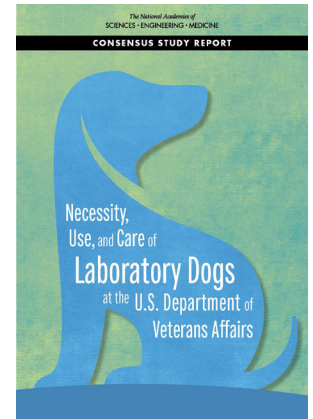




Necessity, Use, and Care of Laboratory Dogs at the U.S. Department of Veterans Affairs

For many years, laboratory dogs have served as important animal models for biomedical research that has advanced human health. However, the role of dogs in American society as companion animals and work partners makes their use in research contentious. This report assesses whether dogs are or will continue to be necessary for biomedical research related to the U.S. Department of Veterans Affairs' (VA) mission. Laboratory dogs remain scientifically necessary for some areas of VA research on cardiovascular disease and spinal cord injury, but are no longer the preferred model for other areas of research, including diabetes and primary pharmacology, the report finds. The report offers parameters to help determine when dogs are necessary for biomedical research, makes recommendations for the VA to promote the development and use of alternatives, and highlights opportunities for the VA to enhance the welfare of laboratory dogs when they are necessary for biomedical research.



Historically and across disease type—from the understanding and treatment of diabetes to the development of cardiac pacemakers and valve replacement—it would be challenging to find an area of biomedical research that has not benefitted from the involvement of laboratory dogs. For thousands of years and up to the present day, dogs have been used in research due to their anatomical and physiological similarity with humans, and because of their ubiquity and comfort around humans.

However, the close bond between humans and dogs raises ethical and social concerns about the continued use of laboratory dogs in research. The use of dogs in biomedical research has notably decreased since the 1970s, but in the last decade has been steady at around 60,000 dogs per year in the United States. Investigators in some biomedical fields continue to perform research using laboratory dogs because of factors including familiarity with dogs as a model species, access to historical data, and biological factors that cannot be modeled effectively in other systems.

The U.S. Department of Veterans Affairs (VA) supports and conducts a wide range of research to help advance understanding of how disease affects veterans. Although most VA animal research uses rodents, laboratory dogs are also used. In 2017, mice and rats constituted 99 percent

of all animals used at the VA; dogs constituted less than 0.05 percent of all animals used. Over recent years public and congressional attention to the use of laboratory dogs in VA biomedical research has increased (see Box 1). In March 2018, the VA announced its intention to conduct an in-depth internal review of its existing canine research projects, and requested the National Academies of Sciences, Engineering, and Medicine convene a committee to explore the necessity of laboratory dogs in biomedical research related to the VA's mission.

LEGAL, SOCIAL, AND ETHICAL CONSIDERATIONS

The committee reviewed 14 animal component of research protocol (ACORP) forms associated with current or recent past studies involving laboratory dogs, together with additional materials provided by the VA. The committee also carried out site visits, held public sessions, and conducted a comprehensive review of the scientific literature regarding VA research that has traditionally used dogs. Based on this information and documentation from other organizations and regulators, the committee concludes that the VA's biomedical research programs appear to adhere to all relevant legal policies surrounding laboratory dogs.

BOX 1

Recent Legislation Concerning the Use of Laboratory Dogs at the VA

Over recent years, there has been increased congressional attention to the use of laboratory dogs in VA biomedical research:

In March 2018 the federal government mandated that:

- No federal funds “may be used to conduct research using canines unless: the scientific objectives of the study can only be met by research with canines.”
- The VA Secretary is required to “directly approve” any studies using canines.

In December 2019, the Further Consolidated Appropriations Act of 2020 reiterated the restrictions above and required that:

- The scientific objectives of VA research involving canines, felines, or non-human primates must be “directly related to an illness or injury that is combat-related.”
- The VA Secretary must personally report all new research on canines, felines, or non-human primates to the U.S. Congress, and to submit a plan by December 31, 2020 for eliminating or reducing research on these species over the next five years.

