28 June 2022

Dear Dr. Panjabi, Dr. Califf, and Ms. O’Connell:

Monkeypox is the first major test of the U.S. government’s pandemic response capabilities since the emergence of SARS-CoV-2, the virus that causes COVID-19. Many of the same problems of bureaucratic incoordination and inertia within the federal government that slowed access to diagnostics, therapeutics, and vaccines for COVID-19 are now unnecessarily inhibiting the deployment of these medical countermeasures for monkeypox.

This letter focuses on ending the current shortage of the JYNNEOS monkeypox and smallpox vaccine in the United States (based on the replication incompetent Modified Vaccinia Ankara - Bavarian Nordic platform), which is the currently preferred option for monkeypox vaccination given its FDA approval for monkeypox, ease of administration and superior adverse event profile compared to ACAM2000.

Since 2007, Americans have spent over $2 billion of taxpayer money to develop, manufacture and stockpile doses of JYNNEOS as part of a federal biosecurity program. Currently the U.S. Government owns more than a million doses—enough to fully vaccinate more than 500,000 people—of JYNNEOS that are filled, finished and ready for administration.

---

1 See U.S. Government Definitive Contracts between the U.S. Department of Health and Humans Services and Bavarian Nordic A/S; Procurement Instrument IDs: HHS0100200700034C (start date 4 June 2007, total amount awarded to date USD $1,510,761,647.00) and HHS0100201700019C (start date 27 Sept 2017, total amount awarded to date USD $517,342,656.00).

2 Conversation Between J. Krellenstein (PrEP4All) and Senior BARDA Official on June, 24 2022.

www.prep4all.org
However, as the monkeypox outbreak spreads uncontained in the gay, bisexual and trans communities in the United States, members of at risk communities are being turned away from monkeypox vaccination because these vaccines are not available in sufficient quantity in the U.S., but instead sitting in freezers in Denmark.

We must not allow the same failures of vaccine production and distribution that hampered the global COVID-19 response cause us to fail to contain the current monkeypox outbreak. We write with three urgent actions the administration must take rapidly to ensure adequate short- and long-term supply of the JYNNEOS monkeypox vaccine, domestically and globally.

I. Free the more than 1 million filled and finished monkeypox vaccine doses from the U.S. stockpile in Denmark

Presently, the U.S. owns more than 1 million doses of JYNNEOS monkeypox vaccine that are filled, finished, labeled, packaged, and in freezer storage at a Bavarian Nordic facility in Denmark. On June 22, the CDC reported these doses will be delivered sometime “this year”. This timeline is unacceptable. According to a senior BARDA official, the reason the U.S. government cannot distribute these doses immediately is because the U.S. Food and Drug Administration (US FDA) failed to conduct a timely inspection of the Bavarian Nordic facility and therefore allowed its Current Good Manufacturing Practices (cGMP) certification to expire.

However, the European Medicines Agency (EMA) did inspect the Bavarian Nordic facility precisely a year ago and deemed the facility to be in compliance with cGMP standards. Of course, the US FDA and the EMA executed a mutual recognition agreement regarding cGMP inspections—allowing each agency to recognize each other's cGMP inspection without inspecting a facility themselves—on 2 March 2017. However, the US FDA and EMA have delayed extending this agreement to vaccine drug substance and product (ostensibly due to the COVID-19 pandemic) despite being required by agreement to notify each other of a decision on this issue by 15 July 2022.

Therefore, it is likely that either the US FDA will soon be able to recognize an EMA cGMP certification without having to perform its own inspection or will be able to successfully inspect
the facility, resulting in the US FDA cGMP certification needed to finally distribute more than a
million doses of vaccine.

_Therefore_, to ensure that the entirety of the filled-and-finished 1+ million dose JYNNEOS
stockpile is out of the facility in Denmark and ready for distribution in the U.S. by July 7,
2022, President Biden should use all authority to either:

a) Immediately recognize the European Medicines Authority’s cGMP certification of the
Bavarian Nordic facility pursuant to the United States–European Union Amended
Sectoral Annex For Pharmaceutical Good Manufacturing Practices (GMPs) or,

b) Direct the US FDA to immediately conduct a cGMP inspection of this facility

II. Liquid fill and finish the 15 million+ additional doses of bulk drug substance currently
in the U.S. stockpile in Denmark

Presently, the U.S. owns at least 15 million additional doses—enough to vaccinate at least 7.5
million more people—of JYNNEOS bulk vaccine drug substance in storage at the Bavarian
Nordic facility in Denmark. These doses are not filled and finished in vials, however. The U.S.
has not contracted with any manufacturing partner to fill and finish this available drug substance
so that all 15.8 million doses may be distributed.

Bavarian Nordic itself has committed to fill and finish just 500,000 doses from this drug
substance stockpile by the end of this year. In May, BARDA executed an option with Bavarian
Nordic to lyophilize (freeze dry) 13.8 million doses from this drug substance stockpile for
long-term storage. However, because this process will start in 2023 and not be completed until
as late as 2025,⁸ BARDA should order a pause of its lyophilization campaign with Bavarian
Nordic, and ensure that the bulk vaccine drug substance is preserved in a form compatible with
liquid fill and finish.

