facility, providing less scrupulous dealers an opportunity to hide violations and alter records. The Committee did not physically inspect facilities but became aware of such discrepancies after examining USDA/APHIS inspection reports for the last 3 years of all currently licensed Class B dealers. These reports revealed there are dealers that fully respected their obligations to the AWA, with virtually no citations accrued in the last 3 years. In contrast, other dealers were the source of repeated, usually minor and occasionally serious infractions of the law. The Committee recognizes that it is unfortunate that legitimate businesses are negatively impacted by less savory dealers.

ALTERNATIVES TO CLASS B ANIMALS

Chapter 3 discussed attributes, both positive and negative, of random source animals, attributes that pertain to random source animals whether they are obtained directly from pounds and shelters, obtained through Class B dealers, or obtained in other ways. Information provided to the Committee by Class B dealers and USDA officials indicates that a signifi-

cant number of dogs from Class B dealers are hounds from private owners (Figure 4-1a, "Individuals") and that only 20% (947 of 4,672 total) came from pounds and shelters in 2008 (Figure 4-1a). In contrast, most cats (230 of only 378 total, or 61%) obtained by Class B dealers come from pounds and shelters (Figure 4-1d), many of which are probably stray and feral animals. These percentages indicate that Class A dealers can fulfill much of the demand for animals with similar characteristics. Justification for the research use of random source animals from Class B dealers is based on their cost, size, age, genetic diversity, infectious and naturally occurring diseases, and other conditions, but these attributes (other than cost) are generally not unique to animals from shelters and pounds.

Furthermore, it is important to emphasize that even if random source animals are considered desirable and necessary for NIH-based research, it is not clear that Class B dealers can ensure their availability from the diminishing number of cooperating pounds and shelters. And as sources of random source animals decline, the animals sold by Class B dealers are becoming increasingly similar in characteristics to those of Class A animals, except that they are of inferior quality to Class A animals for the reasons discussed in this report.

Class A Dealers

One mechanism that has been proposed to ensure continued access to genetically diverse, aged, or large breed dogs (attributes that are desirable in random source dogs) is to encourage these animals to be specifically bred and maintained by Class A dealers. Purpose-bred hounds available from Class A vendors are in fact somewhat genetically diverse. Although the colonies of such hounds have been closed for many years, the original stock was composed of various breeds (red bone, black & tan, blue tick, Tennessee walker, foxhounds, and brindle current) and the "descendants" do represent genetic diversity. In addition, a Class A colony of smaller mongrel dogs, originated from Class B dogs almost a quarter-century ago, is available and represents other mixed breed dogs (personal communication, Covance, to Committee, February 2009). Class A vendors also keep a few retired breeding animals or animals that are larger in size, but these are not always available. If the research community requires specific attributes—such as a particular age, physical conditioning, or physical attributes (e.g., larger size) not normally found in existing Class A colonies—Class A vendors may consider providing these models and the costs may not always be significantly higher than for animals from Class B dealers.

It would be impossible for Class A dealers of laboratory animals to maintain the diversity of dog and cat breeds (and thus the genetic diversity) that exists in the general dog and cat population, which could therefore be

an enormous potential resource of animal models of human disease. But Class B dealers do not provide such animals to the biomedical research community either; rather, they deal with various specific breeds of medium and large-sized dogs and random source cats.

Other Research Institutions

Some research institutions (e.g., the University of Florida, the University of North Carolina, and the University of California, Davis) maintain purpose-bred colonies of various breeds of dogs and cats. The Committee was unable to determine how many such colonies exist, because most are not supported directly by NIH, although their animals are used in NIH-related research. Indeed, these colonies are a relatively untapped resource for NIH for the acquisition of aged, genetically defined, or genetically diverse purpose-bred animals.

