National Association *for* Biomedical Research

Non-Human Primates (NHPs) in Biomedical Research

BACKGROUND: Non-human primates (NHPs) remain a critical resource for the United States biomedical research enterprise. However, the U.S. Fish and Wildlife Service has denied the export of any NHP originating from Cambodia, as well as any tissue sample or blood serum sample from any research animal originating from Cambodia. These models represent 60% of the preclinical research being conducted in the United States. The federal government and the scientific community should continue to work together to develop and validate non-animal test methods where scientifically feasible, but also must work to mitigate a pressing issue facing biomedical research in the United States: the NHP model supply chain crisis. Addressing this crisis is necessary and urgent to ensure the United States remains the global leader in biomedical research, but more importantly, to ensure treatments will be developed for the thousands of unmitigated diseases affecting Americans. The drug development pipeline is grinding to a halt.

NHPs Are a Critical Resource for the Development of Medications and Treatments in the U.S.

- Before a drug or vaccine can be evaluated in the clinic on humans, the FDA often requires testing in two animal species, including one rodent and non-rodent species, to test the safety and efficacy of a drug[1]. Although they represent less than ½ of 1 percent of all animals in biomedical research, non-human primates (NHPs) remain key animal models for specific types of biomedical research because of their close genetic, physiological, and behavioral similarities to humans.

- We support efforts to replace, reduce, and refine the use of animals in drug and vaccine development. However, new drug and vaccine testing technologies to realize this vision at a broad scale and that meet regulatory acceptance are still many years away.

- There are estimated to be 17,752 individual products currently in the US R&D pharmaceutical pipeline, accounting for 47% of the global R&D pipeline.[2] Of these, it is estimated that 56% have used or will require use of NHPs during their development.[3] If NHPs are no longer available, these preclinical drug projects will grind to a halt- this includes drugs for cancer, diabetes, and neurodegenerative diseases, as well as vaccines..

Research Primate Shortage in the U.S. & Global Scientific Competitiveness

- On average, the U.S. imports approximately 30,000 purpose-bred nonhuman primates for research purposes annually, with the majority coming from Vietnam, Cambodia, and the island of Mauritius.[4]

---

[1] International Conference on Harmonization ICHM3(R2): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/m3r2-nonclinical-safety-studies-conduct-human-clinical-trials-and-marketing-authorization

[2] EvaluatePharma database, January, 2021 https://info.evaluate.com/rs/607-YGS-364/images/Evaluate_World_Preview%20Report_Final_30-09.pdf

[3] PhRMA Biopharmaceuticals in Perspective, Fall, 2020 : https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/ChartPack_Biopharmaceuticals_in_Perspective_Fall2020.pdf

[4] Animal Research in a Global Environment: Meeting the Challenge, National Academies, 2011, available online at: https://nap.nationalacademies.org/catalog/13175/animal-research-in-a-global-environment-meeting-the-challenges-proceedings

National Association *for* Biomedical Research

- Escalating tensions between the U.S. and China and the COVID-19 pandemic have stopped the import of monkeys from China. At the onset of the pandemic, China implemented a ban on wildlife trade, including the exportation of research primates to other countries.

- China is importing research NHPs from southeast Asia too, in addition to their domestic resources of NHPs, and this reduces the number of NHPs available to the U.S. and Europe even more.[5] This presents yet another hurdle that only makes it more pressing to find a solution to the NHP shortage we are experiencing.

- The Biden Administration has made U.S. domestic biotechnology and biomanufacturing a national priority, particularly for the security of U.S. supply chains. In September 2022, President Biden signed an executive order for advancing U.S. biotechnology and biomanufacturing innovation by announcing a national strategy and new investments to boost innovation and reduce reliance on foreign suppliers.[6] The Administration also pledged more funding for America's primate research centers as a critical element for bioresearch with the NIH's support.

National Security Issue

- A lack of NHP resources may ultimately lead to Chinese supremacy in pharmaceutical countermeasure R&D:
    - The Biomedical Advanced Research and Development Authority (BARDA), whose mission it is to develop medical countermeasures to address public health threats including chemical, biological, radiological and nuclear accidents, pandemics and emerging infectious diseases, studies SARS, MERS, COVID-19 and other emerging infectious diseases thanks to research monkeys.

    - Likewise, many Department of Defense (DOD) and DOD-funded entities are conducting research with NHPs to study COVID-19 and other infectious diseases.

- China is establishing itself as an international hub of primate research and has invested heavily in NHP breeding operations. In addition, China has made it a national priority to top the United States in biomedical research by 2035 – and become the international leader in science by 2050[7].

