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

Committee on Scientific and Humane Issues in the Use of Random Source Dogs and Cats for Research; National Research Council

ISBN: 0-309-13808-6, 136 pages, 6 x 9, (2009)

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

PREPUBLICATION COPY

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

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

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Washington, D.C.
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This study was supported by the National Institutes of Health through Contract Number N-01-OD-4-2139 Task Order #207. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the organizations or agencies that provided support for the project. The content of this publication does not necessarily reflect the views or policies of the National Institutes of Health, nor does mention of trade names, commercial products, or organizations imply endorsement by the US government.

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[Library of Congress Cataloging-in-Publication Data]

International Standard Book Number
International Standard Book Number

Additional copies of this report are available from The National Academies Press, 500 Fifth Street, NW, Lockbox 285, Washington, DC 20001; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu

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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* 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 passage of the original Animal Welfare Act in 1966, with several subsequent revisions. The enforcement arm of the Act, the United States 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 US 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:

Margaret Snyder, NIH sponsor and contact person
Jerry DePoyster, USDA/APHIS

W. Ron DeHaven, American Veterinary Medical Association (AVMA)
Cathy Liss, Animal Welfare Institute
Bill Yates, University of Pittsburgh
David Kass, Johns Hopkins University
Stacey Pritt, Covance
Kimberley Cohen, Covance

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

* 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.

CONTENTS

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 Plant and 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 Class B dealers as a source of such animals for NIH-funded 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. 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.

[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.

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 Pet Distributors, Exhibitor/Animal Distributors, and Laboratory Animal Distributors. 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 Class B dealers are necessary to provide them. 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

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

research colonies, and owner-donated animals. The Committee therefore determined Class B dealers are not necessary as providers of random source animals for NIH-related research. Regardless of the source however, if NIH deems animals with random source qualities to be important, pro-active 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 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 entire 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, most 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 addresses 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 non-human 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 straight-forward, 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
RSBD	Random Source B Dealer
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

CHAPTER 1: INTRODUCTION

Congressional Mandate for This Study

In response to public concerns that pet animals were being obtained from owners under fraudulent circumstances Senator Daniel Akaka (D-HI), and Representatives Mike Doyle (D-PA) and Phil English (R-PA) 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." This bill was intended to ensure that dogs and cats used in research and education are not pet animals brokered through random source Class B dealers, and would also establish monetary penalties for violations. However, under this bill, purpose-bred and random source dogs and cats, young and old, genetically uniform and genetically diverse would still be available to research facilities from a variety of sources, such as Class A dealers, shelters, pounds, research facilities with breeding programs, and individuals.

The House and Senate versions have received no action since 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. 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 study language (Box 1-1) was substituted. The Senate Fiscal Year 2008 Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriation Bill (S. 1710) report requested a study on this issue.

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." (Referenced in the Consolidated Appropriations Act, 2008, P.L. 110-161, signed 12/26/2007).

Timeline for This NRC Study

As a result of the Fiscal Year (FY) 2008 House Appropriations Committee Report 110-231 and FY 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 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 compile a report that addresses the statement of task found below. 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* (Appendix A for biographies).

Statement of Task

At the request of the National Institutes of Health (NIH), the National Academies, through ILAR, were charged with the following title and specific statement of task:

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.

Committee Approach to Its Charge

To address the Statement of Task, the Committee assessed the use of dogs and cats in research based on USDA reporting data. Then, using information from the NIH, the USDA, and the published scientific literature, the Committee attempted to relate the areas of research and the use of Class B animals. With this information in hand, 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 superimposed the information upon the changes in American culture, laws, regulations, practices, and science related to the care and use of laboratory animals. The Committee was further challenged in understanding 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 specifically identify research projects that employed Class B animals, since NIH does not maintain records that categorize specific sources or numbers of animals, does not maintain records of grants that utilize Class B animals, and individual grants or publications do not identify sources of animals. Nevertheless, the Committee used 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 some degree assess “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 which represent a resource of significant morphological and physiological diversity. This diversity has been utilized in the development of animal models for the study of both human and animal diseases. In total, dogs and cats represent only 8.7 percent[3] of the animals used in research that are covered by the AWA (non-covered

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

species include mice, rats, and birds – see definition of "Animals" below). Table 1-1 summarizes the numbers of each species covered by the AWA that were used in research. 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).

Table 1-1: Numbers of animals used in research, by type and year. 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)

	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	69,990
Hamsters	167,231	180,000	177,991	175,721	176,988	167,571	207,257
Rabbits	267,351	243,838	236,250	261,573	245,786	239,720	172,498
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	242,251	180,488	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

It is important to point out that there are over a thousand Class B dealers registered with the USDA, but there are currently only 11 Class B dealers that sell live random source dogs and cats for research. There are several different categories within USDA Class B Licensed Dealers, such as Pet Distributors, and Exhibitor/Animal Distributors, in addition to Laboratory Animal Distributors. Furthermore, some Class B dealers do not deal with live animals, and some Class B Laboratory Animal Distributors deal with live animals other than dogs and cats. This report focuses on the small number of USDA Class B Licensed Laboratory Animal Distributors 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); provides an evolutionary 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/Class B animals 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).

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:

- A ***dealer*** (Sec 1.1) Dealer 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.

- A ***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.

- A ***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.

- A ***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.

- ***Animal*** (Sec 1.1) means any live or dead dog, cat, monkey (nonhuman primate mammal), guinea pig, hamster, rabbit, or such other warm-blooded animal, as the Secretary may determine is being used, or is intended for use, for research, testing, experimentation, or exhibition purposes or as a pet; but such term excludes 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 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*** are pet animals that are missing, but not stolen, and the owner would like to reacquire.

- ***Stolen pets*** are animals that have been illegally removed from the owners possession.

- ***Abandoned pets*** are animals that have been subject to abandonment by their owners.

- ***Relinquished pets*** are animals that have been voluntarily released by their owners to shelters and pounds.

- ***Feral animals*** are 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:

- The term ***purpose-bred*** is not defined in the AWR and is used in this report to refer to a dog or cat that was bred and raised specifically for research purposes.

- The term ***non-random source*** was used in the AWR but was deleted as a result of a rule change in 2004. This term 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 (source: response from USDA distributed to the Committee January 2009).

- The term ***buncher*** is not defined in the AWR, but it is defined in the USDA/APHIS Animal Care Resource Inspection Guide as a person who collects dogs, cats, or other regulated animals from random sources and

supplies these animals to laboratory animal dealers [4]. All bunchers are now required to be licensed as Class B dealers.

- The term ***mongrel*** is used to describe a random or non-random source dog of mixed or indeterminate breed.

- **Inspection manuals** are internal USDA documents which provide specific instructions and definitions for USDA inspectors to use during their inspections. Currently, there are 3 different manuals in existence (USDA, 1999, 2001, 2004), one each for dealers, research and exhibitors. These manuals allow for the application of different standards for each of these groups.

- A **contract pound** is 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** is 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:

USDA Class A Licensee: A USDA-licensed dealer that breeds animals (purpose bred, 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). The animals that are bought and sold may include random source, or non-random source animals. Regardless of the source of purchase, once the Class B dealer obtains ownership of an animal, that animal is considered a random source animal. There are several different categories of Class B dealers, including Pet Distributors, Exhibitor/Animal Distributors, Other Distributors, and Laboratory Animal Distributors. Some Class B Laboratory Animal Distributors deal with live animals other than dogs or cats, and some Class B Laboratory Animal Distributors do not deal with live animals.

USDA Class B Laboratory Animal Distributor of Live Random Source and Non-Random Source Dogs and Cats: A specific

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

group of USDA-licensed Laboratory Animal Distributor 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. Internally, the USDA refers to these as **random source B dealers**, or **RSBD**.

The statement of task specifically involves **USDA Class B Laboratory Animal Distributors of Live Random Source and Non-Random Source Dogs and Cats**. This designation is important to define as the specific category of dealers under consideration in this report, since the Committee's deliberations and recommendations do not pertain to other types of Class B dealers or animals. For brevity in this report, terms will hereafter be abbreviated as "**Class B dealer,"** "**Class B dog or cat**," **or "Class B animal."** These abbreviated terms shall include both random source and non-random source dogs and cats.

Welfare Compliance Definitions

An abiding principle in biomedical research is that reproducible and valid scientific data evolve from healthy (Although, see Chapter 3 for discussion on rare exceptions) and well-cared-for laboratory animals. The biomedical research community is very much aware of this concept, and subscribes to a number of laws, regulations, guidelines, and voluntary compliance, summarized below, that not only assure humane principles of animal care, but also good science.

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

- **Replacement.** Use of non-animal systems or less-sentient animal species to partially or fully replace animals.
- **Reduction.** Reduction in the number of animals utilized to the minimum required to obtain scientifically valid data.
- **Refinement.** Use of a method that lessens or eliminates pain and/or distress and therefore enhances animal well-being.

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 such time that they are acquired for research.

US Animal Welfare Act (AWA). The AWA [5] was originally enacted in 1966, with a number of revisions over the ensuing years. The AWA names the US Department of Agriculture (USDA) as the responsible federal agency for the

[5] http://www.aphis.usda.gov/ac/awa.html

implementation and enforcement of the act, through the USDA Animal and Plant Health Inspection Service (APHIS). Under authority of the AWA, a number of animal welfare regulations (AWR) [6] define standards and regulations that pertain to animal care and use programs, including research facility registration, implementation of Institutional Animal Care and Use Committees (IACUC), requirements for Attending Veterinarians and veterinary care, record keeping, reporting, and procurement, handling, care, treatment, and transportation of animals. In addition, APHIS has established Animal Care Policies (AC Policies) that further clarify the intent of the AWA. The AWA applies to all animals as defined by the act which 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. Licensure and compliance of Class B dealers is covered by the AWA through the USDA/APHIS.

Public Health Service Policy on Humane Care and Use of Laboratory Animals: The "*PHS Policy*" was originally drafted in 1973, and subsequently revised in 1979 and 1986 (NIH/OLAW, 2002). It 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 Health Resources and Service Administration, the Indian Health Service, the National Institutes of Health, and the Substance Abuse and Mental Health Services Administration. *PHS Policy,* which since 1985 has the force of law, requires research institutions that receive federal funds to establish and maintain appropriate programs for care and use of animals involved in research, research training, and biologic testing. It requires compliance 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*. In addition, it 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 contain description and justification of animal use, which is part of the proposal review by scientific peers and funding agencies.

[6] http://www.aphis.usda.gove/ac/publications.html

Guide for the Care and Use of Laboratory Animals: The "*Guide*" was first published by the Animal Care Panel in 1963 under the title *Guide for Laboratory Animal Facilities and Care*. The Animal Care Panel was a group of professionals with interest in laboratory animal care. 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 published 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 Department of Agriculture, 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*.

US Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training: The "*US 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. Its stated 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 AWA, AWR, *PHS Policy* and the *Guide*). In turn, compliance with the *US Government Principles* is mandated by both the *PHS Policy* and the *Guide*.

Association for Assessment and Accreditation of Laboratory Animal Care International: "*AAALAC International*" 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. Compliance with AAALAC International standards is awarded for a 3 year term, and is achieved through 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 *US 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 Class A and Class B dogs and cats falls under the AWA only until such time that the animals enter a research institution.

Animal Welfare Act Provisions in Regard to Dogs and Cats

Any person operating or desiring to operate as a dealer must have a valid license, which is kept on file with the USDA. There are three classes of license holder (Sec 2.1), each business entity being referred to as a dealer. In general, Class A dealers breed animals, Class B dealers purchase and resell animals and Class C licensees exhibit 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 1000 Class B Dealers licensed in the US, only 11 operate as random source Class B dealers that purchase dogs and cats for resale (USDA, 2007).

The health status of Class B dogs and cats can be the same quality as purpose-bred animals, or it can be an unknown entity. 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 only in a limited number of research studies, such as non-survival surgical training preparations (Fox et al., 2002).

The annual license renewal fee for a Class B dealer is established by USDA 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 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 (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).

Class A dealers breed and raise animals on their own premises 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 and cats 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. A Class B dealer may obtain live random source dogs and cats only from

(AWR, Sec 2.132 (a)): (1) Another licensed dealer (this includes auction houses, see below); (2) State, county, or city-owned and operated pounds and shelters; (3) Contract pounds or shelters. The animals they buy and sell may be random source or non-random source dogs and cats. Once dogs and cats enter the Class B system, they are collectively referred to as random source animals, regardless of source, or Class B animals.

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, and may not hold animals in any facilities. Auction houses are licensed as Class B dealers, but they are not considered random source Class B dealers. Class B animals may be sold to research institutions or to other licensees. Typically, Class B dogs and cats are of various breed-types and ages, and have variable environmental and microbial backgrounds. They have variable vaccination and medical treatment histories.

There are a number of exemptions to the licensing requirement including: (1) Retail pet stores (unless they sell for research, exhibition or sell wild or exotic animals); (2) Any person who derives no more than $500 gross income from the sale to research, exhibitors, a dealer, or a pet store; (3) Any person who maintains 3 or fewer breeding females; (4) Any person who sells fewer than 25 dogs and/or cats per year; (5) Any person who transports animals for breeding, exhibiting in purebred shows, etc.; (6) Any person who buys, sells or transports animals used only for the purposes of food or fiber; (7) Any person who breeds and raises domestic animals for direct retail sales to another person for the buyer's own use and; (8) Any person who buys animals solely for their own use or enjoyment.