Random source dogs are used for age-related research, but a significant degree of aging research involves purpose-bred beagles (Cotman and Head 2008). Beagles are accessible from purpose-bred colonies maintained by a small number of research institutions (e.g., the Lovelace Foundation). Aged beagles from such colonies are particularly valuable models of human cognitive aging, and are actively used by the scientific community for these aging studies. These dogs manifest age-dependent decline in learning and memory and develop neurological disease with features similar to Alzheimer's disease (AD) as well as age-related hippocampal and entorhinal neuronal loss, similar to that which occurs in humans. The aged Beagle model has also been used in immunotherapy studies for AD (Nippak et al. 2007; Siwak-Tapp et al. 2008; Vasilevko and Head 2009). In contrast to random source animals, which typically are of unknown age, defined-age purpose-bred dogs are also ideal for longitudinal studies and for studies evaluating the effects of long-term dietary variables or environmental enrichment.

To its credit, the Comparative Medicine Program of the NIH National Center for Research Resources has capitalized on the many genetic mutations among the pet dog and cat population by supporting the Referral Center for Animal Models of Human Genetic Diseases at the University of Pennsylvania School of Veterinary Medicine. This center has accrued a wealth of dog and cat models of human genetic diseases (e.g., metabolic diseases, bleeding disorders, immunologic disorders, dilatative cardiomyopathy and other cardiac disorders, osteogenesis imperfecta, mucopolysaccharidoses, and many others) through referrals about pets (e.g., from knowledgeable breeders, working dog organizations, and veterinarians). The center acquires, characterizes, and genetically analyzes submitted cases to validate homology to the human disease, and makes

animals available to the general research community by maintaining small nucleus breeding populations, collaborative interactions with colonies at other institutions, and germplasm. This laudable program directly addresses NIH needs for certain types of dog and cat models.

Another outstanding program, the Canine Comparative Oncology Program of the National Cancer Institute (NCI), takes full advantage of naturally occurring cancers in the general dog population. The aged and genetically diverse dog population is prone to many types of cancers that mimic the human disease—including non-Hodgkin lymphoma, osteosarcoma, melanoma, prostate carcinoma, pulmonary carcinoma, mammary carcinoma, soft tissue sarcomas, mast cell tumors, and others—and the rate of occurrence is sufficient to power preclinical trials.

The NCI program, established in 2003, includes a multicenter collaborative network of 18 veterinary teaching hospitals[6] (the Comparative Oncology Trials Consortium; Figure 4-2) that fosters rigorously controlled preclinical trials of new cancer drugs intended for eventual use in humans. These preclinical trials provide guidance on the design of human studies, without the constraints of human phase I, phase II, and phase III trials, while also benefiting the client-owned animal patients. The program is linked to another NIH consortium, the Comparative Oncology and Genetics Consortium, which builds on the publication of the canine genome and maintains a biorepository of canine tumors, fosters collaborative opportunities between comparative oncologists, and initiates preclinical trials using pet dogs with cancers.

These NCI programs make use of naturally occurring cancers in dogs, which have significant similarities to the genomic profiles and biology of human neoplasms. For example, the comparable respiratory anatomy of large dogs and humans (discussed in Chapter 3) and the parallels in distribution of primary and metastatic lung cancers have allowed assessment of inhaled cytokine immunotherapy, which led the way for—and predicted the successful outcome of—early phase trials in humans. These programs benefit from the rich genetic and disease diversity of the general dog population, together with highly qualified veterinary and medical collaboration, client participation, and mutually beneficial advancement of human and animal health.

[6] Auburn University, Auburn University, AL; Colorado State University, Ft. Collins, CO; Cornell University, Ithaca, NY; Michigan State University, East Lansing, MI; North Carolina State University, Raleigh, NC; Purdue University, West Lafayette, IN; Texas A&M University, College Station, TX; The Ohio State University, Columbus, OH; Tufts University, North Grafton, MA; University of California, Davis, CA; University of Florida, Gainesville, FL; University of Georgia, Athens, GA; University of Illinois, Urbana, IL; University of Minnesota, St. Paul, MN; University of Missouri, Columbia, MO; University of Pennsylvania, Philadelphia, PA; University of Tennessee, Knoxville, TN; University of Wisconsin, Madison, WI.