To ensure that the remainder of the U.S. government’s JYNNEOS vaccine drug substance
stockpile is rapidly filled-and-finished, BARDA should work with Bavarian Nordic to estimate its
capacity to rapidly fill-and-finish additional vaccine doses beyond its current 500,000 dose
commitment.

If Bavarian Nordic can not rapidly fill-and-finish all 15 million doses of the JYNNEOS vaccine,
BARDA, Bavarian Nordic, and the FDA should form a joint task force to rapidly find US FDA
cGMP certified partners capable of doing so for the remaining doses.

⁸ https://www.globenewswire.com/en/news-release/2022/05/18/2445603/0/en/Bavarian-Nordic-to-
Manufacture-First-Freeze-dried-Doses-of-Smallpox-Vaccine-upon-Exercise-of-Contract-Option-
by-the-U-S-Government.html
If the US Government commits sufficient resources to this effort, rapidly filing and finishing these doses will likely be successful.

Therefore, President Biden should use all authority to:

a) Ask Bavarian Nordic to immediately pause efforts to lyophilize the United States’ bulk JYNNEOS drug substance stock, preserve it in a form compatible with liquid fill and finish, and work with Bavarian Nordic to rapidly assess their ability to fill and finish the remaining doses by the end of August, 2022.

Bavarian Nordic has committed to only liquid fill and finish 500,000 additional doses of JYNNEOS out of bulk drug substance. As late as June 10, 2022, Bavarian Nordic publicly indicated that it still plans on lyophilizing 13 million US owned doses of JYNNEOS, rather than liquid fill and finish these doses. If Bavarian Nordic cannot liquid fill and finish the remaining doses of JYNNEOS, BARDA and US FDA must work together with other partners to find a US FDA approved cGMP liquid fill and finish facility or facilities capable of filling and finishing these doses as fast as possible.

b) Rapidly assess whether BARDA’s Fill Finish Manufacturing Network (FFMN) can be utilized to rapidly fill and finish JYNNEOS bulk vaccine drug substance.

Starting in 2012, BARDA has awarded over $40 million in contracts to four contract development and manufacturing organizations (CDMOs) to establish the Fill Finish Manufacturing Network (FFMN). According to BARDA, the FFMN is able to fill and finish up to 117 million pandemic influenza vaccine doses in 12 weeks — an average throughput of 9.75 million doses per week. Assuming this average throughput could be achieved, and JYNNEOS bulk drug substance is compatible with the FFMN, the entire JYENNOS bulk drug substance of the US inventory could be filled and finished in less than two weeks. US FDA, BARDA and FFMN partners should work rapidly with Bavarian Nordic to determine whether JYNNEOS can be filled within the FFMN.

c) Rapidly identify additional fill and finish partners for the remainder of the 15.8 million JYNNEOS doses.

If neither Bavarian Nordic nor the FFMN can rapidly fill and finish drug substance, BARDA and the U.S. FDA must work rapidly to identify global US FDA cGMP certified CDMO or originator slack liquid finish capacity that could be rapidly utilized to fill and

---

finish the remainder of the 15.8 million JYNNEOS doses. A rapid surge in fill-finish capacity for JYNNEOS should be possible, as evidenced by the rapid expansion of fill-finish capacity for COVID-19 vaccines. For example, Moderna and its drug substance manufacturing partner Lonza did not utilize their own fill and finish capacity for producing the Moderna vaccine. Rather, Moderna utilized Catalant (an FFMN partner) for the U.S. vaccine supply and Rovi for the European Union and global supply. Despite the Moderna vaccine being a novel drug substance, these CDMO partners scaled capacity rapidly, building hundreds of millions doses per year of fill and finish capacity in less than 3 months. As demand for COVID-19 vaccines has dropped dramatically, there has been a dramatic increase in “slack” full and finish capacity.

III. Establish a manufacturing network for JYNNEOS vaccine drug substance production via tech transfer, licensing, and manufacturing investments to meet global need

To ensure global monkeypox vaccine needs are met, the FDA, BARDA, and Bavarian Nordic form a joint task force that evaluates existing drug substance manufacturing facilities that have the requisite ability to manufacture JYNNEOS vaccine drug substance.

The FDA should immediately release draft guidance on which immunological bridging studies need to be performed given the variations in manufacturing. This is necessary to move manufacturing from originators to contract manufacturing organization facilities. This can likely be done expeditiously, as the correlates of immune protection for smallpox and monkeypox vaccines have already been characterized.

Within 8 weeks, the FDA should make a recommendation to the administration as to which contract manufacturing organizations or originators can receive technology transfer and begin manufacturing scale-up.

We kindly request a meeting with you at your earliest convenience.

Thank you.

Sincerely,

James B. Krellenstein
Co-Founder & Managing Director, Strategy & Policy
PrEP4All Inc.

Garrett Wilkinson, MSPH, MSc
Government Relations & Policy Officer
Partners In Health