

# Vaccine “Dose-Sparing” Update

## Public Health Emergency Explainer

PrEP4All’s M-Pox Alert is a weekly bulletin containing key information for activists, advocates and impacted communities on the evolving response to the monkeypox in the United States and worldwide. We will issue our alerts weekly, updating key data points and progress on action steps.

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### PrEP4All M-Pox Community Monitoring Project

PrEP4All has a community monitoring project focused on access to monkeypox testing, vaccines, and treatments in the United States; we encourage activists and impacted people in diverse communities in the US and in other countries to reach out to share tools, information and updates as we track this outbreak.

## Vaccine Supply and “Dose-Sparing” Update

*What is the dose-sparing approach?*

On August 9th, five days after the United States Department of Health and Human Services declared the US monkeypox outbreak a State of Emergency (see “Public Health Emergency Explainer”), the United States Food and Drug Administration announced that it was granting an Emergency Use Authorization (EUA) to change the way JYNNEOS, the monkeypox vaccine made by Bavarian Nordic and marketed in the United States, is used. To date, the vaccine has been given subcutaneously — or SC — which means that the dose is delivered into the layer of tissue directly under the skin. The vaccine can also be delivered intradermally—or ID—which means the shot is delivered into the dermis, the layer of skin directly below the outermost layer of skin. In phase 2 trial, [published in 2015](#), participants who received the ID dosing strategy developed the same amount of antibodies in the same time period as people who received the SC dosing. ID doses are smaller than SC doses. The US FDA’s EUA states that one vial, which can deliver one SC dose, can deliver five ID doses.

A full course of ID dosing is two shots. The FDA has stated that people receiving ID JYNNEOS will get two shots; people who have received the SC vaccine have, for the most part, only been able to receive one of the two recommended shots due to supply issues. **The EUA specifies that people who have already received one SC can receive a second ID dose.**

This new approach changes both the amount of vaccine a person will receive and the quantity of vaccine doses that states and other US jurisdictions will receive. The White House announcement of the EUA for intradermal dosing of JYNNEOS stated that the Centers for Disease Control and Prevention was looking at needs and supply and would be updating jurisdictions about their allocations based on a shift to the ID dosing approach.

### ***Why is the dose-sparing proposal being made now?***

The dose-sparing proposal is being put forward because the United States government says that there are not enough filled and finished doses for SC IM administration to meet the need in the United States. The US government owns roughly 15 million doses (based on SC dosing) of raw vaccine substance that has to be “filled and finished” to become shots that can go into arms. The US government has projected that it will take months—into 2023—for these additional supplies to become available. US government officials have said, on calls with concerned health activists, that the dose-sparing regimen is the only approach that will avert a complete stock out of vaccines. This decision is primarily guided by supply, not science.

### ***What are the concerns with this approach?***

The US government dose-sparing strategy raises concerns because:

#### **▶ It is based on limited scientific evidence**

The [FDA-authored information sheet for providers on intradermal dosing](#) references one study in which 191 people received ID dosing and 167 received SC dosing. Both groups developed similar levels of vaccine-induced antibodies in roughly the same period of time. While this is positive, supportive evidence, it is also limited. The trial participants were predominantly non-hispanic white and young (with a median age of 27). People living with HIV and/or viral hepatitis were not eligible to enroll in the study. In an August 10 White House-convened health briefing, the White House monkeypox deputy coordinator Dr. Demetre Daskalakis stated that ID dosing is effective in PLHIV (though not necessarily in those who are immunocompromised, ie with low CD4 cell counts). However in spite of this assurance, there are no clinical trial data on SC versus ID in PLHIV—a community highly impacted by monkeypox. The [most recent joint European Centre for Disease Prevention and Control-WHO report on monkeypox](#) in the region states that, among people with monkeypox and known HIV status, 36% are living with HIV. The data on the percentage of people with monkeypox who are also living with HIV are comparable, though less well-tracked, in the United States. For example, in [the most recent update from the state of Georgia](#), more than two thirds of people diagnosed with Monkeypox also were living with HIV.

In community conversations, the FDA has also referenced widespread ID administration of an earlier version of the MVA vaccine in Germany; however these data are not included in the EUA information sheet.

There are no data available at this time on the T-cell responses associated with ID versus SC immunization. T-cells are another key part of the immune response, and may also play a role in protection.

It is important to note that it is possible that ID dosing could be more effective, because the vaccine is delivered in the dermis, which is also the site of exposure. The site of vaccine administration (where the shot goes into the body) can impact where, and in what quantities, vaccine-induced immune responses develop. But right now, this information isn't available, though it could be gathered quickly through a well-designed research study.

### **Action Step:**

The US FDA, CDC and NIH should immediately, in consultation with impacted communities, design and implement a study that can provide high-quality evidence on the efficacy of intradermal versus subcutaneous vaccination in diverse populations. This is important both to ensure the safety and efficacy of the US vaccination campaign, as well as the global vaccination campaigns.

### ▶ **The vaccine manufacturer says it does not have information on how to implement this strategy safely**

The [US provider guidance issued along with the EUA](#) for intradermal dosing states that a vaccine vial can be stored at +2°C to +8°C (+36°F to +46°F) for up to 8 hours. However the Bavarian Nordic Chief Executive Officer [has stated publicly](#) that the company does not know how long the vaccine remains potent after it has been punctured or how many times a vial can be punctured—questions that he says state officials have “bombarded” the company with since the ID dosing regimen was first suggested.