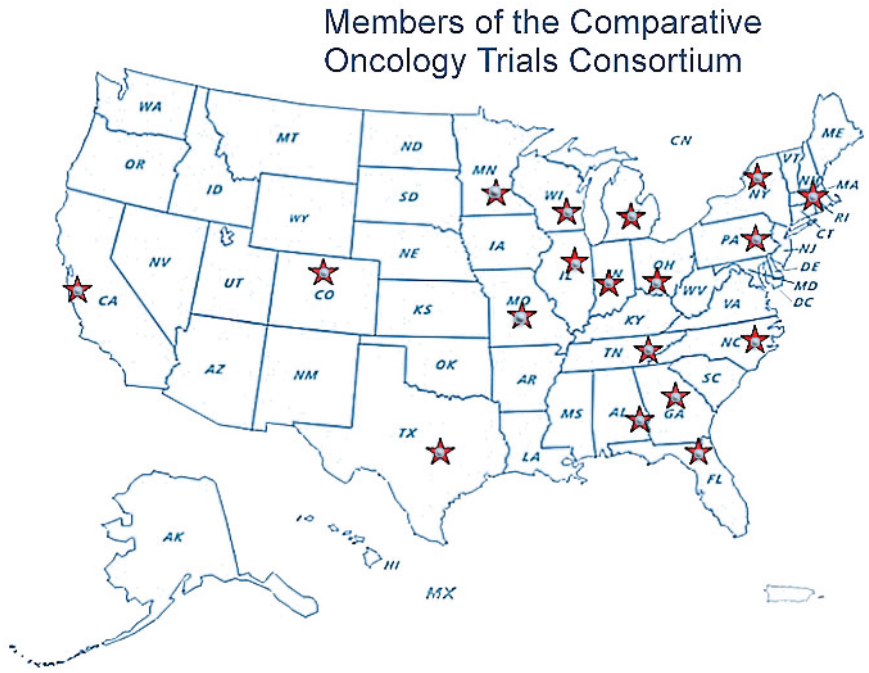

FIGURE 4-2 Map of current institution members of the Comparative Oncology Trials Consortium. *Source:* http://ccr.nci.nih.gov/resources/cop/COTC.asp

UNRESOLVED CLASS B COMPLIANCE ISSUES

The public harbors two major concerns about the use of Class B dogs and cats in research, and the Committee shares those concerns. The first is the perception of pet theft or displacement of lost pets by dealers who may profit through the sale of such animals to research. The second is the deplorable husbandry conditions that have been documented at some Class B dealers (AWI 2007).

With respect to the first concern, loopholes in the AWR permit pets to enter the research pipeline via Class B dealers who acquire and sell dogs and cats that originated from auctions, shelters, and pounds.

The second concern arises from the requirement that Class B dealers adhere to only the AWR, whereas institutions that receive NIH funding for research comply with *PHS Policy*, the *Guide for the Care and Use of Laboratory Animals*, and the *U.S. Government Principles* (defined in Chapter 1). Class B facilities are therefore not held to the same standards as NIH-funded research facilities. In addition, the USDA, which is responsible for enforce-

ment of the AWR, has different internal inspection manuals (see Chapter 1), allowing—and inconsistently applying—different standards of the AWR among dealers, research institutions, and exhibitors. It is difficult for the public to understand why there are different standards of care when the purpose of the AWR was to establish minimum standards.

Finally, the Committee recognizes that the USDA is severely hampered in its ability to implement the AWR standards. USDA has insufficient enforcement powers, including the ability to act more swiftly, assess sufficiently punitive fines, issue temporary injunctions, and impose immediate cease-and-desist orders for serious or repeat animal welfare citations. As explained above, because of insufficient staffing and the time-consuming multiple steps and documentation required for enforcement, only serious and repeated infractions are worth pursuing, allowing many "minor" infractions to persist unaddressed. It is of great concern to the Committee that animals can be removed from Class B dealer sites only if they are in need of immediate veterinary care, leaving the possibility that severely stressed animals or those in need of less intensive care may be left unattended.

These serious unresolved Class B compliance issues and humane concerns were major factors in the deliberations that led to the Committee's final recommendations (Chapter 5).

