June 13, 2022

The Honorable Rosa DeLauro
Chairwoman
U.S. House Appropriations Committee
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies
Washington, D.C., 20515

The Honorable Tom Cole
Ranking Member
U.S. House Appropriations Committee
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies
Washington, D.C., 20515

Dear Chairwoman DeLauro and Ranking Member Cole,

On behalf of the 46 undersigned organizations representing a diverse array of biomedical professional societies, academic institutions, veterinary groups and technical staff, pharmaceutical companies, and individual researchers, we appreciate Congress's steadfast support for science, biomedical innovation, and global competitiveness. To achieve revolutionary change in these areas and strengthen the nation's competitive edge on the global stage, robust federal investments in animal research remain essential. Here we explain the importance of large animal foundational and translational research, the current problems in transporting research animals, and opportunities for reducing the administrative burden placed on investigators and institutions.

Large Animal Foundational & Translational Research

To ensure scientists have the resources necessary to advance the next generation of discoveries, we urge the House LHHS Appropriations Subcommittee to include language in the FY23 appropriations bill and report that supports and expands large animal foundational and translational research supported by the National Institutes of Health (NIH). Scientists agree one of the most critical steps in designing research experiments is identifying the best model to address specific questions. Although most research proposals (e.g., more than 95 percent) involve small animals such as rodents and fish, studies with larger species such as canines, felines, pigs, ferrets, and nonhuman primates can more effectively answer complex research questions that rely on more specific biological similarities to humans. As stated in NIH's policy guidance,[1] studies in animals are essential for all facets of biomedical research—from basic science and preclinical questions to translational, behavioral, and clinical studies.

One example demonstrating how animal research facilitates cutting-edge medical advancements is the discovery of messenger RNA (mRNA) in the 1960s. Subsequent foundational studies in rabbits and pigs enabled researchers to harness the power of mRNA and protein synthesis to create new vaccine platforms, a development researchers routinely leverage to create vaccines against numerous infectious diseases that affect both humans and animals, including rabies[2] and, most recently, COVID-19 in humans. Numerous other examples illustrate the value of research in animals providing the foundation for future, groundbreaking medical discoveries. For instance, brain research with nonhuman primates contributed to the development of deep brain stimulation for patients with Parkinson's disease and will be essential for advancing therapies for cognitive decline and other mental health conditions; canine research is essential

[1] National Institutes of Health, Grants & Funding. "Why are animals used in NIH research?" https://grants.nih.gov/grants/policy/air/why_are_animals.htm.
[2] Zhang C, Maruggi G, Shan H, Li J. Advances in mRNA Vaccines for Infectious Diseases. *Front Immunol*. 2019 Mar 27;10:594. doi: 10.3389/fimmu.2019.00594. PMID: 30972078; PMCID: PMC6446947.

for cancer studies and the development of immunotherapies because canines develop—and similarly present—many of the same cancers as humans. In comparative medicine, the similarities between large animals and humans strengthen research rigor, reproducibility, and translatability compared to models with lower predictability. As a result, large animal studies facilitate accelerated advancement of preventative measures, diagnostics, drugs, therapies, and medical countermeasures, especially those necessary for use in public health emergencies.[3]

The biomedical research community acknowledges the emerging field of research with nonanimal models such as organs on chips, cell culture, organoids, and computer simulations. These models play a vital role in supplementing research with animals, often by providing preliminary information for scientists to differentiate particular drug targets or biological pathways. In turn, studies with nonanimal models have the potential to drive basic research to the next translational step with greater efficiency and precision. However, such techniques cannot be used alone to replace all animal studies because they do not provide comprehensive insight into mechanisms affecting the whole body, including complex diseases and behavioral mechanisms. Additionally, nonanimal models must be validated in animals to ensure safety and efficacy before testing in humans. Because validated models may only be suitable for specific research questions, there is an essential need for continued support for animal studies to fulfill various scientific and public health demands.