Because of the unique bond that many humans have with dogs, it is tempting to infer that dogs bear a higher moral status and therefore deserve greater protection than other species like rabbits or pigs. However, pigs, sheep, and cows—and mice and rats, for that matter—all have moral status; they have feelings, preferences, and the ability to suffer. A preference for dogs does not justify a lower regard for the welfare of non-dog species nor does a preference for dogs necessarily constitute a reliable guide to ethical action. The majority of the committee concludes that it is valid to consider the societal preference for dogs only in situations where the expected burden for substitute animals is anticipated to be equivalent to the expected burden for the laboratory dog – that is, a social preference for dogs can only serve to break a tie between laboratory dogs and substitute animals when the expected burden is equal.

DETERMINING THE NECESSITY OF LABORATORY DOGS IN RESEARCH AT THE VA

The VA provided the committee with documentation from 44 research projects involving dogs conducted by its researchers over the past 50 years, with 14 projects being active in 2018-2019. The Committee surveyed the

use of dogs in ten biomedical research fields; seven areas in which the VA currently uses laboratory dogs or has done recently (cardiovascular disease, spinal cord injury, imaging, diabetes, narcolepsy, osteoarthritis and chronic pain, and experimental pharmacology and toxicology) and three areas of potential future use (cancer, infectious disease, and Alzheimer’s disease). The committee reviewed current practices and recent advances in each of these areas of research to better understand the context for VA’s research using laboratory dogs in these areas.

The committee found that in a few areas of current VA research, laboratory dogs offer the potential for important biomedical discoveries that cannot currently be obtained using other models. These research areas include subsets of cardiovascular disease research, most notably cardiac rhythm disorders, which depend on anatomical and physiological features shared between humans and dogs and not with other laboratory species, or on implantation of devices that rely on restricted growth in addition to some of these other features. Research on some treatments for spinal cord injuries also requires laboratory dogs, particularly cervical injuries resulting in quadriplegia that cannot be modeled effectively in other animal and non-animal systems. Even in these limited fields, however, it will be crucial to remain vigilant for non-dog and non-animal alternatives and actively work to promote the development and use of alternatives. It is not inconceivable that future VA research in other fields could require the limited use of laboratory dogs due to their unique biology.

Recommendation 1:

Adopt an expanded set of criteria for determining when it is scientifically necessary to use laboratory dogs in biomedical research funded by or conducted at the VA.

The VA should adopt an expanded set of criteria for determining if the use of laboratory dogs is scientifically necessary:

1. The scientific question and the knowledge anticipated will advance understanding or medical practices related to veterans health; and
2. Based on unique physiological or other characteristics, there is no alternative to the laboratory dog that will yield scientifically valid results that meet proposed study objectives; and
3. The anticipated harms experienced by the laboratory dog are outweighed by the potential benefits for veterans; and
4. Both the scientific review committee and the IACUC have provide written statements attesting that the laboratory dog is the only species that can yield scientifically valid results.

The majority of the committee found that where multiple species including the laboratory dog could be used to answer the scientific question, the species that will incur the fewest burdens should be selected. Thus, ethical, legal, and animal welfare considerations must also play a role in determining when a proposed protocol is “necessary.” In Recommendation 2, the report presents criteria that should be met before the use of laboratory dogs is approved when other models are also scientifically appropriate.

Five of the fifteen members of the committee believed that the report should be limited only to recommending criteria for the VA to use in determining when the use of dogs is “scientifically necessary,” due to a difference of interpretation of the committee’s statement of task. A discussion of their views can be found in Chapter 3 of the report.

Recommendation 2:

Adopt an expanded set of criteria for determining when to use laboratory dogs in VA’s biomedical research when the dog is not scientifically necessary.

The following criteria should be met before approving the use of laboratory dogs when other animal models are also scientifically appropriate.

