The Honorable Roy Blunt
Chair
Senate Appropriations Subcommittee
on Labor, Health and Human Services,
Education, and Related Agencies
260 Russell Senate Office Building
United States Senate
Washington, DC 20510

The Honorable Patty Murray
Ranking Member
Senate Appropriations Subcommittee
on Labor, Health and Human Services,
Education, and Related Agencies
260 Russell Senate Office Building
United States Senate
Washington, D.C. 20510

November 4, 2020

Dear Chairman Blunt and Ranking Member Murray,

The American Society for Pharmacology & Experimental Therapeutics (ASPET) is concerned about report language accompanying the House FY 2021 Labor-HHS Appropriations bill that targets federally-funded researchers' work with nonhuman primates (NHP). The language duplicates recent oversight efforts and does not acknowledge the critical role of NHP in biomedical research. ASPET urges the committe not to include similar language in its bill.

ASPET is a 5,000-member scientific society whose members conduct essential basic and clinical pharmacological research and are employed by academia, government, large pharmaceutical companies, small biotech companies, and non-profit organizations. ASPET members work in a variety of different fields and their efforts help to develop new medicines and therapeutic agents to fight existing and emerging diseases.

The House committee report language calling for the National Institutes of Health (NIH) to provide a report on efficient and effective alternatives to the use of NHP in its intramural research programs is duplicative of ongoing efforts by NIH to review and assess the need for NHP models. In 2016, NIH held a workshop in response to congressional interest to explore the state of NIH-supported biomedical and behavioral research involving NHP. Researchers, bioethicists, veterinarians, and policymakers—as well as the general public—provided NIH with input on the state of scientific research, ethical concerns, a review of best practices, and a need for alternative models, where appropriate. In February of this year, NIH held another workshop aimed at fostering rigor and reproducibility in NHP research. This workshop emphasized the importance of rigorous experimental design so that research with NHP is necessary, efficient and ethical. Additional reports represented by the House committee language are unlikely to produce any new information on this subject at this time.

In addition to NIH's review of its use of NHP, this research is also governed by a robust regulatory infrastructure that provides strict oversight and accountability. Under the Animal Welfare Act and Public Health Service Policy, research using vertebrate species must be monitored and approved by an official Institutional Animal Care and Use Committee (IACUC). IACUCs inspect an institution's animal facilities, review

and approve activities related to the care and use of animals, and are authorized to suspend activities involving animals, including NHP. IACUCs provide assurance to the public and scientific community that research with animals is legitimate and necessary, and is carried out in an ethically responsible and humane manner. Any unauthorized activities must also be reported back to the Office of Laboratory Animal Welfare at NIH and can directly impact the funding of that research.

Though the vast majority of research with animals takes place with rats and mice, NHP are generally considered the best available animal models for addressing particular research questions because of their close phylogenetic and physiological relationship with humans. Research with NHP has produced enormous advancements in the treatment of diseases and understanding of human health, including the development of the first Hepatitis-B vaccine and a treatment for cataracts in children. Research with NHP is often an essential component for Investigational New Drug (IND) and New Drug Applications (NDA) submissions to regulatory agencies given the prevelance of species-dependent differences in drug exposure and efficacy. And there are many current challenges for which NHP represent the best model for research that could yield enormous breakthroughs. Currently, the use of NHP in research is vital as evidenced by the following examples:

Opioid Epidemic: The opioid epidemic continues and, according to most indicators, has worsened significantly during the pandemic. Drug effects in NHP are the most predictive model of abuse-related effects in humans, both for substances that are abused and for medications to treat substance use disorders. Monoclonal antibodies (mAbs) that rapidly neutralize potentially lethal opioids are being evaluated in NHP and could provide an improved approach for preventing and reversing opioid overdose and abuse. A single dose of new ultra-long acting antagonists blocks the euphoric and toxic effects of opioids for a week or longer in NHP. Still other studies with NHP are discovering new drugs for treating pain that lack the euphoric and dependence producing effects of opioids.

Cancer**:** Biologics like mAbs are also becoming the cornerstone of cancer treatment due to their high specificity for their target and low potential for off-target toxicity. To test the safety of highly-specific human mAbs, NHP are the best animal model to show how these therapies will bind and engage the target to a similar extent as that anticipated in humans. mAbs and similar therapies now make up a significant portion of the drugs in the pipelines of most large biopharmaceutical companies.

Infectious Diseases: Research with NHP is responsible for the ongoing development of therapeutics and vaccine candidates to combat SARS-CoV-2. Before the antiviral therapeutic remdesivir was approved for use by humans by the Food and Drug Administration, it was tested for safety and efficacy in a NIH-funded intramural study using rhesus macaques. Another recent preprint study using the same nonhuman primate animal model showed prophylactic and therapeutic effects of monoclonal antibodies to treat SARS-CoV-2.

Developmental Toxicology: In pregnant women, the Zika virus (ZIKV) can cause miscarriages and congenital malformations. Initially, research on ZIKV was hampered by a lack of relevant *in vivo* experimental models. However, the use of NHP in developmental and reproductive toxicology testing is becoming more common because NHP respond to biological toxins (e.g. virusus) and drugs in a manner that is similar to and highly predictive of responses in humans. The recent development of NHP models has allowed researchers to replicate human ZIKV infection allowing them to study transmission and pathogenesis. Futher research in NHP may contribute to the development of treatments to counteract ZIKV.

Though some proponents of scaling back the use of NHP in research point to computational models as an alternative to animal models, presently those models do not sufficiently simulate the complexities of human behavior, drug, and immune responses. The necessity for NHP for biomedical research is critical given the acute need for therapeutics and vaccines to ameliorate the ongoing effects of the global pandemic.

Research with NHP is key to helping us understand and improve human health, and patients have reaped—and will continue to reap—dramatic benefits as a result of this research. ASPET supports efforts to reduce, refine, and replace animal models, including NHP, when that is in the best interest of public health. However, until suitable replacements are available,

research with NHP is a nececessary and vital tool for biomedical research. ASPET requests that your committee oppose the inclusion of the House FY 2021 Labor-HHS Appropriations report language in the Senate bill or report.

Respectfully,

Charles France, Ph.D.
President
ASPET