[5]Supply and Use of NHP Around the World (subsection) https://www.ncbi.nlm.nih.gov/books/NBK91434/
[6]https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/
[7] "China's overarching national goals to become an "innovative nation" by 2020, be in the "front ranks" of innovative countries by 2035, and a "global scientific power" by 2050." From CGTN News, September 27, 2021, available online at https://news.cgtn.com/news/2021-09-27/Technology-and-innovation-in-China-s-Path-to-2035-13pFsrWVOdq/index.html

National Association *for* Biomedical Research

Transportation of NHPs for Biomedical Research

- In 2011, animal activist campaigns began to pressure major airlines to stop carrying research animals resulting in most airlines refusing transport of research animals and forcing the biomedical research community to utilize other means of transportation, including charter flights and ground transportation. These methods are significantly more costly and time-consuming, leaving researchers unable to keep up with the demand for vital animal models.

- All airline carriers must abide by the International Air Transportation Association's (IATA) guidance, which remains the worldwide standard for ensuring safe animal transport. Accordingly, the IATA Manual indicates that animal transportation is safe when detailed container, feeding, and water protocols are followed (Ch. 8, 210-408). Furthermore, scheduled flights are frequently designed to take the shortest time possible, resulting in less overall stress on animals.

- Considering that good science and animal welfare are complementary objectives, transportation methods that minimize stress and enhance animals' ability to sustain travel are essential for preserving animal health and strengthening critical research necessary for scientific growth. Scheduled air transportation is both cost-effective and can be in the best interest of animal welfare given its often shorter duration with rigorous oversight.

- Airline restrictions continue to endanger the nation's global competitiveness as world leaders in scientific discoveries and limit researchers' access to appropriate animal models. As other nations accelerate investments in research and development, we are concerned that leaving this issue unresolved will unnecessarily delay U.S. research productivity and weaken our nation's ability to respond to future public health crises.

- In 2018, the National Association for Biomedical Research, on behalf of 160 research organizations, filed a USDOT complaint (Docket No. DOT-OST-2018-0124, NABR v. United Airlines et al) alleging violation of common carrier obligations and discrimination of cargo following the refusal of certain airlines to transport animals for research purposes.[8] To this day, the Department of Transportation (DOT) has taken no action.

[8]USDOT complaint (Docket No. DOT-OST-2018-0124, NABR v. United Airlines et al) https://www.nabr.org/about-nabr/news/nabr-dot-complaint-makes-headlines

National Association *for* Biomedical Research

Importation Issues Are Halting the Drug Development Process

The supply of NHPs coming out of Cambodia (about 60% of the market), has come under scrutiny following a Department of Justice (DOJ) indictment on November 16, 2022, alleging that eight Cambodian individuals (representatives of a Cambodian NHP supplier and two Cambodian officials) were illegally importing wild-caught NHPs into the United States as captive bread animals. NABR denounces any illegal importation.

As part of its ongoing investigation, DOJ and the Fish and Wildlife Service (FWS, which has jurisdiction over the importation of NHPs) have proposed new DNA testing requirements for all imports to affirm the animals are NOT wild caught. This has stopped the release of thousands of animals currently in the US completing their quarantine period and future imports.

NABR supports US efforts to ensure that NHPs are not illegally entering the US research supply chain; however, this new requirement, which is beyond the Convention on International Trade in Endangered Species of Wild Fauna and Flora ("CITES") criteria, will freeze the supply chain for up to two years while such a testing regime can be established[9].

According to PhRMA, it takes roughly 10-15 years and $2.6 billion to develop one new medicine. These issues are depriving Americans of the treatments they need most. Therefore, a bridge is necessary to address the concerns of today while allowing time to establish a new DNA testing process. Such an interim step could be to follow current regulations that are consistent with guidance issued by the CITES Secretariat[10] for inspection of captive breeding facilities and require audits to confirm that a supplier currently has—and in the past has had—the appropriate number of NHPs on its farm for breeding purposes to be able to produce the number of juvenile NHPs that are to be shipped into the U.S.

We ask that USFWS and other USG stakeholders with national security and biomedical infrastructure concerns work together to develop a scientifically and logistically justifiable path forward.

---

[9] New testing regimes will take significant time to establish due to the nature and structure of breeding facilities, which are different environments from quarantine and lab facilities. Breeding facilities house the animals socially, often with hundreds of animals tighter, making it both a dangerous and time-consuming undertaking (both to the animals and the human handlers) to locate, isolate and sedate individual animals to obtain a blood samples, especially from large and aggressive males. Sedatives are controlled substances which often require advanced purchase order and purchase limits. In addition, breeding facility staff need to be expanded and trained to perform blood draws and collect, document, and transport samples internationally, without delay or loss of integrity.

[10] *See* CITES Secretariat, Guidance for Inspection of Captive Breeding and Ranching Facilities (Feb. 2017), available at https://cites.org/sites/default/files/eng/prog/captive_breeding/E-InspectionGuidance-FINAL.pdf ("provid[ing] a general framework for national CITES Management and Scientific Authorities, and other relevant agencies, to assist in assessing facilities claiming to produce captive-bred and/or ranched specimens and evaluating their capacity to produce the numbers of specimens being traded each year").