Prior to 2004, these exemptions allowed individuals to traffic in dogs and cats for profit and without obtaining licensure. Individuals, termed bunchers, provided a mechanism for animals that are not bred and raised on an individual's premises to enter the Class B system. Bunchers have been a difficult entity to regulate. In 1987, the AWR were amended 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 that 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* [7] states that "Anyone importing, buying, selling, or trading laboratory animals, either directly to research institutions or through other dealers, **must be licensed**. This

[7] http://www.aphis.usda.gov/ac/awlicreg/awlicreg.html

licensing requirement includes "bunchers," who supply dealers with dogs, cats, and other regulated animals collected from random sources . . ."

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." (source: Animal Care Resource Guide; Random Source Dog & Cat Dealer Inspection Guide) [8]

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. They may be Class A or Class B dealers. Typically, dogs and cats used as blood donors for privately held blood banks come from Class B dealers, but not necessarily from Class B dealers of live random source dogs and cats. The seller of the blood product also requires a Class B license since they deal in parts of animals that have otherwise not been tested.

Research facilities may obtain dogs and cats from Class A or Class B dealers. In addition, they may also obtain dogs and cats directly from pounds or shelters, or persons who have bred and raised the animals on their premises and fall within the exemption requirements (e.g. sell fewer than 25 per year to research, fewer than 3 breeding females, less than $500 annual income) (Letter from Chester Gipson, USDA/AHPIS to the Committee, January 2009). An institution that sells or exchanges dogs or cats that it no longer needs, may be acting as a Class B dealer and needs to be licensed as a dealer. 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.

Holding periods: Holding periods for Class B dealers were established to ensure that lost or potentially stolen dogs and cats had the proper time to become reunited with their owners. Holding periods range from 24 hours to 10 days, depending upon the source of the animal (pound versus private individual versus other USDA licensee) and the age of the animal (Animal Care Resource Guide, Dealer Inspection Guide). If the dog or cat came from another USDA licensed individual, or a private individual who bred and raised the dog/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 the dog/cat is greater than or equal to 120 days of age, it must be held for 5 days. If it came from a private or contract pound, it must be held by the B dealer for 10 days. AWR sec 2.133 states that the sources that Class B dealers may obtain random source dogs and cats from Sec 2.132 (a) (1) – (3) (another licensed dealer, pound or shelter), must hold and care for the dog or cat for a period of not less than 5 full days. This holding period must include at least one Saturday. AWR section 2.132 (e) (3) states that

[8] http://www.aphis.usda.gov/animal_welfare/downloads/manuals/dealer/randomsource.pdf

any Class B dealer who obtains a random source dog or cat from a private or contract pound or shelter, shall hold the dog or cat for a period of at least 10 full days.

Certification requirements: AWR Sec. 2.133 (b) (1) through (6): Upon selling a random source dog or cat to any person or institution, the Class B dealer must provide the recipient of the dog or cat with certification that contains the following information: (1) name, address, USDA license number and signature of the Class B dealer and (2) the name, address, USDA license or registration number, if such number exists, and the signature of the recipient; (3) 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; (4) 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 the person, pound, or shelter was notified that the dog or cat might be used for research; (5) the date the dealer acquired the dog or cat; (6) if acquired from a pound or shelter, a signed assurance that they 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 available sources that B dealers may obtain animals from, there remains a public perception of unlawful theft of pets or lost pets or those fraudulently obtained as a source of animals to Class B dealers. 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 from Chester Gibson to Committee, October 2008).

Although the AWA, and USDA AWR and Policies have equal provisions that cover both Class A and Class B dealers the USDA inspects Class B dealers with more scrutiny and more frequency than other dealers at considerable cost (internal USDA Standard Operating Procedure [SOP] for Conducting Tracebacks from Random Source B Dealers; implemented in October, 2008). Whereas the AWR mandate annual inspections for research facilities and Class A dealers, Class B dealers currently undergo quarterly inspections. 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. The number of tracebacks conducted will depend upon how many dogs or cats were acquired since the previous inspection. However, 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, i.e. once a year each dealer will have 100 percent of its acquisitions since the previous quarterly inspection traced back. However, due to the turnover of the population,

not all animals that pass through a dealer's facility will have a traceback performed. The traceback process is designed to determine where an animal came from and who sold it to ensure regulatory compliance.

During the traceback, an attempt is made to trace the animal back to the person who originally sold it. Inspectors are encouraged to visit the seller's place of business when practical. Telephone tracebacks may occur but only under specific circumstances: such as if the seller is a licensed dealer, a pound, or a person or broker recognizable to the inspector. A mechanism exists whereby sellers identified outside a particular area will be inspected by other USDA inspectors and the results provided to the appropriate inspector. If the last seller is determined to be another Class B dealer, a second traceback is performed for the previous seller. Once contact with a seller is made, the individual is questioned by the inspector to ensure that the person listed on the records did actually sell the dog or cat and that the person bred and raised the animal themselves. If the seller did not breed or raise the dog or cat, they are questioned about the source of the animal. During the early 1990's tracebacks were 40-50 percent successful at correctly identifying the seller. In 2000-2001, this estimate was 95 percent (personal communication, Ron DeHaven, formerly of the USDA, October 2008). The traceback for dogs and cats acquired from an auction ends at the auction house. They are not traced back to the person who sold the animal(s).

During an inspection of a Class B dealer, the inspector will determine that the acquisition and disposition records meet all of the requirements contained under section 2.75(a) of the AWR. The required records shall include: (1) The name and address of the person from whom a dog or cat was purchased; (2) The USDA license or registration number of the person if s/he is not USDA licensed; (3) The vehicle license number and state, and the driver's license number and state of the person, if s/he is not licensed; (4) The name and address of the person to whom a dog or cat was sold or given and that person's USDA license; (5) The date the dog or cat was acquired or disposed of; (6) The USDA tag number or tattoo assigned to the dog or cat; (7) A description of each dog or cat; (8) The method of transportation, including the name 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 may not meet the exemption requirements listed under section 2.1 the name and address of this person is forwarded to the USDA Regional Office for further investigation. The inspection process also includes an evaluation of the animals, husbandry conditions, and medical records.

The Animal Care Policies have also been used since the early-1990s to make Class B dealers more accountable under the regulations and there has been a crackdown on unlicensed dealers. Animal Care Policy #1: *Denial of AWA License Applications* strengthens the existing regulations that entitle APHIS to deny license if an awardee does not comply with the regulations and standards as specified in Section 2.11(a)(3) of the Regulations. The regulations define

those business entities or relations that may be impacted by using broad terms so as to have wide impact. The policy further states that licensure can be denied where "Applicant has been fined or sentenced to jail under state or local animal cruelty laws as specified in Section 2.11(a)(4)." Or that "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. Animal Care Policy #8: *Guidelines for the Confiscation of Animals* provides guidance to APHIS officers to confiscate regulated animals if they are suffering. This policy spells out who defines suffering and how suffering is defined. It establishes the authority to require proper care and relief "as soon as possible, but typically not to exceed 24 hours." If confiscation occurs, APHIS has the power to immediately suspend the license of the agent.

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CHAPTER 2: USE OF DOGS AND CATS IN RESEARCH

Public Perception and Evolution of Laws and Guidelines

Dogs and cats occupy a very large and valued niche in American society in their roles as companion, work and hobby animals. In addition, they have served as important animal models for research, which has advanced both human and animal health. This complex relationship with humans has fostered an uneasy tension between general society and the scientific community, which has intensified as the stature of pet dogs and cats has risen in many households to that of equal members of the family. The public is generally concerned about research animal welfare, but concern for the welfare of dogs and cats, because of their iconic stature, has been particularly instrumental in the evolution of laws, guidelines and policies that affect research with all types of animals. The specter of lost or stolen pets being used for research has been a particularly galvanizing concern, which has evolved into increasing resistance to using any former pet for research. Assessment of the desirability and necessity of using random source dogs and cats for research, and in particular random source dogs and cats from Class B dealers, cannot be accurately assessed without consideration of public perceptions, the impact of the animal protection movement on public attitudes and availability of these animals for research, changing trends in the use of these models for research, and responses of the scientific community to these issues. The progressive evolution of laws, policies, and guidelines regarding the use of dogs and cats in research has been an accurate barometer of these changing trends. These issues are reviewed in order to define the context for subsequent chapters of this report that focus on random source animals and Class B animals.

Public Perceptions on the Use of Dogs and Cats in Research

The public's perception of their pets and animals in general, has been one of the main driving forces behind the legislation creating and refining the AWA. It is estimated that nearly half of all households have at least 1 dog or cat, with a total population of 72 million dogs and nearly 82 million cats (American Veterinary Medical Association, 2007). In a survey conducted by the American Animal Hospital Association (2004), approximately 95 percent of owners imbued human-like personality traits in their pets, and stated that they would risk their lives for their pet. In urban disasters, human behavior poses significant risk to owners due to failure to evacuate or attempts at re-entry to save a pet (Heath et al., 1998) (Also see Box 2-1). The pet products industry contributes over $50

billion to the U.S. economy, with exponential growth of pet superstores, play parks, day care centers, and training centers. Pet owners spend over $11 billion per year on veterinary care (American Pet Products Association 2008 survey[9]).

When assessing the pet ownership and the state of affairs of dogs and cats in the U.S., one must also consider the plight of homeless animals. It is impossible to provide a current, accurate estimate of the numbers of animals entering shelters or being euthanized because there is no reliable public list of shelters and no federal requirement to gather or release accurate data. In fact, shelters may obscure or refuse to release data to avoid negative publicity. It must also be stated that, although "shelter" is defined for purposes of this report as "facilities owned and operated by a state, county, or city, or as privately owned pound/shelters, such as a humane society, that is under contract with a state, county, or city", estimates and shelter data provided here may include statistics from other facilities commonly referred to as shelters. According to Clifton (Clifton 2002), the estimated number of animals euthanized in shelters was 4.5 and 4.6 million respectively for 1999 and 2000. More recently Scarlett (2004) states

> "…the inflow of animals into shelters varies considerably by area of the country and even by shelters within an area. Several sources have suggested that 6-12 percent of the dog population entered shelters in the 1990s and that approximately 50-55 percent were euthanatized (representing 4% of the dog population) (Patronek and Glickman 1994; Wenstrup and Dowdichuk 1999), and that 5-8 percent of the estimated owned population of cats entered shelters and that 65-80 percent of those entering were euthanatized (Arkow 1994; Wenstrup and Dowdichuk 1999). These figures represent 4-6 percent of the owned cat population (Arkow 1994)"

Although those percentages are likely to have changed since the 1990's, one might be able to make a rough estimate of the shelter intake numbers for any given year by taking AVMA demographic numbers regarding owned dogs and cats and multiplying them by the percentages given 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). That would indicate 4.3 to 8.6 million dogs and 4.1 to 6.5 million cats may have entered shelters, and that up to approximately 7 million animals may have been euthanized.

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

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 may be either animal protectionist groups or scientific organizations), in particular, may be biased in how questions are worded, in the selection of the group to be polled, the numbers of respondents, the types of questions and the conditions under which they are answered, and in how the data are eventually analyzed (Crespi, 1989; Herzog et al. 2001). In addition, the decision to release the results of a poll or survey by special interest groups may be influenced by whether the results support their position on a given issue (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, etc)—especially when they formulate the questions—should be regarded as being more objective (Crespi, 1989).

Based on the limited survey evidence currently available, it appears that a majority of the American public is generally supportive of the use of animals in biomedical research, but that the proportion of people supporting this issue has declined significantly over the last several decades from around 85 percent in 1950 to around 50-60 percent in the late1990s and early 2000s (Herzog et al., 2001; Rowan & Loew, 2001; Moore, 2003). The reasons for this decline are unknown, although they appear to mirror parallel changes in public attitudes to a wide variety of animal-related issues over the same period (Herzog et al., 2001). The Foundation for Biomedical Research (FBR) commissioned Zogby International to conduct a nationwide telephone survey in 2008. That survey revealed that while a majority of those polled still supported the use of animals for medical and scientific research, they were much less supportive than those polled in 2004 (FBR, personal communication). Other survey findings also suggest that public support for animal research is influenced by the perceived importance of the medical problem being researched, and the type of animal that is used. The use of animals 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 serve to illustrate the higher value that the American public tends to place on dogs, cats, and other companion animals (Kellert, 1989).

Animal Protection Movement

As discussed in the following section on history of U.S. Laws and Guidelines, the animal protection movement has had a profound impact upon public attitudes toward the use of animals in research, and the evolution of public law, policies, and voluntary compliance by the scientific community. Jasper and Nelkin defined three types of animal protectionists, including 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" (Jasper and Nelkin, 1992). Clearly, it is impossible to classify every individual into each of these categories.

