United States Senate
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
WASHINGTON, DC 20510–6300

July 19, 2023

VIA ELECTRONIC TRANSMISSION

The Honorable Joseph R. Biden, Jr.
President of the United States
The White House
1600 Pennsylvania Ave
Washington, D.C. 20500

Dear President Biden:

I am deeply concerned about the critical shortage of non-human primates (NHPs) used for biomedical research, and the negative implications this shortage will have for patients and on our reliance on China. The NHP shortage compromises our ability to create new medicines, jeopardizing our preparedness for potential public health threats. Actions by the U.S. Fish and Wildlife Service (FWS), along with the U.S. Department of Justice (DOJ), have caused this shortage. These actions run counter to the administration's stated goals of securing supply chains that power the American bioeconomy.[1] It is critical that your administration work with urgency to address this problem.

NHPs are integral to the development of new therapies for patients. Animal testing is commonly used to create new medicines and assess whether potential medicines are safe to be given to humans in clinical trials. Manufacturers often hire contract research organizations (CROs) to conduct such animal testing. For certain types of drugs, manufacturers rely on NHPs because of their close genetic relationship to humans. Indeed, U.S. Food and Drug Administration (FDA) officials recognize that many biologics should be tested in NHPs because those biologics only show their intended activity in primates, and not other types of animals.[2] At the direction of Congress, the National Academies published a report last month finding that for several areas of biomedical research, NHPs "are regarded as the best available model to reproduce the human

[1] Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy, EO 14081 (Sept. 12, 2022).
[2] *See, e.g.*, U.S. Food and Drug Administration, *CDER overview of Non-Human Primate (NHP) use in drug development and pathways for the qualification of New Alternative Methods (NAM)* at slide 9, https://www.nationalacademies.org/documents/embed/link/LF2255DA3DD1C41C0A42D3BEF0989ACAECE3053A6A9B/file/DE8A40CC45A67F0139A353BD9927B131C9ECDB570A38?noSaveAs=1.

condition."[3] NHPs are especially important to support cutting-edge products for cancer, sickle cell, and other debilitating diseases.

Prior to the current shortage, estimates show that more than 20 percent of all NHPs used in biomedical research in the U.S. came from Cambodia, including 60 percent of our imported supply of NHPs.[4] Prior to 2020, the United States relied on China for a huge proportion of the NHPs used in research. According to FDA, China was the largest supplier of NHPs used in pharmaceutical development—60 percent of NHPs imported into the U.S. came from China.[5] However, in early 2020, China halted exports of NHPs.[6] China instituted this ban to halt the spread of the COVID-19 virus and retain this supply for its own biomedical research needs, and it remains in effect today. In response, American firms looked to Cambodia, Mauritius, Vietnam, Indonesia, and the Philippines for new suppliers, with a significant majority—around 60%—coming from Cambodia alone.[7]

The events that led to the current NHP shortage began with an investigation conducted by DOJ and FWS. On November 16, 2022, DOJ announced that it indicted multiple individuals, including two officials from the government of Cambodia, for the alleged smuggling of wild-caught primates that were falsely presented as captive-bred primates.[8] In February 2023, two leading U.S. CROs reported that they received subpoenas from DOJ related to this investigation.[9]

Since November 2022, I understand that FWS has effectively halted the import of NHPs from Cambodia by refusing to grant the required permits. This has also impacted the export of tissue, blood, and other specimen samples collected from Cambodian NHPs to laboratories located out of the United States (a common practice). As part of the ongoing investigation, stakeholders have conveyed that FWS has proposed new DNA testing requirements to verify that the animals presented for import were not caught in the wild.[10] But these requirements are opaque, and we are not aware of FWS vetting these requirements with stakeholders or other agencies to ensure that they are feasible from a scientific, cost, and logistical perspective. Moreover, it is unclear

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[3] *Nonhuman Primate Models in Biomedical Research: State of the Science and Future Needs, National Academies of Sciences, Engineering, and Medicine* at ix (May 2023), https://www.nationalacademies.org/our-work/nonhuman-primate-model-systems-state-of-the-science-and-future-needs.

[4] The 20 percent estimate is based on numbers from the U.S. Department of Agriculture's 2021 research facilities annual report, available at https://www.aphis.usda.gov/animal_welfare/downloads/annual-usage-summary-report.xlsx. *See also* The Wall Street Journal, *Monkey Business Threatens U.S. Drug Discovery* (March 3, 2023), https://www.wsj.com/articles/monkey-business-threatens-u-s-drug-discovery-e9e71409?ns=prod/accounts-wsj.

[5] U.S. Food and Drug Administration, 87 Fed. Reg. 10373, 10374 (Feb. 24, 2022).