1. The scientific question and the knowledge expected to be gained will advance understanding or medical practices related to veterans’ health; and
2. The research objective cannot be adequately addressed using New Approach Methodologies (NAM) or ethically using human subjects or companion animals; and
3. Where multiple species [excluding non-human primates], including the laboratory dog, can be used to adequately answer the scientific question, the non-primate species that will incur the fewest burdens should be selected. If the species that will incur the fewest burdens cannot be selected for any reason, including legal and/or funding restrictions (e.g. the laboratory dog), the VA cannot ethically proceed and should consider forgoing the research; and
4. The expected harms experienced by the selected animals are sufficiently outweighed by the expected benefits to veterans. Both the IACUC and the VA’s Central Office ethics review should concur in this assessment

IMPROVING RESEARCH PROTOCOLS AND REVIEW PROCESSES

The committee’s analysis of the ACORP forms provided by the VA revealed some deficiencies in the

justification for using laboratory dogs. Some protocols lacked a serious attempt to exclude other species, and literature searches for alternative species were often of poor quality. In other cases, investigators cited previous experience with dogs and historical data in dog models as justifications for using laboratory dogs, but the committee found that these justifications are insufficient alone, and constitute a form of circular reasoning that perpetuates the use of laboratory dogs. The ACORP analysis also revealed instances where the investigators did not adequately explain the relevance of the study to veterans’ health.

The committee recommended that VA should enhance its scientific and ethical review process so that it better integrates the assessment of harm and burden (of study animals) with assessments of value and impact associated with biomedical research using laboratory dogs.

Recommendation 3:

Improve biomedical research protocols and review processes, and track the impact of research.

ALTERNATIVES TO THE USE OF LABORATORY DOGS

The committee considered four broad categories of alternatives to the use of laboratory dogs: companion dogs; laboratory animals other than the dog; new approach methodologies (NAMs), a diverse array of non-animal approaches including in vitro, ex vivo human tissue, computational, and in silico models; and human clinical trials.

Each of the potential alternatives offers advantages and disadvantages. For example, although none of the NAMs considered by the committee can serve as an immediate or complete replacement for animals, they do enable researchers to investigate aspects of human biology that cannot be addressed in dogs or other animals. Companion dog studies, in which diagnostic, preventative, or therapeutic approaches are investigated in companion dogs with naturally occurring conditions of interest, could reduce the use of laboratory dogs while also benefitting the companion dogs. The VA has an opportunity to enhance the administrative infrastructure to identify and support new collaborations with veterinary researchers conducting trials in companion dogs.

Incorporating any of the alternatives into an animal-based research program will require a dedicated and comprehensive effort. The VA will need to develop strategic plans prioritizing protocol review processes that require and support the consideration of all alternatives and incentivizing the use of NAMs.

Recommendation 4:

Develop a strategic roadmap to create, track, and sustain internal efforts to incorporate NAMs in VA biomedical research.

Recommendation 5:

Establish long-term external collaborations to optimize the use of companion dogs and humans in biomedical research.

ENHANCING THE CARE AND WELFARE OF LABORATORY DOGS

Over the past fifty years, there have been several key conceptual advances regarding the welfare of animals. These advances reflect developments related to animal sentience; a consideration of positive and negative welfare states; and the recognition that welfare assessments must incorporate both resource-based and animal-based considerations.

Based on the information gained during site visits and in submitted materials, the committee concludes that the VA appeared to meet or exceed all regulatory requirements. Nonetheless, the Committee observed several areas where the VA's animal program could be enhanced.

Recommendation 6:

Enhance the welfare of laboratory dogs used for biomedical research.

- Submit to voluntary USDA inspections of dog facilities to increase transparency.
- Modify dog enclosures and staffing to enhance opportunities for social interaction, exercise, and sensory stimulation.
- Address current experimental impediments to dog-dog interactions.
- Conduct enhanced assessments of laboratory dog welfare.

COMMITTEE ON ASSESSMENT OF THE USE AND CARE OF DOGS IN BIOMEDICAL RESEARCH FUNDED BY OR CONDUCTED AT THE U.S. DEPARTMENT OF VETERANS AFFAIRS

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For More Information . . . This Consensus Study Report Highlights was prepared by the National Academies of Sciences, Engineering, and Medicine based on the Consensus Study Report *Necessity, Use, and Care of Laboratory Dogs at the U.S. Department of Veterans Affairs* (2020). The study was sponsored by the Department of Veterans Affairs. Any opinions, findings, conclusions, or recommendations expressed in this publication do not necessarily reflect the views of any organization or agency that provided support for the project. Copies of the Consensus Study Report are available from the National Academies Press, (800) 624-6242; <http://www.nap.edu> or via the project webpage at <http://www.nas.edu/dogstudy>.

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