Since the early beginnings 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 non-human primate. The U.S. animal protection community is large and varied. In 1994, there were over 400 animal advocacy groups in the U.S., with a membership of greater than 10 million (Blum, 1994). These figures have likely grown substantially since that time. These groups include organizations such as the Animal Welfare Institute (AWI[10]), which is concerned about research animal welfare, and published graphic documentation of animal dealer abuse which was provided to the Committee (AWI, 2007), the Humane Society of the United States (HSUS[11]) which seeks to eliminate animal-based research that is harmful to animals, and People for the Ethical Treatment of Animals (PETA[12]), which seeks to eliminate the exploitive use of animals by humans, including those used for research, food, fiber, and entertainment. At the more extreme end of the spectrum of the animal rights organizations, is the Animal Liberation Front (ALF[13]), which uses acts of intimidation, terrorism and violence to disrupt the scientific enterprise, as well as to free animals from use in sport, textile, research or agriculture. Organizations such as the ALF have become so strident as to result in passage of the *Animal Enterprise Terrorism Act* (S.3880), which was originally introduced by Congressman Thomas Petri of Wisconsin, and signed into law on November 27, 2006. John E. Lewis, Deputy Director, Counterterrorism Division of the FBI, 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] www.awionline.org
[11] www.hsus.org
[12] www.peta.org
[13] www.animalliberationfront.com

Response of the Scientific Community to Animal Protection Activism

Since its beginnings in the 1800s, the scientific community has had a long and contentious relationship with animal protection groups (reviewed in Rudacille, 2000). In the past, the research community could be described as maintaining an imperious attitude toward the public, with over-confidence 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. Part of this trend arose internally within the research community itself, which promulgated voluntary compliance beyond that which is mandated by law. The ILAR *Guide* originated from the efforts of a professional group known as the Animal Care Panel, which appointed a *Committee on Ethical Considerations in the Care of Laboratory Animals* and a *Professional Standards Committee* to evaluate laboratory animal care and use. NIH funded a contract to the Animal Care Panel to "determine and establish a professional standard for laboratory animal care and facilities," resulting in publication of the first edition of the *Guide* in 1963 (reviewed in the *Guide*, NRC, 1996). NIH also led the way in development of the *PHS Policy* that applies to most federally-funded animal research. Other significant events arising from within the biomedical research community have been the creation of AAALAC International, and the American College of Laboratory Animal Medicine (ACLAM[14]), whose mission is to advance the humane care and responsible use of laboratory animals through certification of veterinary specialists, professional development, education and research .

While the scientific community has come to embrace changes leading to 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. Animal protection groups have pushed for greater and greater regulation of animal research. The cost of regulatory compliance in terms of dollars and time is recognized as one of the fastest rising burdens to biomedical research; however, it is not clear that the increased regulatory oversight directly benefits the health and welfare of the animals (Goldman et al., 2000; Decker et al., 2007; Haywood and Greene, 2008). When regulations do not improve animal health and well-being, the regulations and policies become regulatory burden. This problem was noted in an earlier National Academy of Sciences report in which the diminishing availability of random source animals was specifically addressed nearly 20 years ago (NRC, 1988). Attacks and intimidation against scientists by extremist organizations have increased dramatically in recent years (Foundation for Biomedical Research [FBR[15]] Illegal Incidents Report). 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[16]), and Americans for Medical Progress (AMP [17]). These

[14] www.aclam.org
[15] www.fbresearch.org
[16] www.nabr.org
[17] www.amp.org

organizations attempt to educate the public in regards to the importance of animals in research. Although difficult to prove, there is resistance among some members of the scientific community to terminate the use of Class B dealers as a source of research animals, regarding this as another step forward by the animal rights movement to eliminate animal-based research altogether.

Animal Protection Activities Affecting Access to Random Source Dogs and Cats, and on Class B Dealers

With these trends within the biomedical research community, random source dogs and cats and Class B dealers/animals continue to be a highly contentious and publicly visible issue. The consequences of the animal protection movement and public opinion have increasingly closed access to random source dogs and cats from pounds and shelters, have resulted in greater effort by USDA to inspect and enforce the AWA in regards to Class B dealers, and have pressured research institutions to use purpose-bred animals from Class A dealers, to explore alternative sources of animals such as donation programs or direct acquisition, to use alternate non-animal models, and to use less iconic species, such as pigs and small ruminants in lieu of dogs. The downward trends in use of dogs and cats in research are multi-factorial, including reduced research funding, changing NIH program priorities, regulatory burden, and availability of other models. Thus, animal protection activity represents a significant, but certainly not the only, factor that has contributed to these trends.

Trends in the Use of Dogs and Cats 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 2-1 indicate an increase in the use of all dogs and cats in research between 2006 and 2007. The reasons for this latest 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 Class B animals, 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, 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, 34,828 between 1988 and 1997, and 23,737 between 1998 and 2007 (Table 2-1). Similar decreases occurred in the use of guinea pigs, hamsters, and rabbits. Only the use of non-human primates increased from 57,007 to 69,990. It is estimated that rats and mice also increased although numbers are not reported for these species. These numbers indicate a dramatic fall in the use of dogs and cats in research over the last 30 years.

Table 2-1: Total numbers of dogs and cats used in teaching, research, experiments and tests. Animals were counted once, regardless of the number of protocols in which they were used. Animals used in multi-year studies were counted once each year regardless of when they were acquired. Data source USDA in response to Committee request, 2008.

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

History of U.S. Laws and Guidelines Regarding the Use of Dogs and Cats in Research

Many of the influences in societal thinking that eventually led to the Animal Welfare Act of 1966 (Public Law 89-544) may have been catalyzed by animal protection activities that occurred in the United States and prior to that in Britain. In the 1820's, 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. However, it was not until forty years later that policies were developed that related to animal experimentation. Between 1863 and 1876, four important policies or acts were enacted. During this period, the RSPCA adopted a policy against painful animal experiments. Slightly later, the British Association for the Advancement of Science produced guidelines calling for the minimization of suffering and discouraged illegitimate experimentation (Public Law 89-544). Thomas Huxley and Charles Darwin composed a bill, the provisions of which regulated painful experiments and called for the licensing of experimenters. Finally, at the end of this period, the Cruelty to Animals Act required experimenters to obtain yearly licenses and placed restrictions, to some extent, on potentially unnecessary experimental duplication.

Early in the history of the colonies that formed the nucleus of what would be the United States, there were also concerns about the treatment of animals. 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 (for instance see Massachusetts Society for the Prevention of Cruelty to Animals Historical Timeline [18]) 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. However, it was not until 1921 that all states had such laws. The State of New York was also the site for pivotal legislation. In 1867 Henry Bergh, founder of American Society of the Prevention of Cruelty to Animals (ASPCA), was instrumental in persuading New York law makers to prohibit animal baiting and fighting and to require that impounded animals be treated and transported humanely.

The first federal law prohibiting cruelty to animals, known as the "28-hour Law", took effect in 1873. The 28-hour Law regulated the time and conditions of confinement for animals being transported by the meat packing industry. Subsequently, the USDA was tasked with inspection and enforcement roles of this industry as well as for other instances of animal transportation, use and processing.

From the turn of the 19th century and throughout much of the early 20th century there were a few unsuccessful attempts at legislation that would further protect animals. For example, in 1896, the District of Columbia was the focus of a congressional bill designed to regulate the use of animals in medical research. Interestingly, this bill was opposed by both the National Academy of Sciences and the American Medical Association. In the 1940s, the National Society for

[18] http://www.mspca.org/site/PageServer?pagename=aboutus_MSPCA_Angell_Historical_Timeline

Medical Research helped various states formulate “pound release laws”. The State of Minnesota passed one of these in 1949; other states soon followed. Laws of this sort were designed to require states and local municipalities to have their animal shelters relinquish unclaimed cats and dogs to biomedical research institutions for experimentation and teaching. Conflicts immediately arose over the humane treatment of research dogs and cats among animal welfare advocates and those supporting medical research, and these conflicts became more overt in the ensuing years.

During the late 1950s and early 1960s, groups concerned with the humane treatment of animals called for federal regulation of research animal use. These calls were to be 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 his owner, in a newspaper photograph along with several other dogs being unloaded from a dog dealer’s truck (Kreger et al. 1998, p. 19). Pepper was never located but may have been used in a medical experiment and euthanized before it could be recovered, according to the report above. The owners eventually were aided by Joseph Resnick (D-NY) who sponsored H.R. 9743, one of the bills that sought to regulate the use of dogs in medical research. Later that same year, Coles Phinizy of *Sports Illustrated* wrote “The Lost Pets That Stray To Labs”, chronicling the story of Pepper. On February 4, 1966 “Concentration Camps for Dogs” was published in Life Magazine. The text of the article was written by Michel Silva, but it was largely a photographic essay by award-winning photographer Stan Wayland. It documented the conditions of dogs at the White Hall property of Lester Brown as found during an investigation by Frank McMahon, Chief Investigator for HSUS.

Heightened public awareness arising from 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 be the **Laboratory Animal Welfare Act** into signing by President Lyndon B. Johnson on August 24 of that year. It established minimal standards for the care, housing, sale, and transportation of dogs and cats as well as other animals kept by animal dealers and laboratories. Portions of the Act also set standards for identification of dogs and cats by dealers and research facilities in order to prevent acquisition of animals that had been obtained inappropriately. This act also required the licensing of dog and cat dealers. Authority to promulgate regulations was given to the Secretary of Agriculture to oversee appropriate treatment of animals pre-research or “for other purposes.” Moreover, it provided a definition of “animal”, limiting the term to dogs, cats, non-human primates, guinea pigs, hamsters, and rabbits (so-called “covered species”).

The Animal Welfare Act (AWA) of 1970 (Public Law 91-579) was essentially a revision of the Laboratory Animal Welfare Act of 1966. In the AWA, all species of warm-blooded ‘laboratory animals’ (covered species) came under the purview of the Secretary of Agriculture. However, the AWA excluded 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

addition, all animal dealers were required to be licensed. Humane treatment of animals in research was broadened to all phases of experimentation. Notably, the sale of pet animals other than in stores, and those animals used in exhibitions were also included under the AWA.

Revisions to the AWA in 1972 excluded mice, rats and birds as well as some farm animals from regulation by the Secretary of Agriculture. As a finer point, these species had not been regulated because they were not defined previously as "animals". With the 1972 revisions, they were specifically excluded for regulatory purposes. In 1976 amendments to the AWA categorized research institutions and exhibitors and dealers similarly when evaluating fines that could be levied for violations. With these amendments, government research facilities begin to be held to the same standards that were expected of private institutions.

In commenting on the Food Security Act of 1985 Subtitle F, Animal Welfare, Public Law 99-198 (also known as the Improved Standards for Laboratory Animals Act), Senator Robert Dole stated "…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 and keeping painful experiments to a minimum." (Congressional Record (1985), December 17, U.S. Government Printing Office, Washington, D.C.).

The Food Security Act of 1985 defines Humane Care to include specific criteria such as sanitation, ventilation, and housing. It directs the Secretary of Agriculture to establish regulations, enforced by the USDA, covering exercise for dogs and the physical environment adequate to promote the psychological well being of non-human primates. The Food Security Act notably establishes requirements for an Institutional Animal Care and Use Committee (IACUC). Details of requirements in their current form are found in the Animal Welfare Act Regulations (9 CFR Part 1, Subpart C, 2.31). The regulations 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. They also require that the principal investigator must consider alternatives to any procedure likely to cause pain or distress.

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, Food and Drug Administration, National Institutes of Health, and Office of International Health), Department of Agriculture, Department of State, Department of the Interior, the Environmental Protection Agency, the National Aeronautics and Space Administration, the National Science Foundation, and the Veterans Administration, formulated and published the "*U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training."* 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 vertebrate animals.

The same year, the Health Research Extension Act of 1985, Public Law 99-158, "Animals In Research" (November 20, 1985) was passed into law. This law provides the statutory mandate for the Public Health Service (PHS) to establish an over-arching Policy on Humane Care and Use of Laboratory Animals (*PHS Policy*), which includes the "*U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*." The *Principles* were incorporated into *PHS Policy* in 1986 and continue to provide a framework for conducting research in accordance with *PHS Policy*. *PHS Policy* requires institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities conducted or supported by the PHS. The *Policy* is applicable to all PHS-conducted or supported activities involving animals, whether the activities are performed at a PHS agency, an awardee institution, or any other institution. The PHS agencies include Centers for Disease Control and Prevention, the Food and Drug Administration, and the National Institutes of Health. The NIH Office of Laboratory Animal Welfare (OLAW) has responsibility for the general administration and coordination of *PHS Policy*. Although the USDA enforced AWA excludes rats, mice, and birds, *PHS Policy* includes all vertebrate animals used in PHS supported research, training or testing.

Years before the 1966 enactment of the original AWA and the 1985 Research Animals Congressional Mandate, the biomedical research community was engaged in organized efforts to improve and assure the humane care and use of animals in research. Most notable among these organizations are the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) founded in 1965 as the American Association for Accreditation of Laboratory Animal Care (AAALAC) and the National Research Council's Institute for Laboratory Animal Research (ILAR; formerly the Institute for Laboratory Animal Resources). Since 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 these ILAR guideline reports is "*The Guide for the Care and Use of Laboratory Animals*". The first edition of the "*Guide*" was published in 1963, three years before the "Laboratory Animal Welfare Act" became law (See Chapter 1). The *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training* refers to the "*Guide*" for guidance through these principles. *PHS Policy* also requires that institutions eligible for receiving PHS funding use the "*Guide*" "as a basis for developing and implementation of an institutional program for activities involving animals." Since 1965, AAALAC International has used compliance with the "Guide" as the standard for institutions voluntarily seeking accreditation. In 2008, 770 institutions reported having chosen to voluntarily maintain AAALAC International accreditation.

The AWA was amended by the Food, Agriculture, Conservation, and Trade Act in 1990 to improve the humane handling, care, treatment and transportation of dogs and cats. This was in response to public attitudes (as

determined through public comments) and APHIS' experience in administering and enforcing the regulations (Animal Welfare; Standards, Proposed Rule. Federal Register Vol. 55, No. 158 [15 August 1990], 33448-33531) (Food, Agriculture, Conservation, and Trade Act of 1990. [Public Law 101-624], United States Statutes at Large. Section 2503 - Protection of Pets. Approved 28 November 1990 [19]). Specifically, regulations were strengthened to prohibit the use of stolen pets in research and to provide owners the opportunity to locate their animals (Random Source Dogs and Cats, Final Rule. Federal Register Vol. 58, No.139 22 July 1993 [20]). These amendments established a minimum 5-day (including one weekend day) holding period for 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 Department of Agriculture before being sold to a [Class B] dealer. They also require [Class B] dealers to provide written certification regarding each animal's background to the recipient. (For additional details about the Pet Theft Act of 1988, Pet Protection Act of 1990, and public perception about pet theft, see Kreger et al., 1998, pp. 32-34)

The Farm Bill of 2002 contained an amendment by Jesse Helms (R-NC) designed to redefine "animal" in the law to match the 1972 change by the Secretary of Agriculture 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 June 4, 2004, with publication by USDA of the "Final Rule" in the Federal Register to include the language contained in the 2002 Farm Bill excluding mice, rats and birds from regulation by USDA under the AWA.