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5

Conclusions and Recommendations

The *Committee on Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research* was assigned three specific tasks. The first task required an analysis of the available data to determine the important biomedical research questions and common research topics in contemporary NIH-funded research where dogs and cats from Class B dealers are desirable or necessary as well as the number of grants where the potential exists or the animal is identified as coming from a Class B source. The second task asked for a description of the special characteristics (e.g., physiological, anatomic, or genetic) of the animals that make them particularly well suited for the types of research described in task one. Unfortunately, given the inaccessibility of specific data, it was impossible to ascertain if animals from Class B dealers (as opposed to animals from other sources) were used specifically in these studies. Furthermore, because "Class B" refers to a system of acquisition of random source animals and not the animals themselves, it could not be determined if animals from Class B dealers were desirable for use in these studies (e.g., studies of aging, naturally occurring infectious disease, genetic disease) simply because of their lower cost and availability, or necessary for some other compelling scientific reason. The Committee determined that while there were a few studies that required animals with characteristics not currently provided or available only in limited numbers by Class A dealers (e.g., naturally occurring infectious disease, larger size, deeper chest, and older age) these specific characteristics are not unique to random source or animals from Class B dealers, and the demand for animals with these specific characteristics appears to be small. Concerns that the elimination of the Class B dealer

would hamper a few research projects were based largely on speculation that other sources of animals could not meet this very small demand. The third task was to make recommendations, if necessary, for new or revised scientific parameters to guide their use, if Class B dogs and cats are deemed to be necessary for research.

Despite passage in 1966 of the Animal Welfare Act (AWA) in response to public concerns about the use of lost or stolen pets in research, these concerns persist. The Committee found that the USDA has made significant strides recently in enforcement of the AWA regulations and that the number of Class B dealers, who obtain some animals (including lost or stolen pets) from shelters and pounds, has decreased dramatically, particularly in the last 15-16 years. Whereas animals from Class B dealers represented 20 percent of dogs and cats used in research in 2002, by 2008 they represented only 3 percent and only a fraction of that percentage were used for NIH research. Of that fraction, animals from pounds and shelters, which is the group of animals with potentially valuable or unique attributes for NIH research, accounted for 20 percent of dogs and 61 percent of the very small numbers of cats from Class B dealers.

However, testimony provided to the Committee by USDA officials made it clear that despite new enforcement guidelines and intensified inspection efforts, not all origins of animals are or can be traced; therefore the USDA simply cannot ensure that lost or stolen pets do not enter research laboratories via the Class B dealer system. Furthermore, the administrative and judicial procedures necessary to enforce the AWA and ensure remediation of conditions that cause animal distress and suffering are inordinately slow, cumbersome, and ineffective. The Committee felt strongly that this is unacceptable.

Thus, in evaluating the information provided through testimony and from other sources, the Committee found the following:

- Trends in the use of dogs and cats from Class B dealers in research suggest that for a variety of reasons (public opinion, pressure from animal protectionists, regulatory and financial burden, institutional policies, research trends, investigator choice), the Class B dealer system may soon become unavailable as a source of animals for research.
- As long as the Class B dealer system persists, the biomedical research community will be subject to "negative press" and public concerns about lost or stolen pets ending up in research, no matter how rare such occurrences are or how well enforced the regulations.
- The husbandry standards and humane treatment of animals are unacceptably variable among Class B dealers and not consistent with NIH standards of research animal care and quality.
- In the absence of reported data, it is not possible to identify the

actual number of random source dogs and cats or animals from Class B dealers with the unique characteristics needed for or used in specific NIH research projects. However, the number of random source animals from pounds and shelters used in research is very small, and the number used in NIH-based research is smaller. Nonetheless, this small number of animals may have potentially high value to the NIH mission.

- Alternatives are available for filling much if not all of this limited need. It is therefore not necessary to continue to obtain random source dogs and cats for NIH research from Class B dealers, provided that alternative sources of animals with similar characteristics can continue to be assured.