Scientists are dedicated and strictly adherent to the established ethical, legal, and scientific standards and policies that strictly regulate animal research, as cited in the United State Department of Agriculture Animal and Plant Health Inspection Service 2021 Annual Impact Report, which found 96 percent of licensees and registrants in substantial compliance with the Animal Welfare Act.[4] Beyond the regulatory requirements, scientists, veterinarians, and animal care staff extend compassionate care for research animals because they recognize high-quality oversight ensures excellent science and, more importantly, that humane care for animals is our societal responsibility. Finally, scientists give significant consideration to the 3Rs— reducing animals to the most appropriate numbers, refining research practices, and replacing animals with nonanimal options where possible—when designing, reviewing, and conducting research studies. **We encourage the House LHHS Appropriations Subcommittee to consider these aspects while drafting bill language and consult with the scientific community during the decision-making process to ensure future requirements are evidence-based and in the best interest of human and animal health.**

Availability, Transportation, & Protected Use of Nonhuman Primates

The biomedical research community urges the House LHHS Appropriations Subcommittee to acknowledge the critical need for nonhuman primate research and allocate additional funding for NIH and the National Primate Research Centers (NPRCs) to allow researchers to conduct this essential work. The COVID-19 pandemic presented numerous scientific and infrastructural challenges that can inform future appropriations strategies. Chief among these challenges was the lack of availability of nonhuman primates, animals that comprise less than half of one percent of all NIH-funded animal research but remain indispensable for biomedical and vaccine research. Furthermore, the NPRCs—a network of seven medical research centers across the U.S.—remain a steadfast pillar in advancing human health by breeding and caring for nonhuman primates. These centers were instrumental in carrying out

[3] Food and Drug Administration, MCM Regulatory Science, "Animal Rule Information." https://www.fda.gov/emergency-preparedness-and-response/mcm-regulatory-science/animal-rule-information. May 2022.

[4] United States Department of Agriculture Animal and Plant Health Inspection Service, 2021 Annual Impact Report, "Keeping U.S. Agriculture Healthy for America and the World." Published April 6, 2022. https://www.aphis.usda.gov/aphis/newsroom/stakeholder-info/administrator-letters-to-stakeholders/2021-impact-report

research studies essential for the development of the COVID-19 vaccines at record speed. However, the capabilities of nonhuman primate researchers are limited due to diminishing funds and national supply constraints, as noted in a 2018 report from the NIH Office of Research Infrastructure Programs that underscored the need for an adequate supply of nonhuman primates in the U.S.[5] The pandemic significantly exposed the challenges associated with supply and demand for nonhuman primates when researchers struggled to acquire nonhuman primates to meet the rising need for studies on SARS-CoV-2.[6] The shortage was further exacerbated when China banned exports at the beginning of the pandemic. The unexpected pivot to COVID-19 research and enduring lack of nonhuman primates forced numerous scientists to delay and, sometimes, even temporarily halt ongoing studies into other diseases that rely on these animals and impact millions of American patients, including cancer, tuberculosis, HIV/AIDS, Alzheimer's, Parkinson's, and numerous psychiatric and neurological diseases such as depression, substance abuse disorder, and addiction. To maintain U.S. leadership in science and technology, nonhuman primate researchers must have the resources, staff, and infrastructure to conduct their research and swiftly respond when the country faces challenging times.

Additionally, we urge the House LHHS Appropriations Subcommittee to address the current shortage of nonhuman primates for research use, including the ongoing refusal of numerous airlines to transport animals for research purposes. This issue has compounded the current shortage of nonhuman primates and jeopardizes both biomedical research and national security by inhibiting researchers' access to the appropriate animals necessary for addressing pressing public health concerns. As competing nations accelerate investments in research and development, we are concerned leaving this issue unresolved will unnecessarily delay U.S. research productivity, reduce our ability to respond to future public health crises, and compel scientists (both academic and private) to either pursue opportunities elsewhere or rely on other countries entirely, including China. In a dynamic 21st-century economy, retaining domestic talent and safeguarding U.S. scientific resources—including the supply and transport of nonhuman primates—is critical for achieving national and economic security. **Thus, the biomedical research community encourages the House LHHS Appropriations Subcommittee to include language that directs the NIH, the Centers for Disease Control and Prevention, and the Food and Drug Administration to form an interagency committee that develops and routinely evaluates a federal plan that ensures the long-term support, breeding locations, veterinary oversight, and enrichment and social needs of nonhuman primates in the U.S.**, similar to language included in the Senate LHHS FY22 Appropriations explanatory statement (see pg. 161, *"Research with Nonhuman Primates*").[7] To accompany these efforts, we request House Appropriators collaborate with the House Transportation, Housing, and Urban Development Appropriations Subcommittee to resolve the 2018 complaint against the Department of Transportation regarding animal research transportation.[8]

<u>Reducing Administrative Burden</u>

To maximize federal investments and foster accountability with stakeholders, we recommend the House LHHS Appropriations Subcommittee include language that directs NIH to provide a list of