On February 28, 2007, during the first session of the 110th Congress, 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 act, called the Pet Safety and Protection Act of 2007, was intended to modify Section 7 of the AWA (7 USC 2137). The bill entitled S. 714 was one in a series of related proposed legislative efforts designed to ensure that dogs and cats used in research have been obtained by appropriate means. A list of other related proposed legislation may be found in Table 2-2. This bill never became law, although it received two readings and was referred to the Senate Committee on Agriculture, Nutrition, and Forestry.

[19] http://www.nal.usda.gov/awic/legislat/pl101624.htm
[20] http://www.nal.usda.gov/awic/legislat/cat1.htm

Table 2-2: Pet Safety and Protection Act (and related legislation) during the last ten years [21] to amend permissible sources for obtaining dogs and cats for research.

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

*"Sessions of Congress last two years, and at the end of each session all proposed bills and resolutions that haven't passed are cleared from the books. Members often reintroduce bills that did not come up for debate under a new number in the next session." [22].

The year 2007 also re-focused the public's attention on the potential for pet theft with an incident involving the discovery, by a research institution's veterinarian, of a micro-chipped dog among a group of animals received from a Class B dealer (Fayetteville Free Weekly, 2005). A brindle Labrador-mix dog named "Echo" originally received the identifying micro-chip prior to being adopted from the Fayetteville Animal Shelter. It appears that Echo made his way to the University of Minnesota via a USDA-licensed Class B dealer from Michigan, who in turn reported buying Echo from another Class B dealer in Missouri.

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.

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[21] http://www.govtrack.us/congress
[22] http://www.govtrack.us/congress/bill.xpd?bill=s110-714

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CHAPTER 3: USE OF RANDOM SOURCE DOGS AND CATS FOR RESEARCH

The statement of task given to this Committee by NIH was rather specific to Class B animals, but the report encompasses random source dogs and cats, per the intent of Congress, as previously 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 Class B dogs are clearly identified as random source animals from pounds and shelters. Therefore, the majority of Class B dogs are non-random source, and thus 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 interest, 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 chapter of the report.

Dogs and cats, regardless of source, have been used in American biomedical research for over a century. Random source dogs and cats have contributed toward advancing both human and animal health. The American public is divided in its opinions regarding the use of random source dogs and cats from shelters and pounds in research. Public attitudes are difficult to measure accurately, since opinion polls are often biased to serve the needs or perspective of the polling agency. For example, in a 1990's public opinion poll conducted by the Survey Research Center, Institute for Social Research, University of Michigan, 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 the passing of a law that would prevent unclaimed pound animals from being used in medical research for the public benefit (Michigan Society for Medical Research [MISMR]).[23] 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 of this report), viewing shelters as havens for homeless animals and not a resource for biomedical research (American Humane Shoptalk, 1988). This perspective has

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

been reflected by some academic institutions, exemplified by the Colorado State University College of Veterinary Medicine and Biological Sciences (CVMBS) policy on animal use which also reflects the public's concern about the use of pound animals in research and the quality of care the animals receive. It states: "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, 2006a) In another closely related statement on the subject, the CVMBS policy goes on to state: "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, 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 (88 percent of pet owners view their pets as family members according to a 2007 Harris poll), but also by increased spending on veterinary care, food, toys, clothing, day care, and the PETS Act passed by Congress in 2006 (The Harris Poll, 2007). Following the Hurricane Katrina disaster in which scores of people either refused to evacuate and/or returned home early out of concern for their pet, the PETS Act mandated that disaster plans now include provisions for companion animals (The White House, 2006). The public has become increasingly vocal in support of improved care for pound animals and opposition to euthanasia of adoptable shelter animals as seen by the increased number of "No Kill" pounds and shelters and increased veterinary professional 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, through 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."[24] The American Physiological Society (APS) supports the continued use of random source animals, recognizing these animals have attributes that are important in the fields of study relevant to its members. "The American Physiological Society recognizes the importance of research that

[24] http://www.avma.org

depends upon animals of large size, advanced age, and diverse genetic background. These are known as "random source animals…"[25]

The "3-Rs" Principle.

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. The universal principle used among the biomedical research community is to follow the **"3-Rs"** doctrine of Russell and Burch (1959; see also NRC, 2003) that promotes **reduction**, **refinement** and **replacement** of research animals whenever scientifically feasible. 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 utilize unwanted pound and shelter animals for research runs counter to the "reduction" component of the 3-Rs 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 being used. Thus, even this issue is not straight-forward.

Desirability of Random Source Dogs and Cats for Research

According to the AWA, *PHS Policy*, and the *Guide*, justification for the use of a particular species is required prior to approval of a scientific protocol, but justification of the source of such animals is not required. Maintaining records of the source of various research animal species is not a part of any regulatory requirement and, as such, documentation and justification for the use of dogs and cats from random sources (such as Class B dealers, pounds, and shelters) is not available. The Committee was therefore left to identify 'common research topics' where random source dogs and cats are 'desirable' and 'where the potential exists' for the use of these animals. 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. When animal models are less than optimal, the quality of knowledge is lessened and the chance for adverse drug and device events increases. As a result, the search for the best animal model is essential in understanding and developing treatments for disease.

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, David Kass, to Committee, October 2008) indicated that random source animals

[25] http://www.the-aps.org

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 in no sense 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, when properly socialized, purpose-bred animals can be as tractable as former pets. Therefore, generalizations regarding tractability cannot be made, and depend upon individual animals, their socialization, and history.

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. It is incumbent for readers of this report to understand that this Committee was tasked with identifying ‘common research topics’ where 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 purpose-bred animals nor was it tasked to identify attributes that were ONLY unique to random source or Class B dogs and cats. In addition, given the lack of information in proposals or publications justifying the source of the animal or uniqueness of a particular breed or even individual animal, the ‘necessity’ of the use of these animals is nearly impossible to determine. However, the Committee was able to determine ‘common research topics’ where these animals were desirable and/or where the potential exists to utilize these animals in contemporary NIH-funded research. The following areas were identified as fields where the potential exists to utilize random source animals and describes the particular characteristics that would make these animals well suited for this research. It is important to emphasize that these characteristics may not be unique to random source animals and in many cases other sources, including Class A animals, may also hold these same particular characteristics.

Random Source Dogs – Anatomic and Physiologic Attributes

Scientific investigation may require the utilization of older, larger, or genetically diverse dogs, or dogs with naturally occurring disease, 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, healthy dogs, including beagles, “mini-mongrels” and hounds weighing between 23-27 kg (50-60 pounds) with defined genetic background and disease-free status suitable for many biomedical research endeavors. A common argument for the use of random source dogs is the need for larger, 27-37 kg (60-80 pounds), and older animals that are physically and physiologically similar to humans (Parsons, 1996; Sasajima, 1999). Demand for these larger and older animals is usually not great

and maintaining even small numbers of these 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 utilized in the study of cardiac diseases, as well as procedures and devices to alleviate these diseases because of their large 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 to be utilized.

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). Differences in coronary artery anatomy and cardiac physiology have been identified between random source dogs and purpose-bred dogs. This 'conditioning' can affect the physiological status of the animal. 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., 2001; personal communication, Bill Yates, to Committee, October 2008). Furthermore, the incidence of idiopathic extramural coronary arteritis occurred less often in purpose-bred animals compared to random source animals (Hartman, 1989). The coronary sinus, or venous drainage of the heart in the dog, is also similar to human anatomy allowing for investigation of chronic resynchronization therapy and development of devices and procedures to ameliorate severe congestive heart failure (Williams et al., 1994; Reising et al., 1999). Physiologically, the cardiac electrical conduction system in the dog mimics humans, and dogs are used for studies investigating 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) within the heart chambers similar to those observed in end-stage human heart failure (Fuller, 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 while random source dogs did develop the characteristics of this arrhythmia (Antzelevitch, 2008).

Pulmonary

Scientists investigating diseases in pulmonary medicine and utilizing thoracic surgical procedures seek to use deep, barrel-chested, large breed dogs.

Pulmonary function studies utilize 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, 1999) and acute lung injury (Kaczka, 2005). 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 in prosthetic device development for hip and knee replacements, development of fixation devices and techniques, vertebral fusion models, tendon and ligament repair and assessment of biomaterials for orthopedic procedures (Arnoczky, 1982; Greis, 2001). In some circumstances, the larger animal's size accommodates human prosthetic devices and 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 such as hip and knee replacement, arthroscopic ligament repair, menisectomy 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 (Smith et al., 1998; An and Friedman, 1999; Hunter et al., 2004). Cervical disc degeneration occurs 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 utilize older, skeletally mature animals to reflect an adult human population rather than younger (less than one year) 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 yr 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 (Hasegawak, 1994; Katsuura, 1994; Nguyen-minh, 1997).

Age-related disease

Rodent and primate studies indicate that older animals are physiologically different than younger animals (Ferrari et al., 2003). Advanced age is an attribute that is commonly found in random source animals, which 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 making it attractive for studying 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 (Dun et al., 2003; Taylor et al., 2004; Anyukhovsky et al., 2005; Studzinski et al., 2006; Goralska et al., 2007; Goralska et al., 2009).

Advanced age itself may be a factor independent of disease conditions that 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 used: For example, the recent case in which a COX-2 inhibitor that was intended to treat older, arthritic animals, was developed and toxicologically tested using only young beagle dogs. Once on the market, it was discovered that older dogs metabolized the drug very differently leading to severe side affects including gastric ulcers, liver and kidney damage and death[26] [27]

Acquisition of aged dogs poses a logistical and financial challenge that can be addressed with random source animals. One purpose-bred vendor testified that they could provide older animals (retired breeders) on a limited basis but currently this resource is unavailable in substantial numbers. Purpose-bred animals generally are sold as young as possible (usually 6-9 months) to minimize the expense of housing the animals (personal communication with Class A vendors). The average duration of NIH grants usually prohibits an investigator from requesting animals years before they are required, since the availability of funds beyond a single grant cycle is unclear. Vendors of purpose-bred animals would be unlikely to sustain the costs of maintaining the animals for a long period of time unless they knew a customer base was available to purchase them once they reach a certain age. 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).

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

[26] http://www.the-aps.org/pa/policy/animals/ pethealth.htm
[27] http://www.fda.gov/ohrms/DOCKETS/dockets/04n0559/04N-0559_emc-000003-01.pdf

Genetic diversity

The genetic diversity that is represented among the many breeds in the general dog population cannot be reproduced in purpose-bred colonies. Furthermore, in order to maintain maximal genetic diversity within a single colony of dogs, it would require more than 200 breeding pairs to maintain the diversity (personal communication, Stephen O'Brien, to Committee, January 2009). Genetic diversity may be an attribute necessary for some aspects of current and future biomedical research. Nobel laureate, Dr. E. Donnall Thomas, awarded for his work in bone marrow transplantation, stated that "marrow grafting could not have reached a clinical application" (Thomas, 1990) without the use of outbred dogs. Non purpose-bred dogs have been critical in the development of hematopoeitic cell transplantation or bone marrow transplantation because of their random-bred nature, large body size, long life span, wide genetic diversity and, other than humans, are the only mammals to possess these qualities (Ostrander and Wayne, 2005). Genetically diverse animals have also been instrumental in studies in 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

Naturally occurring infectious diseases are found in random source dogs that are exposed to outdoor environments and various vectors that may be carrying disease. Vector-borne diseases such as heartworm (*Dirofilaria immitus*), Lyme disease (*Borrelia burgdorferi*), Rocky Mountain Spotted-Fever (*Rickettsia rickettsii*), Babesiosis (*Babesia microti*) and 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, 2008). Random source animals may also have Sarcoptic mange (*Sarcoptes scabiei*), Demodectic mange (*Demodex canis*) or coccidiosis from natural exposure to parasites. In an effort to maintain a naturally infected condition, random source animals in some cases may not undergo standard conditioning or treatments for these parasitic diseases. These animals have then been available as larger cohorts for studies involving these natural 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 (Guidance 61), states that natural infections are ideal, while induced infections are acceptable for dose determination studies. In addition, Guidance 90 "Guidance for Industry – Effectiveness of Anthelmintics: 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 Anthelmintic Efficacy Guidelines (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 general pet population has been the source of unique animal models that cannot be obtained from vendors of purpose-bred animals. Several spontaneously occurring disease models have been developed. Most often, these colonies have been identified in a particular breed and established using non purpose-bred animals. But some of these same diseases have been identified among a mixed population of pet animals in Germany (Neumann, 2005) and random source animals have been used as controls for studies in comparison to the purebred animals (Smucker, 1990; Basso, 2004). 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).[28] No large animal models, other than these naturally occurring models, exist for these diseases. In some circumstances, breeding colonies have been established by individual investigators desiring to study these diseases. Specific 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 Duschene's 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 that are currently being used for gene-based therapy. The Swedish Briard (RPE65-/-) is the only dog 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, 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, Portugese Water Dogs are maintained at the University of Pennsylvania as a model for dilatative cardiomyopathy (Sleeper, 2009).