The Committee cautions that NIH must either respond with alternate approaches or accept that random source animals are increasingly difficult to obtain, whether through direct acquisition or through Class B dealers. the Committee identified the following existing options to ensure the continued availability of random source dogs and cats in the absence of Class B dealers:

- **Direct acquisition from pounds and shelters.** Some institutions acquire random source animals directly from pounds and shelters in the three states that mandate pound seizure and from some municipal shelters in the 21 states that have no formal policy. While it is impossible to know with any degree of certainty until the question is posed, direct acquisition is most likely to occur at pounds that have inadequate funding, a high euthanasia rate, a strong animal control component, a weak adoption program, and/or an apathetic animal welfare community. It is unlikely that private shelters or humane societies that receive public funding would ever relinquish animals for research. However, it is important to note that Class B dealers are not a solution for the diminishing access to animals of this type. Furthermore, research institutions that engage in direct acquisition take on not only the responsibility and added cost of conditioning and veterinary care but also the responsibility of ensuring the animals' welfare.
- **Donation programs.** Direct acquisition of animals by research institutions from small breeders, hobby clubs, and individual owners is a source that is already in use and represents a significant percentage of the animals acquired by Class B dealers. There is no reason such animals cannot be acquired directly rather than through Class B dealers.
- **Cooperative preclinical consortia.** The current use of pet animals

with owner consent for comparative preclinical investigations is a viable model for both human and veterinary medical research. An outstanding example is the NIH/NCI Canine Comparative Oncology Program (CCOP), a multicenter collaborative network of 18 veterinary teaching hospitals that provides controlled preclinical trials of new cancer drugs with the goal of supporting the design of human studies. In addition, the Canine Comparative Oncology and Genomics Consortium (CCOGC) includes a broad array of private and academic entities focused on the biology and genetics of canine cancers. Cooperative efforts such as these capitalize on the rich genetic diversity and variety of cancers that arise in the canine population as well as dogs' anatomic and disease characteristics, which more accurately reflect the human condition than those of rodents. In addition, these programs ensure the outstanding clinical care of the animals and are free of the constraints of human phase I, II, and III clinical trial designs. Such consortia could be readily developed for virtually any comparative disease research of interest to categorical institutes of NIH.

- **Class A dealers.** Class A dealers of laboratory animals breed primarily beagles, hounds, and mongrel dogs that typically range in size from 15 to 27 kg (33-60 lbs) and in age from 6 to 12 months. However, some of these vendors indicated that larger dogs, 27-37 kg (60-80 lbs), are available or in some cases could be bred if needed. In addition, although most dogs sold for research are less than 1 year old, a small number of older (2-5 years) retired breeding animals are available (personal communication with Class A vendors). If more of these animals are needed, Class A vendors could provide them, albeit at a greater cost. In addition, a significant number of dogs from Class B dealers are hounds obtained from hobby breeders, and these animals overlap with those available through Class A dealers. The number of cats provided by Class B dealers is so small that they are likely to be available through other mechanisms such as Class A dealers.
- **NIH-supported resource and research development.** Random source animals from shelters, pounds, or Class B dealers do not address the need for capitalizing on the plethora of potentially valuable genetic animal models in the general pet population, yet this is often used as an argument for continued access to random source animals (Chapter 3). In addition to the CCOP mentioned above, programs such as the *Referral Center for Animal Models of Human Genetic Diseases* at the University of Pennsylvania School of Veterinary Medicine (Chapter 4) directly address the needs of NIH for discovery, accurate characterization, and access to these

valuable dog and cat models of human disease that arise in the general dog and cat population. These programs are examples of the public's willing contribution of animals for research in order to advance both animal and human health, and they foster a positive public image for NIH. If there is a need for genetic or other disease models, NIH should invest in the expansion of such programs and in technology for the improved preservation and archiving of germplasm of important models, but additional, directed funding for such resources would be needed.

In addition to these options, the Committee recommends consideration of the following means to ensure access to random source animals or animals with the attributes thereof:

- **Existing NIH-supported and privately owned colonies.** Some NIH categorical institutes support dog colonies at U.S. research institutions, including defined-age animals for use in aging research. Indeed, the purpose-bred beagle is the dominant aging dog model. In addition, other privately supported colonies at academic institutions include mixed breed and large breed dogs such as golden retrievers. Similarly, there are colonies of mixed breed cats. Since most of these colonies are not supported by NIH, the Committee was unable to determine how many exist. If access to such animals is important to the NIH mission, NIH should make a "trans-NIH" effort to coordinate such access and offer subsidies to cooperating institutions to maintain access to animals.
- **NIH request for proposal.** Various NIH categorical institutes commonly use the request for proposal (RFP) mechanism to acquire needed items or to perform research and development on a contractual basis. This mechanism has several merits. Examples of NIH animal-related RFPs include contracts to develop specific animal models, operate NIH animal facilities or other animal facilities that serve NIH, provide quality animals for NIH research programs, develop animal-related reagents that enhance research, and explore the application of animal models to test the efficacy of vaccines or therapeutic regimens, among many others. A variety of laboratory animals, ranging from rodents to nonhuman primates, are the subject of RFPs, and since the RFPs are NIH-supported, all such animals fall under *PHS Policy*. Thus the RFP mechanism is quite suitable for fulfilling the need for random source animals.

  The RFP can define the specific criteria for acquisition, husbandry, traceback assurance, and veterinary care of animals in keeping with *PHS Policy*. Respondents to the RFP would need

to provide a detailed Animal Welfare Assurance, similar to any research institution that receives NIH funds, also in keeping with *PHS Policy*. The RFP statement of work can also include specifics of number, age, breed, and size, and can be flexible in response to changing needs of NIH. Under the RFP, animals destined for research would immediately become the responsibility of NIH, an arrangement that would both ensure the optimal care and welfare of the animals and enhance NIH's research through the use of healthier animals. Continuation of the contract would be subject to periodic (usually quarterly) review. The contractor's failure to meet the statement of work, including accurate traceback documentation, could result in the immediate curtailment of support, in contrast to AWA/APHIS enforcement, which requires substantial effort to "build a case," suspend a license, or correct violations. Thus, there is a far higher incentive for, and more rapid response to, compliance compared to contractors working with the existing Class B dealer system.

To reiterate, the RFP mechanism would not be equivalent to a Class B dealer, as animals acquired through the RFP would become NIH property and thus be subject to the *U.S. Government Principles* and *PHS Policy* (as well as the AWA). Furthermore, the RFP mechanism could allow coordination of scientific need with availability of specific types of animals from geographically diverse sources.

The Committee acknowledges that NIH will need supplemental funding to facilitate these options and, in the absence of specific allocations from Congress, anticipates that NIH will be reluctant to take on these responsibilities at a time when the NIH budget is uncertain. As noted throughout the report, the Class B dealer system is declining, and availability of random source animals from pounds and shelters is diminishing, independent of the decline of Class B dealers. Therefore, if NIH deems random source animals, or their qualities, necessary for research, it will need to explore and support alternatives before these animals become altogether unavailable from either Class B dealers or pounds and shelters.

Appendix

Committee Biographies

Stephen W. Barthold *(Chair)*, DVM, Ph.D., IOM, is Director of the Center for Comparative Medicine, University of California–Davis where he is the Distinguished Professor of Veterinary Pathology, Microbiology and Immunology, and of Medical Pathology and Laboratory Medicine through joint appointments of the Schools of Veterinary Medicine and Medicine. Dr. Barthold received his Doctor of Veterinary Medicine degree from the University of California, his Ph.D. in experimental pathology from the University of Wisconsin, and is a Diplomate of the American College of Veterinary Pathologists. He is nominated as chair because of his expertise in experimental pathology of infectious disease, and pathology of laboratory animals. His research involves mechanisms of persistent infection and antibiotic tolerance with *Borrelia burgdorferi* (the agent of Lyme disease), using mouse models. Dr. Barthold is the recipient of several research career awards, including the AALAS Nathan R. Brewer Award, University of California Alumni Achievement Award, the Francis Schofield Medal from the Ontario Veterinary College, Honorary Diplomate of the American College of Laboratory Animal Medicine, and the AVMA Charles River Prize. He has served on numerous national scientific advisory and review committees, and editorial boards. Dr. Barthold is an IOM member and currently serves as Chair of ILAR Council.