[6] *Id*.

[7] Centers for Disease Control and Prevention, *Nonhuman Primate Importation and Quarantine United States, Fiscal Year 2022*, Presentation to the Association of Primate Veterinarians Annual Workshop (Oct. 21, 2022).

[8] *Cambodian Officials and Six Co-conspirators Indicted for Taking Part in Primate Smuggling Scheme*, U.S. Attorney's Office, Southern District of Florida (Nov. 16, 2022), https://www.justice.gov/usao-sdfl/pr/cambodian-officials-and-six-co-conspirators-indicted-taking-part-primate-smuggling-0.

[9] *See* Charles River Laboratories International, Inc., Form 10-K for Fiscal Year 2022 (filed Feb. 22, 2023); Inotiv, Inc., Form 10-Q (filed Feb. 14, 2023).

[10] Because FWS has not published any rulemaking, guidance, or other public-facing information on the requirements that it is imposing through its review of individual permit applications, and has failed to respond to questions posed to the agency on this topic, we are left to rely on representations made by stakeholders about their experience in applying for permits from FWS.

when companies will be able to establish testing regimes that could comply with such requirements. The result may be disruptions in research that could last months, or even years.

Based on information from researchers, I understand that FWS' actions have disrupted studies needed for drug development. The shortage of available NHPs has also increased the costs to develop drugs. I also understand that innovators are now turning to other countries, including China, to conduct the time-sensitive research needed to bring new medicines to patients.

Unfortunately, FWS has failed to respond to multiple attempts to obtain more information about this problem and how FWS is working with other agencies to solve it. FWS has ignored repeated follow-up requests from staff for information about the FWS DNA testing requirements, whether or not there is a *de facto* ban in place on imports from Cambodia, and how FWS envisions resolving this issue, in addition to questions seeking factual information about NHP import trends. And I have yet to receive responses to questions on this issue that I submitted to the Department of the Interior in connection with Secretary Haaland's appearance before the Senate Committee on Energy & Natural Resources on May 2, 2023. Multiple stakeholders have raised similar concerns about the lack of responsiveness and transparency from FWS.

While our country seeks to reduce the need for NHP testing over the long term, NHP testing is still critical to ensuring that patients have safe, effective drugs. Cambodia is a major source of NHPs, and DOJ and FWS need to work with stakeholders to avoid disruptions to important studies. We cannot cede global leadership in biomedical research to China by allowing China to establish a near-monopoly on NHP research. It is imperative that the White House ensure that all relevant agencies are coordinating to solve this problem, and that these agencies are transparent with Congress about their efforts.

I ask that you answer the following questions on a question-by-question basis by **August 11, 2023**:

1. What intergovernmental conversations have taken place on this topic, on which dates, and which agencies were involved? More specifically, please identify the conversations that DOJ and FWS have had with FDA and the National Institutes of Health about the impact of this investigation on biomedical research. Please also identify conversations in which the White House has been involved, and the specific White House offices that participated.

2. Since November 16, 2022, when DOJ indicted officials with the Cambodian government, how many permit applications related to such NHPs has FWS received, and how many has FWS granted?

3. What is the current status of the import of NHPs for biomedical research from Cambodia, and the export of samples derived from such NHPs?

4. For parties who wish to import primates from Cambodia into the United States, including parties that may be included within the scope of the ongoing investigation, what are the specific requirements or case-by-case requests (particularly those related to DNA testing to establish parentage) that such parties will need to follow, in addition to complying with the

Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), for a shipment to be accepted by FWS for import?

5. Which external organizations has FWS met with to receive technical feedback on such requirements or considerations for case-by-case requests? Please provide a list of such organizations, and the dates of such meetings.

6. Why has FWS not published new rules or guidance documents to help facilitate the lawful import of monkeys from Cambodia, to help avoid the negative consequences seen with the current investigation?

7. How and when does FWS envision its new requirements or considerations for case-by-case requests being made public or shared with importers?

8. How is FWS working with DOJ to resolve this investigation? What is the relationship between the date of DOJ investigation resolving and the publication of FWS's new requirements or considerations for case-by-case requests?

9. What percentage of imports of primates into the United States come from Cambodia? Please provide this data for each of the past five years.

Thank you for your attention to this letter.

Sincerely,

Bill Cassidy, M.D.

Bill Cassidy, M.D.
United States Senator

Copy:

The Honorable Debra Haaland
Secretary, U.S. Department of the Interior

Martha Williams
Director, U.S. Fish and Wildlife Service

Dr. Robert Califf
Commissioner, U.S. Food and Drug Administration

Dr. Lawrence A. Tabak
Acting Director, National Institutes of Health