These valuable models are examples of how access to random source animals as genetically diverse control animals may be desirable or necessary, or as of yet undetermined animal models that may occur as a result of naturally occurring single nucleotide polymorphisms, epigenetic occurrences, or other genetic alterations (personal communication, Stephen O'Brien, to 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 prior knowledge of their availability from random sources. The process by which novel dog models of

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

human disease can be developed includes a sophisticated process of referral by breeders or veterinarians aware of nuances of their breed, veterinary medical workup, scientific characterization, and validation as an animal model. Such programs are ongoing with NIH support for discovery of novel models in dogs and cats, and are discussed in Chapter 4.

Random Source Cats – Anatomic and Physiologic Attributes

Cats have long been a mainstay of NIH funded studies investigating neurological, cardiovascular, 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 that is derived from studies utilizing cats as models of human disease. As with dogs, the genetic diversity within the general cat population, as well as 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. There are over 200 hereditary human diseases with correlates in cats (O'Brien et al., 2008).

Feline Immunodeficiency Virus

Cats are naturally susceptible to infection by feline immunodeficiency virus (FIV), which induces an immune suppressive disorder that is very similar to human immunodeficiency virus (HIV) infection in humans (Willett and Hosie, 2008). Currently there is a considerable current research effort underway into the mechanisms of FIV infection in cats as a model for HIV infection and the cat represents an important element in efforts to understand HIV and 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, after as much as 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 FIV and induced FIV may be due to infectious co-factors 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. Random source animals that have been naturally-infected with FIV represent a critical resource for understanding FIV, its sequela, and its transmission between hosts.

Feline Interstitial Cystitis

Human interstitial cystitis is a serious bladder disorder characterized by pain, urinary frequency, and nocturnal urination (Roppolo et al., 2005). Interstitial cystitis can occur 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 spontaneously develop feline interstitial cystitis, which is clinically indistinguishable from the human disorder (Westropp and Buffington, 2002). Random source cats are a source of feline interstitial cystitis and there are no other known naturally occurring experimental models of human interstitial cystitis (Westropp and Buffington, 2002).

Feline Infectious Peritonitis

This disorder is almost always fatal and is associated with vascular inflammation in a variety of organs and is caused by an infectious agent in the coronavirus family, feline infectious peritonitis virus (FIPV) (Olsen, 1993; Takano et al., 2008). This virus is thought to mutate from a more commonly found coronavirus, feline enteric coronavirus (FECV) (Vennema et al., 2008). FECV is very common in random source animals, but does not induce life threatening disease (Olsen, 1993). The conditions that are responsible for mutation of FECV to FIPV are not well understood, but may be promoted in immuno-suppressed animals in which viral replication is significantly increased (Haijema et al., 2004). Replication of FECV is also radically increased when previously 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). Antibody-dependent enhancement may be important in human viral diseases, such as Dengue fever and human immunodeficiency virus infection (Olsen, 1993). FIPV infected animals represent important resources in efforts to understand the pathogenesis of significant human viral diseases. Purpose-bred animals can be infected with FIPV and the virus can be cultured in feline kidney cells (Takano et al., 2008). However, random source animals are an important initial resource for FIPV, 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 of animals in biomedical research from species considered by society to be companion animals, poses several unique challenges to Principal Investigators (PI). Institutional Animal Care and Use Committees (IACUC) that must evaluate protocols describing research involving dogs and cats are often challenged as well. 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 for each entity conducting research with, for example, funds provided by NIH. IACUC have been tasked

with institutional oversight of animal care and treatment. Both PI and IACUC at institutions receiving NIH and other federal funds to support research must consider 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 IACUC and the institutional community that these animal models are not only appropriate, but that these models have scientific benefits that outweigh the use of purpose-bred animals. Thus, both PI and IACUC may need to consider strain, breed, and in some cases, source when determining the appropriateness of animal models chosen for particular studies. Certainly, animal models may be defined as exploratory, explanatory, and/or predictive (Hau and Van Hoosier, 2003). However, cost alone has not routinely been a sufficient justification for the choice of an experimental model. Clear guidance related to cost and its inadequacy as the sole factor for determining the appropriateness of survival surgery models is given in the *Guide* (p.12) and in the AWR. Regardless of these considerations, cost is a significant determinant. Limitations of NIH grant budgets tend to favor lower costs of random source animals over the higher costs of purpose-bred animals. Further discussion of relative costs of Class B animals vs. purpose-bred animals is presented in Chapter 4.

This chapter previously summarized public attitudes toward the use of random source animals in research, as well as the anatomic and physiologic attributes that make random source animals desirable and necessary for a few types of NIH-sponsored research. Because these animals have unknown health and care histories the potential health and animal welfare problems associated with their use are discussed below. Not all IACUC may have the collective experience to conduct a thorough risk versus benefit analysis of the ramifications of using random source animals at their institutions. 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 those IACUC members representing the concerns of the institutional community before, during, and after research involving random source animals. As in all research involving animals, ethical and health concerns vary based on the state of the animals when acquired and during their housing on premises. Community concerns will vary based on the type of animal and the source from which it is obtained. 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 prior to the consideration and approval of any animal use protocol involving animals of this type.

IACUC and PI, when considering the use of random source animals may face challenges resulting from Principle VII, which in part states "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 to uphold the high standards of animal care and welfare within their PHS assurance. Thus, from the time that a research animal is received on premises until the end of the research involving that animal, certain standards are met. Conditions of care and housing are subject to oversight by IACUC and veterinarians periodically, and animal care and laboratory staff on perhaps a daily basis. Institutions, IACUC and PI are less likely to oversee similar 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 when compared with 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 prior to obtaining animals from them.

While the team approach has been stressed above, Principle IX reminds PI and IACUC alike of their shared responsibilities in experimental model selection. It states "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 any research done on premises. *PHS* Policy tends to be scrutinized more completely than the AWA because institutions accepting PHS funding are also more likely to be AAALAC accredited and therefore may be subject to more numerous instances of oversight. Thus, if receipt of animals of a given type or from a given source is considered (by the IACUC, the PI, or the institution itself) to be different from best veterinary and animal welfare practices, exceptions to the *US Government Principles*, *PHS Policy*, and perhaps the *Guide*, should be evaluated by all of these groups.

In summary, IACUC, PI, and institutions are faced with several challenges when studies are proposed and conducted that involve the use of random source companion animals, regardless of the nature of the sources from which they are obtained. It is imperative that review committees conduct careful and thorough reviews of the justification for animal use.

Deleterious Infectious Disease Issues

Random source animals may be derived from multiple sources, and mixing of animals from multiple sources may contribute to the spread of infectious disease. For example, 20 percent of dogs and 61 percent of cats used in research are derived from shelters and pounds (USDA data submitted to the Committee, January 2009). The health status of dogs and cats from shelters and pounds is often unknown. Animals in shelters and pounds do experience outbreaks of infectious viral diseases, including canine distemper, canine parvovirus, canine parainfluenza virus, feline panleukopenia, feline calicivirus, and feline herpes virus, among others. 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. Based on discussions with various shelter experts (There is no published literature) the Committee found that many shelters do not have veterinarians on staff or serving as advisors. In Miller and Zawistowski (2004) it is also noted that shelters are not required to isolate, vaccinate, de-worm or otherwise provide routine treatment for illnesses in the animals.

The quality of care provided for shelter animals varies widely across the country. While some animals are very well cared for, dogs and cats in shelters and pounds often have undocumented vaccination histories, may be parasitized with heartworms, fleas, ticks, mites, lice, ringworm, or intestinal parasites. They may be placed into different types of group or communal housing with unreliable sanitation practices that contribute to disease spread. They may be behaviorally abnormal, and infected with a variety of disease agents that spread more readily than would normally be expected because they are mixed with other animals with unknown histories, are stressed, and frequently enter the shelter with compromised health. Research has shown that the longer animals are held in shelters and pounds, the more likely they are to develop respiratory disease (Edinboro, 2004). Even if vaccinated immediately upon entry, animals that are held in shelters for several days are at higher risk for respiratory disease because respiratory vaccines do not prevent 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 including instances of false negatives or positives.

Random source dogs and cats enter research institutions by acquisition of animals from shelters and pounds, from Class B dealers, or other legal sources. Animals are **conditioned** by either the research institution or the Class B dealer (or both). This process generally includes a period of quarantine, treatment for parasites, vaccination, de-worming and other procedures that make the animal more suitable for research. Despite these procedures, random source 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 have a higher degree of assurance of being microbiologically defined.

Zoonotic Disease Hazards among Random Source Animals

Some infectious disease agents that are associated with dogs and cats in the general pet population, and therefore among some random source animals, pose a potential threat to humans. The National Association of State Public Health Veterinarians published "*The Compendium of Veterinary Standard Precautions for Zoonotic Disease Prevention in Veterinary Personnel*" (2008), in which Appendix 1 lists fifty four "zoonotic diseases of importance in the U.S., 2008.". Twenty-six of these zoonoses include the dog and/or cat in "most common species associated with transmission to humans." The NRC report (1994), "Dogs – Laboratory Animal Management" (Table 2.1, p 8) lists twenty seven "Selected Canine Zoonoses Causing Disease in Humans". The litany of zoonoses associated with dogs and/or cats begins with "Acariasis" (mange) and ends with "Yersiniosis" which is described in the NRC (1997) report, "Occupational Health and Safety in the Care and Use of Research Animals" (p 95). The WHO Collaborating Center for New and Emerging Zoonoses lists numerous common to rare zoonotic agents in domestic dogs and cats.[29] Some agents are very common, such as *Pasteurella spp*., which are found in the oral and nasal cavities of 12-92 percent of dogs and 52-99 percent 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 mange; 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. Undetected (subclinical) infections can compromise or confound research studies. A recent example (Scorpio et al., 2008) of silent infections that may complicate research was a study that documented exposure of dogs to three frequently reported tick-borne bacterial pathogens. Molecular analysis and serology were conducted on 21 random-source dogs procured from Class B Dealers. Test results were positive in 17 dogs, but none of them showed any overt signs of clinical disease. The authors concluded that "Exposure to and potential for infection with these

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

bacteria and other pathogens may contribute to blood and tissue alteration that could confound experiments and lead to misinterpretation of data in canine models." Even though heartworms (*Dirofilaria immitus*) are generally considered to be associated with dogs, there may be very high prevalence of infection in cats in endemic areas, reaching 76 percent prevalence in one study of outdoor-housed cats in North Carolina (Atkins et al., 2005). Overt infection makes the animals unsuitable for most research, but it has also been shown that Dirofilaria-seropositive cats that lack adult worms in the heart and lung may have significant pulmonary disease, making them potentially unsuitable for cardiopulmonary studies (Brown et al., 2005).

Animal Welfare Issues

In order to discuss humane issues and animal welfare in the context of this report and the statement of task, it is essential to have a basic understanding of the terms animal welfare, stress, and distress. The term "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 tend to give priority to different aspects of an animal's state when assessing its welfare: Some emphasize unpleasant or pleasant subjective feelings (Dawkins, 1980; Duncan, 1993; Boissy et al., 2007), 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 they all agree on is that there is no single, reliable measure of an animal's welfare (Mason and Mendl, 1993; Appleby, 1999). Most animal welfare experts therefore advocate taking multiple measurements of things that are likely to reflect an animal's welfare—e.g. behavioral responses, physiological indicators, immune function, etc.— while at the same time recognizing that the final determination inevitably involves a degree of subjectivity (Dawkins, 1980; Mason and Mendl, 1993; Fraser, 1995).

A recent report from the NRC (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 various behavioral and physiological efforts to restore homeostasis. Potential stressors may be either physical or emotional, including overcrowding; changes in routine, diet, environment, temperature or humidity; perceived threats to safety; sources of pain or discomfort; malnutrition, illness, physical restraint, and so on. A certain amount of stress is a normal part of any animal's life, and should not in itself be considered detrimental to welfare. Only when the degree of perturbation is sufficiently acute or prolonged that an animal's capacity to restore homeostasis is exceeded should stress be regarded as a significant welfare problem. 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" is generally applied 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 there are no published studies available that address this specific 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, etc.—consistent with the effects of moderate to severe stress. Typically these responses may take from 2-5 weeks to return to 'normal' baseline levels, although some animals may remain in a distressed state for several months (Kessler and Turner, 1997, 1999; Rochlitz et al., 1998; Beerda et al., 1999a, b; Hennesey et al., 2001; McCobb et al., 2005; Väisänen et al., 2005; Stephen and Ledger, 2006; Siracusa et al., 2008). Chronic stress is immunosuppressive and reduces both cell mediated and humoral immunity, leading to an increased susceptibility to infectious disease, vasodepressive syncope, an increased tendency for 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 (McCrave, 1991; Carlstead et al., 1993; Hubrecht et al., 1995; Beerda et al., 1999a, b). Given that some random source dogs and cats are likely to be 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 not only for the welfare of random source animals but also for their overall reliability as research models. Stress and distress are known to significantly alter animals' physiological and behavioral responses to experimental manipulations, and they will therefore also affect the quality of the scientific results that are obtained from such animals (Reinhardt, 2004; NRC, 2008).