Donald Bolser, Ph.D., Professor, Respiratory Physiology, Department of Physiological Sciences, College of Veterinary Medicine, University of Florida (Gainesville). Dr. Bolser received his Ph.D. from the University of South Florida and completed postdoctoral work at the University of Calgary and

University of Oklahoma. He worked as a staff scientist at Schering-Plough Research Institute prior to his current position. Dr. Bolser is on the editorial board of the *Journal of Applied Physiology*, has helped develop evidence-based clinical practice guidelines for the diagnosis and treatment of chronic cough for the American College of Chest Physicians, and has served as a consultant for the pharmaceutical industry. His research involves investigations in pathology and physiology of cough as well as the use of rat and feline models to observe spontaneously active and recruited brainstem neurons during cough. He aims to model the configuration of the brainstem neural network controlling airway protection, and to identify the mechanism of action of cough suppressant drugs.

Kelly D. Garcia, DVM, Ph.D., Clinical Veterinarian, University of Illinois at Chicago. Her experience with supervising the care and husbandry of large animals at UIC includes a colony of over 80 dogs in addition to sheep, pigs, cows, rabbits, chinchillas, and guinea pigs. She has published several papers in journals such as the Proceedings of the National Academy of Sciences and the Journal of Neurosciences. Dr. Garcia has collaborated on a research project studying G-protein regulation of ion channels and completed a post-doctoral training program in laboratory animal medicine. She is a Diplomate of the American College of Laboratory Animal Medicine. Currently, Dr. Garcia oversees operations at the UIC Biologic Resources Laboratory surgical facility. At UIC, Dr. Garcia has served on numerous committees including as a Council Member on the National Institutes of Health National Advisory Research Resources Committee and as a past president of the Chicago Branch of AALAS. Dr. Garcia currently serves on the ACLAM Foundation Committee and the American Society of Laboratory Animal Practitioners Communications and Outreach Committee.

Joseph R. Haywood, Ph.D., is Professor and Chairperson, Department of Pharmacology and Toxicology, and Assistant Vice President for Regulatory Affairs at Michigan State University. He uses rats and non-human primates to study central and peripheral actions of hormones and drugs that regulate the sympathetic nervous system and blood pressure. His work has specifically targeted the mechanisms of the renin-angiotensin-aldosterone system as stimuli for sodium- and obesity-dependent hypertension. Dr. Haywood has been an advocate for the humane use of animals in research and education for over 20 years. He served on the Council on Accreditation for the Association for the Assessment and Accreditation for Laboratory Animal Care for 10 years. He is presently on the Governing Board of the International Council of Laboratory Animal Science representing the International Union of Basic and Clinical Pharmacology. Dr. Haywood has served on faculties for national meetings for the American Physiological Society, IACUC

101, Public Responsibility in Medicine and Research, and Scientists' Center for Animal Welfare discussing the humane use of animals in research and teaching.

Stuart Leland, DVM, Director, BioResources at Wyeth Research where he is the Attending Veterinarian and Chair of the Government and Public Policy Working Group. Dr. Leland oversees an NSF vivarium supporting rodent and nonhuman primate research for neuroscience and a genetically modified animal program. Previously, he has served as Head, Research Support and Veterinary Services at Aventis and as Associate Director for the Institute for Human Gene Therapy at the University of Pennsylvania. His research has involved molecular and pathogenic characterization of rat parvovirus and parvovirus-induced oncosuppression. He is board certified by the American College of Laboratory Animal Medicine. He currently serves on the Board of Directors for the NJ Association for Biomedical Research and is Chair, Program Committee for the 2009 National AALAS Meeting in Denver, Colorado.

Lila Miller, DVM, Vice President of Veterinary Outreach, American Society of Prevention of Cruelty to Animals (ASPCA) in New York. She is also an Adjunct Assistant Professor at the University of Pennsylvania's School of Veterinary Medicine and at Cornell University's College of Veterinary Medicine. Dr. Miller has over 30 years experience working in the field of animal sheltering and shelter medicine at the ASPCA in New York City. She is coeditor of the textbook *Shelter Medicine for Veterinarians and Staff* and just completed editing a textbook on the management of infectious diseases in animal shelters. She coordinated the first course on shelter medicine offered at a veterinary college in the U.S. (Cornell), on the Veterinary Information Network, and in Turkey. Dr. Miller co-founded and is past president and past member of the board of directors of the Association of Shelter Veterinarians. She writes a regular shelter medicine column for Animal Sheltering magazine and has written and lectured extensively on animal cruelty. She received the 2008 American Veterinary Medical Association (AVMA) Animal Welfare Award and 2005 Hills Animal Welfare and Humane Ethics award from the American Animal Hospital Association (AAHA). She was a member of the New York State Veterinary Board and board of directors of the American Association of Human Animal Bond Veterinarians (AAHABV), and is a current member of the National Board of Veterinary Medical Examiners (NBVME).