[5] National Institutes of Health Office of Research Infrastructure Programs, "Nonhuman Primate Evaluation and Analysis. Part 1: Analysis of Future Demand and Supply." 2018. https://orip.nih.gov/sites/default/files/508 NHP Evaluation and Analysis Final Report - Part 1 Update 30Oct2018_508.pdf

[6] *The New York Times*, "Future Vaccines Depend on Test Subjects in Short Supply: Monkey." February 2021. https://www.nytimes.com/2021/02/23/business/covid-vaccine-monkeys.html

[7] Senate Explanatory Statement for Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations Bill 2022. Summary of Budget Estimates and Committee Recommendations. https://www.appropriations.senate.gov/download/lhhsrept_final2.

[8] National Association for Biomedical Research v. United Airlines, Inc., British Airways, PLC, China Southern Airlines Co., Ltd. and Qatar Airways Company, Q.C.S.C. DOT-OST-2018-0124. https://www.regulations.gov/docket/DOT-OST-2018-0124.

steps the agency intends to take over the next year to reduce investigator burden; this should be accompanied by implementation timelines and planned strategies for communicating new information with the extramural community. A central tenet of the bipartisan 21st Century Cures Act was to accelerate biomedical research to improve human health and reduce the administrative burden animal researchers experience to provide more time to conduct research. As outlined in the 2018 Federal Demonstration Partnership Faculty Workload Survey, investigators spend nearly half (44.3 percent) of their research time consumed by regulatory burden.[9] This is particularly problematic for small institutions that have limited staff and resources. Due to lack of clear guidance from funding agencies, many institutions enforce additional policies for fear of non-compliance with federal regulations and policies. While we appreciate Congress's support for this law and NIH's ongoing efforts to address inconsistent policies related to animal research, several policy concerns remain unaddressed more than five years after the law's enactment.

Continued investments in animal research are essential for maintaining U.S. scientific leadership, upholding national security, and improving the quality of life for humans and animals alike. The biomedical research community urges the House LHHS Appropriations Subcommittee to sustain support for large animal research and ensure the availability and transportation of nonhuman primates. Importantly, federal support for these areas should be coupled with policies that enhance rather than hinder research productivity, as administrative burden continues to unnecessarily delay critical research studies and, therefore, improved human and animal health.

Sincerely,

American Academy of Neurology (AAN)
American Association for Laboratory Animal Science (AALAS)
American Association of Universities (AAU)
American Association of Veterinary Medical Colleges (AAVMC)
American Federation for Medical Research (AFMR)
Americans for Medical Progress (AMP)
American Heart Association (AHA)
American Physiological Society (APS)
American Psychological Association (APA)
American Society for Bone and Mineral Research (ASBMR)
American Society for Investigative Pathology (ASIP)
American Society for Nutrition (ASN)
American Society of Laboratory Animal Practitioners (ASLAP)
American Society for Pharmacology and Experimental Therapeutics (ASPET)
American Veterinary Medical Association (AVMA)
Association of American Medical Colleges (AAMC)
Association for Research in Vision and Ophthalmology (ARVO)
Association of Primate Veterinarians (APV)
Association of Public and Land-Grant Universities (APLU)
California National Primate Research Center (CNPRC)
Columbia University Irving Medical Center
Emory National Primate Research Center (ENPRC)
Environmental Mutagenesis and Genomics Society (EMGS)

[9] Federal Demonstration Partnership. 2018 Faculty Workload Survey. Research Report: Primary Findings. Accessed May 2022. https://thefdp.org/default/assets/File/Documents/FDP FWS 2018 Primary Report.pdf

Federation of American Societies for Experimental Biology (FASEB)
Federation of Associations in Behavioral and Brain Sciences (FABBS)
National Association for Biomedical Research (NABR)
New Jersey Association for Biomedical Research (NJABR)
Northwest Association for Biomedical Research (NWABR)
Oregon Health Sciences University (OHSU)
Oregon National Primate Research Center
Public Responsibility in Medicine and Research (PRIM&R)
Society for Neuroscience (SfN)
Society for Redox Biology and Medicine (SfRBM)
Society for the Study of Reproduction (SSR)
Society of Toxicology (SOT)
Southwest National Primate Research Center (SNPRC)
Texas Biomedical Research Institute
The American Brain Coalition
The Jackson Laboratory (JAX)
The Shock Society
Understanding Animal Research
University of Colorado Anschutz Medical Campus
University of Pittsburgh
University of Washington
Washington National Primate Research Center (WaNPRC)
Yale University