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CHAPTER 4: CLASS B DEALERS AND ANIMALS

The previous chapters of this report have emphasized areas that indirectly relate to determination of the desirability and necessity of Class B animals, since use of Class B 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 regarding "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)." The Committee was able to determine that a number of studies with NIH funding utilized random source dogs, based on the fact that 'mongrel' dogs were cited as being used. However, the Committee was unable to determine if such dogs were Class B animals, because mongrel dogs are available from various sources, including purpose-bred mongrel dog dealers. Therefore, the Committee relied upon its own expertise, input from scientific organizations provided to the Committee, testimony of individual investigators and an NIH representative, and the biomedical research literature to obtain evidence of general areas of research and specific examples of research, including physiological, anatomical, and genetic, in which **random source** animals have been utilized and may be desirable. These perspectives are provided in Chapter 3 of this report, but a case was not forthcoming that specifically identified any unique or irreplaceable features that made it necessary to obtain **random source** animals from Class B dealers.

This chapter addresses issues specific to Class B animals, but once again, must do so within context of trends in research, sources of animals for Class B dealers, law, and both public and scientific perspectives.

Trends in the Use of Class B Dogs and Cats in Research

As noted in Chapter 2, there has been a significant decline in the use of dogs and cats in research over the last 30 years. Statistics were not maintained by the USDA that discriminated between Class A and Class B dogs and cats for the last 30 year period; however, data were obtained from the USDA regarding Class B animals 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 2-1). Combined dog and cat usage in research totaled 94,724 animals,

roughly 9.2 percent 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. These numbers of Class B animals represent only 4 percent of the dogs and 1.2 percent of the cats used in research. The combined total of Class B dogs and cats used in research represents only 3 percent of the total dogs and cats used in research and 0.3 percent of all animals reported to the USDA for research purposes.

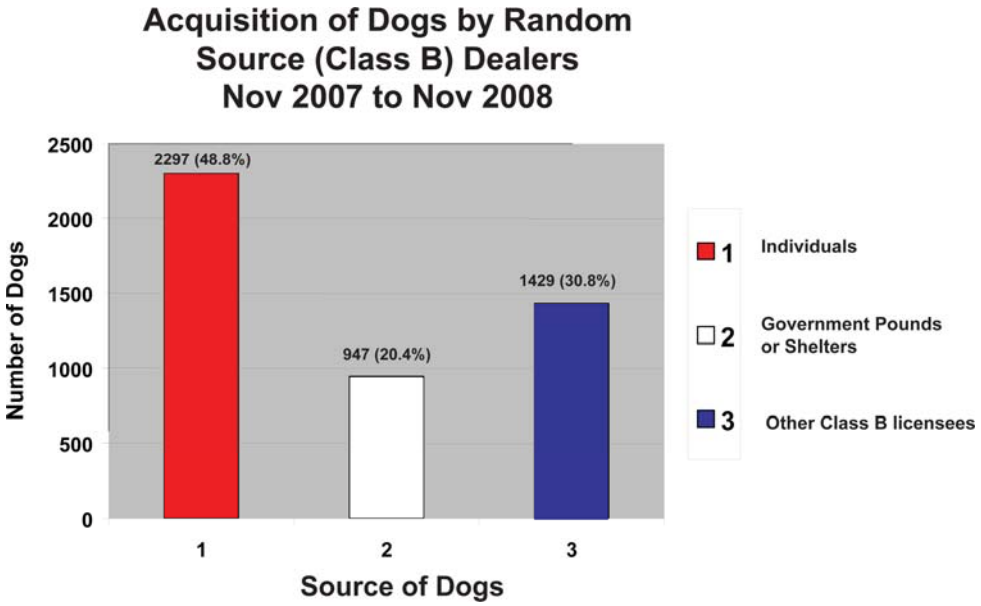

Figure 4-1a: Disposition and acquisition data for Class B dogs and cats November 2007 to November 2008. Disposition regulation (9 CFR 2.80) requires Class B dealers to maintain records for at least one year after an animal is disposed of, so the twelve-month period represents the greatest amount of data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

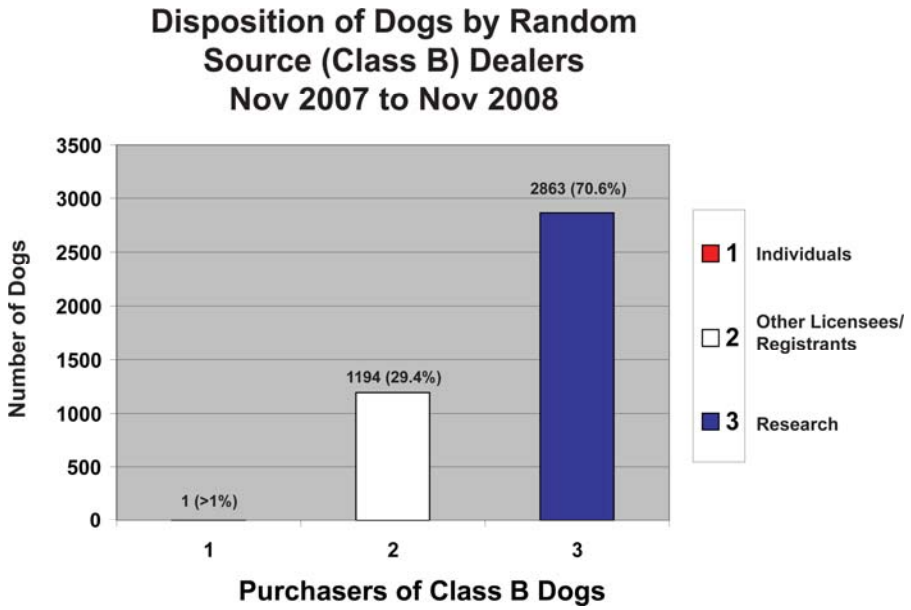

Figure 4-1b

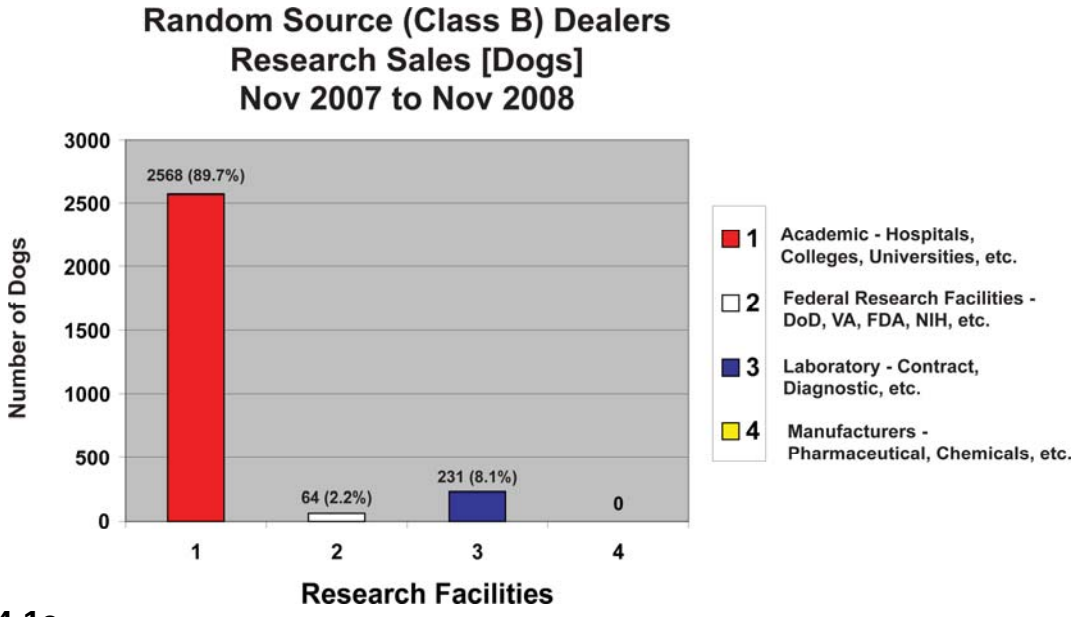

Figure 4-1c

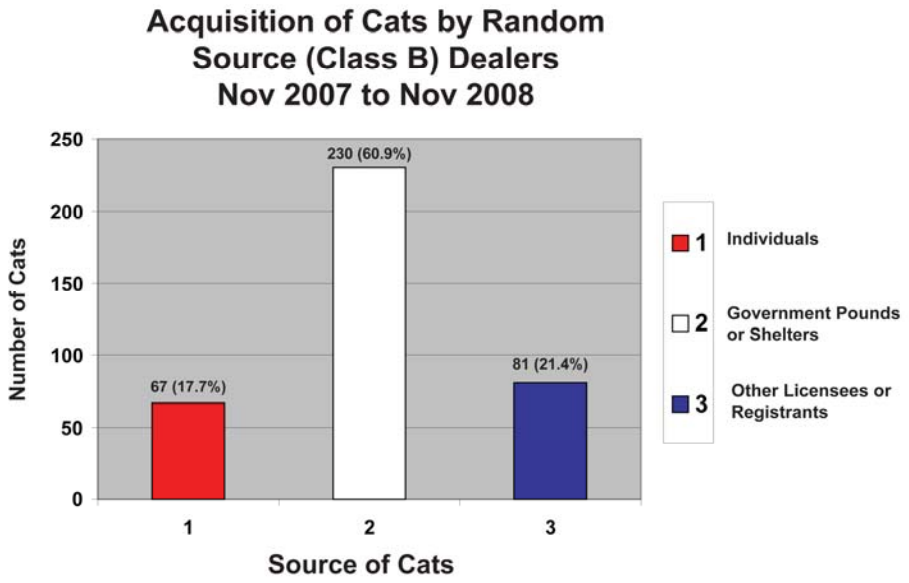

Figure 4-1d

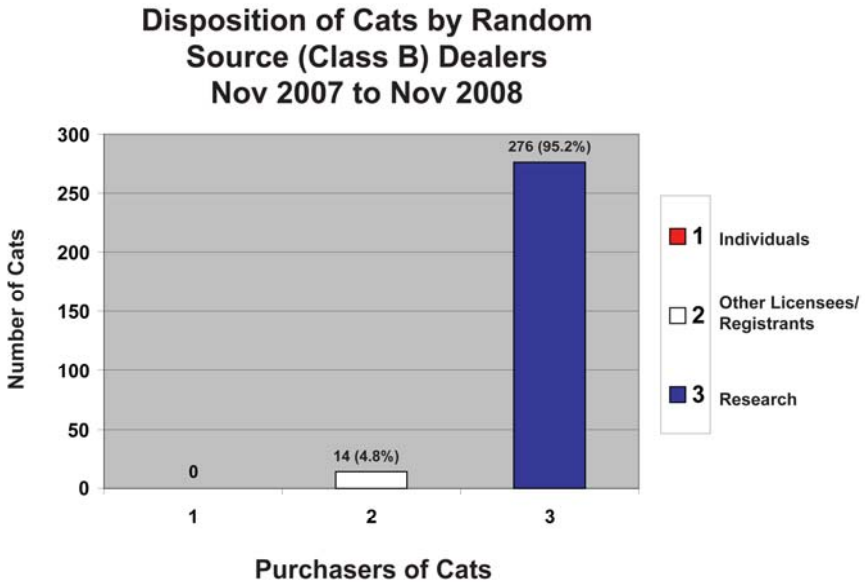

Figure 4-1e

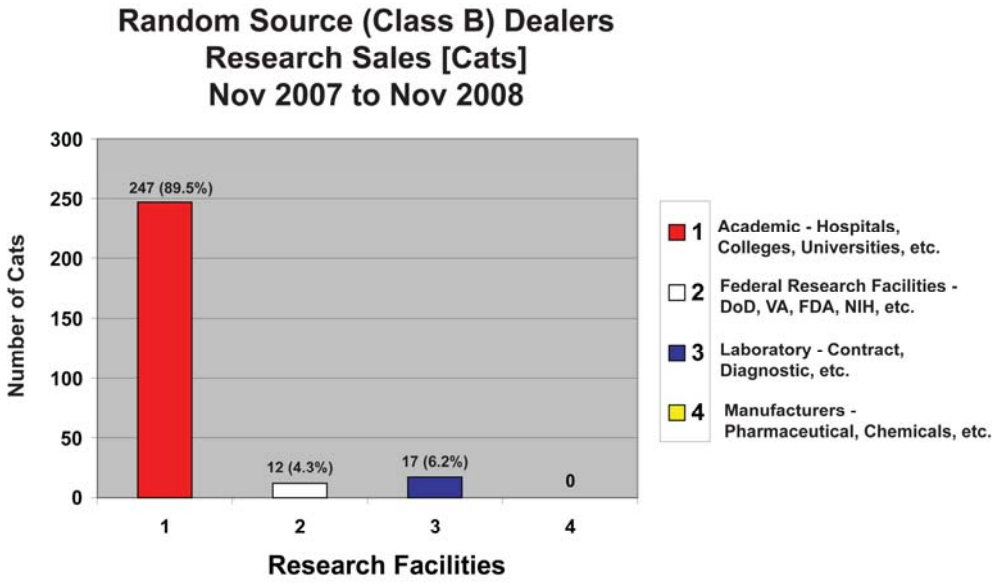

Figure 4-1f

When compared to all of the animals used in research, assuming 90 percent of all research animals are mice and rats, all dogs and cats represent only 0.9 percent (Table 1-1) of animals used in research, and Class B animals represent only 0.03 percent of all animals studied (USDA, 2007). 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 would be that Class A dealers provide most of the dogs and cats used in research.