Randall J. Nelson, Ph.D., Professor of Anatomy and Neurobiology and Associate Vice Chancellor for Research at The University of Tennessee Health Science Center (UTHSC). He has extensive experience in reviewing proto-

cols and directing IACUC activities. He received a B.S. in Psychology from Duke University in 1975 and completed his doctoral degree in anatomy from Vanderbilt University in 1979. Following a postdoctoral fellowship at the University of California at San Francisco, he was a Staff Fellow at the National Institutes of Health, first in the Laboratory of Neurophysiology, and finally in the Laboratory of Neuropsychology, both at NIMH. He came to UTHSC in 1984 and since then has conducted research into the control of hand movement and taught Human Gross Anatomy. He has served as a member of several NIH study sections. He is a former member of the Committee on Animal Research of the Society for Neuroscience and is currently the Secretary of the Board of Trustees of the Scientist Center for Animal Welfare and serves as an ad hoc consultant for the Association for Assessment and Accreditation of Laboratory Animal Care International. He also served as a scientific delegate to an international harmonization workshop held in conjunction with the 5th World Congress on Alternatives and Animal Use in the Life Sciences. He is also a former member of ILAR Council.

James Serpell, Ph.D., is the Marie A. Moore Professor of Humane Ethics and Animal Welfare at the School of Veterinary Medicine, University of Pennsylvania, where he also directs the Center for the Interaction of Animals & Society (CIAS). He has extensive knowledge of animal behavior and welfare of companion animals, the development of human attitudes to animals, and the history of human-animal relationships. He established the Companion Animal Research Group at the University of Cambridge in England before moving to his current position at the University of Pennsylvania. Dr. Serpell is the immediate past president of the International Society for Anthrozoology (ISAZ), and serves on the editorial boards of most of the major journals on animal welfare, applied animal behavior, and human-animal interactions.

Michael R. Talcott, DVM, Director of Veterinary Surgical Services, Division of Comparative Medicine and Research Assistant Professor of Surgery at Washington University School of Medicine, St. Louis. His expertise is in clinical and post-operative care of most non-rodent species including dogs, cats, rabbits, sheep, goats, and pigs. He also provides surgical services in cardiology, orthopedics, vascular surgery, interventional radiology, and general surgery. In addition to his clinical/surgical duties, Dr. Talcott reviews all experimental protocols, advises investigators regarding animal models and experimental design, and provides oversight of all experimental use of these species. He is responsible for inspecting, certifying, and approving dog and cat vendors for Washington University. Dr. Talcott is board certified by the American College of Laboratory Animal Medicine and has served on the Public Policy Committee and Chair of the Career Pathways Commit-

tee. Dr. Talcott is also active in the Academy of Surgical Research, serving as President in 2008, and is on the Board of Trustees for the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). He is also involved in many efforts to educate the public about the use of animals in research, including presentations at local and national meetings and educational tours for groups from elementary school age through college age and adult.

Robert Whitney, DVM, RADM, Retired, U.S. Public Health Service. Dr. Whitney is CoFounder of Earthspan—a non-profit organization providing advanced technologies for the conservation of ecosystems, biodiversity, and environmental health. In the U.S. Public Health Service he served as Chief Veterinary Officer, Deputy Surgeon General, and Acting Surgeon General of the United States. Before 1992, he was Director of the NIH National Center for Research Resources. Prior to joining PHS, Dr. Whitney directed the U.S. Army training program in laboratory animal medicine and served in Vietnam as commander of a veterinary medical detachment. He is a Diplomate of the American College of Laboratory Animal Medicine. Dr. Whitney also serves on a number of boards of or is consultant to animal welfare or environmental awareness groups.