Over the past two decades, a trend has emerged among research institutions to move away from the use of Class B dogs for research protocols or to require justification for the use of these dogs. 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."[30] The document lists questionable health status, poor condition, aggressive temperament and that the institution cannot guarantee that an animal was not someone's pet as reasons that contribute to their default position. 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 examples of the growing number of institutions to adopt similar policies.[31]

[30] http://vetmed.duhs.duke.edu/documents/iacuc/pdf/policy_on_source_of_canines.pdf
[31] http://www.hsus.org/animals_in_research/class_b_dealers/does_your_university_buy.html

Trends in the Number of Class B Dealers

The declining trends for the use of dogs and cats for NIH-based research is reflected in a concomitant and more rapid decline in the number of Class B dealers selling animals for biomedical research. When demand for random source dogs and cats were highest in the 1970s and 1980s, there were approximately 200 Class B dealers that sold research dogs and cats. In the 1990s, the number of these Class B dealers declined to approximately 100. In 2005, inspections performed by the USDA of Class B dealers selling research dogs and cats increased to a minimum of 4 times per year, with an emphasis on trace back verification. This coincided with a significant decline in the remaining dealers. At the present time, there are only 11 Class B dealers, one of which is on a 5 year suspension due to violations of the AWA and not likely to resume operation (personal communication, Robert Willems, USDA, to Committee, January 2009), and 5 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 veterinary product (non-NIH) research.

Sources of Dogs and Cats for Class B Dealers

A review of 2007 *acquisition* data provided by the USDA revealed the following data specific to Class B dealers (See Chapter 1 for AWR eligible sources):

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

378 cats acquired by Class B dealers in 2008:
- 18 percent came from individuals (for example hobby breeders)
- 61 percent came from government pounds or shelters
- 21 percent came from other licensees or registrants (for example other Class B dealers).

Pounds and Shelters as Sources of Class B Animals

Animal pounds and shelters can serve as points of acquisition of animals for research, either directly or through Class B dealers. Usually, these are contract pounds (government sponsored), or private shelters, but since private shelters rely on donations and public support to exist, 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. It was viewed as a betrayal of trust, as shelters are defined as facilities that provide care, adoption services and law enforcement. Modern day shelters also provide a variety of services to both the public and animals, such as spay neuter services, behavior counseling, veterinary care, humane education and so on.

The Iowa statute (145B 2003, and was repealed in 2008) was an example of how pound seizure works. It stated "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 Fee). Thus, the law allowed that after three days a dog could be seized by a research institution providing only a short time frame for reunion of lost animals with their owners or for a new home to be found for relinquished animals. Once the minimum holding period had expired, the shelter operators seeking to find a home for a highly adoptable animal are in competition with research institutions or Class B dealers for those animals. In Utah the statute (UT26-26-4) regarding pound seizure states "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 and the APS, fifteen states and the DC ban pound seizure (CT, DE, HI, IL, MA, ME, MD, NH, NJ, NY, PA, RI, SC, VT, WV) four states (IA, MN, OK, UT) mandate it, seven states allow it (AZ, CO, MI, OH, SD, WI) and the rest of the states leave it up to the discretion of the municipality to decide.[3233] These data may already be out of date or inaccurate, as the American Humane Association's Office of Public Policy reported that in 2008, 18 states now ban pound seizure and only 3 states (MN,

[32] www.aavs.org
[33] http://www.the-aps.org/pa/policy/animals/14states.htm

OK, UT, but no longer IA) mandate it.[34] These statistics reflect changing attitudes and diminishing access to random source animals from pounds for research. California is interesting in that the state allows unclaimed animals to be released for research, but the individual counties have all enacted bans. A major reason for these bans is California Civil Code 1834.7, which requires any pound or shelter where live or dead animals are provided to a biological supply company or research facility to post a publicly visible sign stating: *"Animals turned in to this shelter may be used for research purposes or to supply blood, tissue, or other biological products."* When given a choice, the public has chosen not to allow the resale of pound or shelter animals to research. A survey that gathered 2,438 responses involving 26 shelters conducted in 1988 by the American Humane Association, found that people overwhelmingly stated they would not bring a lost animal to a shelter that released unclaimed animals to research (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).

Alternate Sources of Animals for Class B Dealers

In lieu of obtaining random source animals from 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 example of hobby breeder derived dogs that are bought and sold for research. Class B dealers may 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, USDA, to Committee, January 2009). Dog auctions are primarily involved with the pet trade, which is not covered by the AWA. If auctions move into the research animal trade, the USDA would consider them random source Class B dealers and deal with them as such.

Value of Class B Dealers to Biomedical Research

The declining accessibility to random source dogs and cats from pounds and shelters due to changing state and local laws makes it more difficult for research institutions to directly obtain such animals, 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 serve as a conduit of access to animals for research institutions that would be otherwise difficult to obtain directly.

[34] www.americanhumane.org/assets/docs/advocacy/ADV-laws-state-pound-seizure.pdf

The potential desirability of random source animals for research has been described in Chapter 3 including size, age, genetic diversity and naturally occurring infectious disease. The relatively small number of dogs (<1000, Figure 4-1a) and cats (<300, Figure 4-1d) obtained by Class B dealers from pounds and shelters draws into question the genetic diversity of these animals and how much they truly represent the general population. Class B dealers primarily buy and sell generic dogs (mongrels and hounds) and cats, and are seldom involved or skilled in selection of specific diseases or models. Diseased animals are likely to be culled by dealers. However, at least one existing Class B dealer actually accrued animals with parasitism that could be used for veterinary research. In fact, the majority of dogs, but not cats, sold by Class B dealers are not random source animals, and are therefore similar to animals provided by purpose-bred animal dealers.

Cost of Animals from Class B Dealers

In an ideal world, costs 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 Class B animals, since Class B dogs and cats putatively cost less than Class A animals. Depending on circumstances, the financial incentives to use Class B animals may or may not be substantial.

According to information obtained from two Class B dealers and three Class A dealers (personal communication with Class A vendors), the purchase price of a young, 20-25 kg dog runs $325 - $350 for random source and $600 - $900 for purpose-bred. However, oftentimes dogs and cats from Class B dealers are not free from disease. In addition to being a potential threat to other animals and people in the research facility, they may need to undergo prolonged quarantine, socialization, treatment, or be removed from the study all together. These hidden costs 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 incurred by NIH, the research institution, nor the research investigator.

There are instances in which the difference in costs between Class A and Class B dogs might be prohibitive. The cost for using Class B dogs without conditioning for an acute purpose would be substantially less than Class A dogs. Much of the acute work in which a Class B unconditioned dog would be an appropriate model, such as in a surgical training class, are beyond the scope of this report. The purchase price of Class A animals increases with the age of the animal. For example, one Class A vendor charges a base price of $730 for a six month old beagle and an additional $4.10 for each day the dog is over 195 days. Thus, to obtain a skeletally mature Class A beagle for orthopedic research would cost over $1400/dog and the purchase price of an aged animal would be

considered by some to be prohibitive (Class A vendor beagle price list 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. In many cases, 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 imposed on airlines, may not be an attractive or even viable mode of animal shipping in the future. Obviously, the closer the source providing the animals, the less impact shipping has on the overall cost of them. In fact, based on the locations of the current Class B dealers and the institutions using these animals, this appears to be a factor that may influence utilization of Class B animals. Currently the locations of Class B dealers are limited to Illinois, Indiana, Kentucky, Michigan, Minnesota, and Pennsylvania.

AWA Enforcement

The specter of stolen or lost pets illegally or inadvertently being used in research has been a driving force in the creation of increasingly rigorous revisions of the AWA and USDA/APHIS interpretation and execution of the law. It is the responsibility of the USDA/APHIS to assure that Class B dealers are abiding by the statutes outlined in the AWA and the AWR. However, in the more than forty years since the inception of the AWA, the USDA/APHIS has been unable to completely enforce the AWA in regard to activities of Class B dealers, and consequently at easing the concerns of the American public. The reasons for this failure are multiple, as discussed in the subsequent text, but underscore that laws must be carefully crafted and enforced if they are to have their intended effect.

A notorious recent example is the case of the Class B dealer C.C. Baird[35]. For a number of years prior to 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 multi-agency (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 (HBO, 2006) of these events was produced by Tom Simon and Sarah Tealer for Home Box Office, entitled "*Dealing Dogs*." Because of the importance of this case in regards to recent public perspectives (including Congressional action) and resulting decline in numbers of Class B dealers, the documentary was viewed by the Committee to become familiar with this case.

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

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 prior to the situation becoming public. Baird avoided imprisonment by agreeing to testify to USDA and others in regards to multiple other ongoing Class B dealer investigations. 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. Coinciding with increased USDA oversight and decreasing demand, the number of Class B dealers selling dogs and cats to research facilities in the U.S. decreased from nearly 200 to 11.

Various veterinary officers of the USDA who testified before the Committee were appropriately circumspect about their personal opinions, but reflected ongoing and recent problems with the Class B dealer system. All stated that enforcement of the AWR was feasible, with emphasis on tracebacks. When the Committee queried Dr. 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. Likewise, Dr. Robert Willems, Assistant Director for the Eastern Region, testified that when he was involved in west coast operations, over 800 hours and 1½ years was invested in the investigations of violations of a single dealer. He testified that Class B dealers are regulated more heavily than any other USDA licensee. W. Ron DeHaven, while serving as a USDA Regional Director for Animal Care and Use, discussed with the Committee proposed regulatory changes, including a possible 2-year phase-out of Class B dealers 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 provided to the Committee by Dr. Willems, APHIS has responded to these incidents and public pressure by increasing its regulatory oversight of Class B dealers, which is now more feasible with the greatly reduced number of dealers. In October of 2008, the USDA implemented a new 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. A major focus of these inspections is the acquisition of random and non-random source animals. The legality of acquisition is evaluated by conducting tracebacks on a representative 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 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 percent of Class B Dealers are

now being subjected to 100 percent 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 percent 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.

In the past, the USDA has expressed confidence that their increased scrutiny of Class B dealers is sufficient to address issues in 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 percent of the dogs brokered by Class B dealers (HSUS, 2007; CBRA, 2009). Dr. DeHaven stated in testimony before the Committee that for the years 2000/2001 USDA was able to trace back original ownership for 95 percent of the dogs brokered by Class B dealers. 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. While a more than 90 percent success rate is admirable, the origins of up to 5-10 percent of animals in the Class B system are potentially uncertain. 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, it seems that auction sales could be used as a mechanism to legitimize the sale of illegally acquired animals, although there is no evidence that auction houses are currently used to sell animals to research institutions or Class B dealers.

There is little evidence to prove that pets are stolen for research (HBO, 2006). Conversely, 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 descriptions of thefts provided by informants in prison (personal communication, Robert Willems, USDA, to Committee, January 2009). Additionally, there are 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 a dog from a Class B dealer that through microchip scan was identified as a missing pet named Echo (Fayetteville Free Weekly 2005). The Committee requested FOIA access to USDA inspection reports over the past three years of all existing Class B dealers. These revealed that one dealer purchased two cats from a private individual that upon trace back investigation admitted that they 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, albeit few, are an undeniable breach of the public trust. The reasons for these deficiencies are multi-factorial. First and foremost, acquisition and resale of animals by dealers, bunchers and individuals is profit-driven, which may foster corrupt practices and less attention to animal welfare issues. The system therefore requires intense 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 before violators can be legally prosecuted. 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. 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.

The question has been posed whether animals are still being stolen for research. While the Committee could not make a determination from the evidence provided, it should be acknowledged 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. Among the reasons accounting for lost pets not being reunited with their owners are poor breed identification, and lack of resources. One tool being used currently to identify animals is microchips that are provided by three different companies. 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, and such equipment as computers, fluorescent lights, stainless steel exam tables can interfere with a scan (Lord, 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 owner is further complicated by the fact that an effective universal scanner that can detect all of the microchips currently in use in this country is not always available. This means that lost animals may escape detection despite efforts by their owner to recover them. The individual owner is understandably upset when a lost animal is euthanized at a shelter, but 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 for veterinary care, nor is there a requirement to maintain medical records unless an animal is receiving 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. 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. This issue became evident when the Committee examined USDA/APHIS inspection reports spanning the last 3 years of all currently licensed Class B dealers. Although the Committee did not physically inspect Class B dealer facilities, the reports indicated that 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. 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 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. Only 20 percent (947 of 4,672 total) of dogs purchased by Class B dealers were obtained from pounds and shelters in 2008 (Fig. 4-1a). Information provided to the Committee by some of the Class B dealers and USDA officials indicated that a significant number of Class B dogs are hounds from private owners (Figure 4-1a “Individuals”) as well as from pounds and shelters. In contrast to dogs, the majority, 61 percent (230 of only 378 total), of cats obtained by Class B dealers come from pounds and shelters, many of which are stray and feral animals. These percentages indicate that Class A dealers can fulfill much of the demand for animals with similar characteristics. Evidence provided indicates the justification of Class B random source animals is based on cost, size, age, genetic diversity, cancer, infectious disease, and other conditions but these attributes pertain primarily to availability of animals from shelters and pounds, and those animals obtained from these sources are generally not unique (other than cost). It is important to emphasize that if random source animals are considered desirable and necessary for NIH-based research, it is uncertain if Class B dealers can assure their availability from the diminishing number of cooperating pounds and shelters. 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, but the Class B animals are of lesser quality than Class A animals for the reasons discussed in this report.

One mechanism that has been proposed to assure continued access of genetically diversified, aged or large breed dogs (attributes that are desirable in random source dogs) is to encourage these animals to be specifically bred and maintained as Class A animals. The current source of purpose-bred hounds that are available from Class A vendors are in fact somewhat genetically diverse. Although these colonies have been closed for many years, the original stock was comprised of various breeds of hounds (Red Bone, Black & Tan, Blue Tick,

Tennessee Walker, Foxhounds and Brindle Current) and they do represent genetic diversity. In addition, a smaller 'mongrel' Class A dog colony is available as well which represents other mixed breed dogs and which was originated from Class B dogs approximately 23 years ago (personal communication Covance, to Committee, February 2009). Class A vendors also have retired breeding animals or animals that are larger in size but these occur infrequently and are not always available. If specific attributes are required by the research community, such as specific age requirements, physical conditioning, or physical attributes that are not normally found in existing Class A colonies (for example larger dogs), Class A vendors may consider providing these models, but it is unknown if the costs will always be significantly greater than Class B 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). Although beagle colonies were more common in the era of radiobiology research, beagles are still accessible from purpose-bred colonies that are maintained by a small number of research institutions, such as 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. They 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 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 ideal for longitudinal studies or for evaluating the effects of long-term dietary variables or environmental enrichment. Other research institutions maintain purpose-bred colonies of various breeds of dogs and cats, such as the University of Florida, the University of North Carolina, and the University of California, Davis. The Committee was unable to determine how many such colonies exist, because most are not supported directly by NIH, even though animals from these sources are used in NIH-related research. Nevertheless, they offer a relatively untapped resource for NIH for acquisition of aged, genetically defined or genetically diverse, purpose-bred animals.

It would be impossible for Class A dealers to maintain the diversity of dog and cat breeds, and therefore genetic diversity, that exists in the general dog and cat population. These animals indeed represent an enormous potential resource as animal models of human disease. However, in reality, Class B dealers do not provide such animals to the biomedical research community either, but rather deal with various breeds of medium and large-sized dogs and random source cats (Figure 4-1a and 4-1d). To its credit, the Comparative Medicine Program of the National Center for Research Resources at NIH has capitalized upon 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 through referral from

the pet sector (such as knowledgeable breeders, working dog organizations, and veterinary referrals), including metabolic diseases, bleeding disorders, immunologic disorders, dilatative cardiomyopathy and other cardiac disorders, osteogenesis imperfecta, mucopolysaccharidoses, and many others. The center acquires, characterizes and genetically analyzes the submitted cases to validate homology to the human disease, and makes the animals available to the general research community by maintaining small nucleus breeding populations, collaborative interactions with colonies at other institutions, and provision of germplasm. This program is a laudable paradigm that directly addresses the NIH's needs for certain types of dog and cat models.

Another outstanding program that is supported by the National Cancer Institute (NCI), takes full advantage of the aged and genetically diverse dog population, which 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. The general dog population develops a cancer rate that is sufficient to power pre-clinical trials. The NCI program, founded in 2003, is known as the Canine Comparative Oncology Program that includes a multi-center collaborative network of 14 veterinary teaching hospitals (Comparative Oncology Trials Consortium). This program fosters rigorously controlled preclinical trials of new cancer drugs that are intended for eventual use in humans. These pre-clinical trials provide guidance on design of human studies, without constraint of human phase I, phase II, and phase III trials, while also benefiting the client-owned animal patients. This program is linked to another consortium, the Comparative Oncology and Genetics Consortium, which builds upon publication of the canine genome and maintains a biorepository of canine tumors, fosters collaborative opportunities between comparative oncologists, and initiates pre-clinical trials using pet dogs with cancers. These programs take full advantage of naturally occurring cancers in dogs, which have significant similarities with 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 and predicted the successful outcome for early phase trials in humans. These programs take full advantage of the rich genetic and disease diversity of the general dog population, with highly qualified veterinary and medical collaboration, client participation, and mutually beneficial advancement of human and animal health.

Unresolved Class B Compliance Issues

The Committee engaged in considerable debate in regards to its final recommendations (Chapter 5), since there could be, as discussed in this report, potential value of Class B dealers to the NIH research mission. However, the Committee could not reconcile the serious unresolved Class B compliance

issues, and felt that these issues, as well as humane concerns, were major factors in the Committee's final recommendations.

There are two major concerns the public harbors 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 misplacement 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 (but not all) Class B dealers (AWI, 2007). In regards to the first concern, there are existing loopholes whereby pets may still enter the research pipeline. For example, Class B dealers acquire and sell dogs and cats that originated from auctions, shelters, or pounds.

The second concern is that Class B dealers are only required to adhere to the AWR, while those institutions that receive NIH funding for research comply with *PHS Policy*, the *Guide for the Care and Use of Laboratory Animals* and the *US Government Principles* (Defined in Chapter 1). The Committee was concerned that Class B facilities are not held to the same standards as research facilities receiving NIH funds that mandate compliance with *PHS Policy*, the *Guide* and *US Government Principles*. For example, the USDA has different internal inspection manuals (See Chapter 1), allowing different standards of the AWR to be applied for research, dealers and exhibitors, thereby inconsistently applying standards among dealers, research institutions and exhibitors. It is difficult for the public to understand why there would be different standards of care when existing AWR are meant to establish minimum standards.

Finally, the Committee recognizes that the USDA is severely hampered in its ability to implement the standards described in the existing AWR. USDA has insufficient enforcement action powers, including the ability to act more swiftly, assess sufficiently punitive fines, power of temporary injunction authority and power of immediate cease-and-desist authority for serious or repeat animal welfare citations. Because of the nature of law enforcement, only serious and repeated infractions are worth pursuing, at the expense of many minor infractions that need attention.

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CHAPTER 5: RECOMMENDATIONS

The *Committee on Scientific and Humane Issues in the Use of Random Source Dogs and Cats in Research* was assigned 3 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 Class B dogs and cats are desirable/necessary as well as the number of grants where the potential exists or the source of the animal is identified as coming from a Class B source. The second task asked for a description of the special characteristics, such as 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 Class B animals (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 Class B animals were desirable for use in these studies simply because of their lower cost and availability, or necessary for some other compelling scientific reason. The Committee found 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 (examples include naturally occurring infectious disease, larger size, deeper chest, and older age) these specific characteristics are not confined to random source or Class B animals, 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.

In order to complete its tasks, it was necessary to closely examine the Class B dealer system that provides random source animals for research. The AWA was enacted in 1966 largely due to concerns about lost or stolen pets being used for research and this concern continues to be expressed by the public. The number of Class B dealers has decreased dramatically, particularly in the last 5-6 years, and the USDA has made significant strides in enforcement of the regulations during recent years. 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. The USDA simply cannot assure that stolen or lost pets will not enter research laboratories via the Class B dealer system. Furthermore, administrative and

judicial procedures that are necessary to enforce the AWA and ensure remediation of conditions that lead to animal distress and suffering are inordinately slow, cumbersome, and ineffective. The Committee felt strongly that this was unacceptable.

Trends in the use of Class B dogs and cats in research suggest that for a variety of reasons (public opinion, animal protectionist pressure, regulatory and financial burden, institutional policies, research trends, investigator choice), the Class B dealer system may soon become unavailable to provide animals for research. As noted in previous chapters, Class B animals represented 20 percent of dogs and cats used in research in 2002, whereas in 2007/2008, they represented only 3 percent of dogs and cats used in research, and a fraction of that percentage represents animals used for NIH research. That small fraction is further diminished in regards to random source animals from pounds and shelters, since only 20 percent of Class B dogs and 61 percent of the very small numbers of Class B cats were random source animals from pounds and shelters, which is the group of animals with potentially valuable or unique attributes for NIH research. The actual number of random source animals with characteristics needed for specific NIH research projects that are unique to Class B animals could not be identified by the Committee, but is clearly quite small. The Committee acknowledges that a small number of random source animals may have potentially high value in regards to the NIH mission, but available alternate avenues currently exist for filling much if not all of this limited need.

The Committee also recognized that access to random source animals from pounds and shelters is diminishing, but that trend impacts availability of these animals for Class B dealers as well. Therefore, regardless of recommendations of this Committee, NIH must either respond with alternate approaches or accept the reality that random source animals are becoming increasingly difficult to obtain, either through direct acquisition or through Class B dealers. Furthermore, as long as the Class B dealer system persists, the biomedical research community will continue to evoke the “negative press” of public concerns about lost or stolen pets ending up in research, no matter how rare such occurrences are, or how well enforced the regulations. In addition, the Committee determined that the husbandry standards and humane treatment of animals was unacceptably variable among existing Class B dealers, and not commensurate with NIH standards of research animal care and quality.

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. However, the Committee did not find that it is 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 determined that alternative options are currently available to fill NIH needs for random source animals, but the Committee also recognized that these options are limited and diminishing. In order to assure continued availability of random source dogs and cats in the absence of Class B dealers, the Committee identified the following existing options:

- **Direct Acquisition from Pounds and Shelters:** The number of random source animals from pounds and shelters being used in research is very small, the number used in NIH-based research is smaller, and some random source animals are currently acquired directly by some institutions. While it is unlikely that private shelters or humane societies that receive public funding would ever relinquish animals for research, animals can still be obtained directly from the three states that continue to mandate pound seizure and from some of the municipal shelters in the 29 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 are poorly funded, have a high euthanasia rate, strong animal control component, weak adoption program and/or an apathetic animal welfare community. Research institutions that engage in direct acquisition must take on the responsibility and added cost of conditioning and veterinary care, but in so doing also take on the responsibility of assuring their welfare. It is important to note that Class B dealers are not a solution for diminishing accessibility to animals of this type.

- **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 animals currently being acquired by Class B dealers. There is no reason that such animals cannot be acquired directly, in lieu of through Class B dealers.

- **Cooperative Pre-clinical Consortia:** The current use of pet animals with owner consent for comparative pre-clinical investigations is a viable model for such systems to be employed for advancing both human and veterinary medical research. An outstanding example is the Canine Comparative Oncology Program (CCOP) of the NIH/NCI. The CCOP is a multicenter collaborative network of 14 veterinary teaching hospitals that provides controlled preclinical trials of new cancer drugs with the goal of assisting in 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 upon the rich genetic diversity in the canine population, the variety of cancers that arise in the canine population, anatomic and disease characteristics that are more accurately reflective of the human condition than rodents, assure outstanding clinical care of the animals, and 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 commercial dog vendors breed primarily beagles, hounds and mongrel dogs. These vendors advertise standard sizes ranging from 15-27 kg (33-60 lbs) and generally these dogs are 6-12 months old. However, further information provided by some of these vendors indicated that larger animals, 27-37 kg (60-80 lbs), are currently available or, in some cases, larger dogs could be bred if needed. In addition, although most of the dogs sold for research are less than one year of age, a small number of older (2-5 years) retired breeding animals are available (personal communication with Class A vendors). If a greater number of these animals are needed, Class A vendors could provide them, albeit at a greater cost. In addition, a significant number of Class B dogs are hounds obtained from hobby breeders, which overlaps with what is 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 upon 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). 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 addresses 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. Another laudable program is the *Canine Comparative Oncology Program* that links NCI with a network of 14 cooperating veterinary teaching hospitals for cancer research, discussed above. These programs serve as examples 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. If the need for genetic models or other disease models is warranted, NIH should invest in expanding such programs, as well as invest in technology for improved preservation and archiving of germ plasm of important models, but additional, directed funding for such resources would be needed.

In addition to the above existing options, the Committee recommends consideration of the following options to assure access to random source animals, or animals with attributes thereof:

- **Existing NIH-Supported and Privately Owned Colonies.** Some NIH categorical Institutes currently support dog colonies at U.S. research institutions, including defined-age animals that are available and used for 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 dogs and large breed dogs, such as golden retrievers. Similarly, there are colonies of mixed breed cats. Since most of these various colonies are not supported by NIH, the Committee was unable to determine how many exist. If access to such animals is important to assuring the NIH mission, NIH should make a "Trans-NIH" effort to coordinate access to animals in these colonies, as well as offer subsidy to cooperating institutions to maintain access to animals.

- **NIH Request for Proposal:** Various NIH categorical Institutes commonly utilize the *Request for Proposal* (RFP) mechanism to acquire items that the government needs, or to perform research and development on a contractual basis. The RFP mechanism has several merits. Examples of NIH animal-related RFPs include contracts to develop specific animal models, contracts to operate NIH animal facilities or other animal facilities that serve NIH, contracts to provide quality animals for NIH research programs, contracts for development of animal-related reagents that enhance research, and contracts for application of animal models to test efficacy of vaccines or therapeutic regimens, among many others. A variety of laboratory animals, ranging from rodents to non-human primates, are the subject of RFPs, and since the RFPs are NIH-supported, all such animals fall under *PHS Policy*. Therefore, the RFP mechanism is already in place and is quite suitable for fulfilling this need.

  The RFP can define the specific criteria for acquisition, husbandry, traceback assurance, and veterinary care of animals in keeping with *PHS* Policy. Since OLAW does not have investigative authority, respondents to the RFP would need to provide a detailed Animal Welfare Assurance, similar to any research institution that receives NIH funds, according to *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, assuring optimal care and welfare of the animals, as well as enhancing NIH's research mission through the use of healthier animals. Continuation of the contract would be subject to periodic (usually quarterly) review. If the contractor fails to meet the statement of work, including accurate traceback documentation, support can be immediately curtailed, 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 property of NIH, and animals would fall under *US 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.

In the absence of specific allocations from Congress, NIH will be reluctant to take on these responsibilities at a time in which the NIH budget is uncertain. Therefore, the Committee acknowledges that supplemental funding to NIH directed at facilitating these options will be needed. As noted throughout the report, the Class B dealer system is declining, and availability of random source animals from pounds and shelters is diminishing, regardless of Class B dealers. Therefore, if NIH deems random source animals, or the qualities that they possess, to be necessary for research, alternatives need to be explored and supported by NIH before their demise.

APPENDIX A: 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 University of California, his Ph.D. in experimental pathology from 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 PhD 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, CO.

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 protocols and directing IACUC activities. He received a BS 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 Committee. 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 of 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.