### ▶ **It will erode trust in the vaccine and the US public health approach among BIPOC communities who have already been impacted by and mobilized around racial disparities in access to IM JYNNEOS.**

This announcement was made without prior consultation with community groups and leaders working with and representing BIPOC and LGBT communities, and neither the official announcement nor officials speaking on government-convened calls have offered any information about funding for addressing concerns arising from what is justifiably perceived as an experiment with a reduced dose of a crucial medical countermeasure.

**Based on these concerns, the August 9 announcement is poorly planned and poses risks of vaccine hesitancy and mistrust. The US government must work with speed and transparency to address questions and concerns raised by this approach.**

***What is behind the reported supply constraints of existing vaccines that are driving the dose-sparing proposal?***

The reported supply constraints are due to the US government's lack of urgency in responding to this crisis over the past ten weeks. All of the roughly 16 million doses of the Bavarian Nordic vaccine in the world right now exist in one of two forms: filled and finished doses (ready to go into arms) and raw vaccine substance (that needs to be filled and finished). The US government owns the vast majority of these doses. The main reason that there is a supply constraint is that the US government is not working, with urgency, to fill and finish all of the doses. PrEP4All and other activists have been asking the US government to identify additional contractors who could fill and finish doses quickly, since BN itself has limited capacity. Repeated requests for updates on identifying and engaging a contractor have been ignored.

Right now, the US government is accepting a slow timeline instead of setting new precedents for speed in fill-and-finish, as the crisis demands. This speed is crucial for building a global supply of vaccines, not just vaccines for the United States.

**Action Steps:**

- ▶ The United States government must share, immediately and on an ongoing basis, the rate at which vaccines are being administered nationwide. Existing data show states' allocations and orders. But information on use is the basis for the assertion that a stock out is imminent.
- ▶ President Biden must invoke, and the White House-appointed monkeypox outbreak coordinators must implement, the Defense Production Act to quickly fill and finish the 15.8 million (SC) US-owned doses that are currently bulk raw vaccine substance

***What needs to happen to make more vaccines in addition to those already available in raw and finished form?***

Turning all of the already manufactured doses into shots is just one of the steps needed to increase supply. The next step is to ramp up manufacturing of the vaccine. Bavarian Nordic can make roughly 30 million doses per year, but it had recently shut down the facility where the vaccine is made. It is now re-opening up this facility with the intention of maximizing production. But this process will take months, and a vaccine monopoly is not a sustainable, safe or equitable approach to monkeypox—or any pathogen.

The Bavarian Nordic is, at present, the only facility in the world that can manufacture the vaccine based on the current approach (or recipe). There is an urgent need for the World Health Organization, Gavi, the vaccine

alliance, CEPI and WHO member states to quantify the global need and activate steps to expand its supply. In [the July report issued after declaring monkeypox a public health emergency of international concern \(PHEIC\)](#) the World Health Organization specifically stated that: States Parties who have manufacturing capacity for smallpox and monkeypox diagnostics, vaccines or therapeutics should raise production and availability of medical countermeasures. (para 4.a.)

### **Action Step:**

WHO must, with full cooperation of and funding from, the United States, Europe, the UK, and in coordination with CEPI and Gavi, Africa CDC and other LMIC stakeholders, develop and fund research to support and direct changes in the production process to be utilized in more facilities worldwide, particularly those in LMIC regions. The current approach requires highly specialized equipment and pathogen free fertilized chicken eggs; alternate approaches like the use of immortalized cell lines could be used for production of MVA.

### ***If the US goes ahead with the dose-sparing strategy and I am offered the ID shot series, what should I do?***

Members of PrEP4All have received this question repeatedly—and posed it to each other as we have sought to understand the implications of the dose-sparing strategy. We repeat it here because it has come up and will likely come up for others. It is a question that shifts the responsibility to individuals to interpret and advise on the actions of a state that has not worked with urgency, transparency and equity in this crisis. Simply put,

### **The Biden administration is attempting to turn health advocates and activists in their communities into messengers for a dosing switch that is necessitated by a series of errors the Biden administration made — and we tried for months to prevent. We will not do your work for you.**

The situation we face today is dire and was completely avoidable. PrEP4All does not think that any individual at risk of or exposed to monkeypox should be faced with the choice of ID vaccine or no vaccine at all until there is additional data from diverse populations. But this may be the exact dilemma that the Biden-Harris administration created. This data must come from diverse populations. The US government had months to scale up fill and finish capacity and avert a short-term dose shortage. It did not. It still possibly can. The critical question, at this point, is will it? Despite being asked for months to publicly share information on what steps it is taking to fill and finish additional doses, the administration has refused to do so.

We are also concerned that changing the dosing strategy in the middle of the rollout, and without a communications/messaging plan or engagement of public health leaders in those communities, will create further vaccine hesitancy and medical mistrust in BIPOC communities. Black and Latino LGBTQ people in several major cities reported not being able to book appointments for monkeypox vaccinations only to walk past lines of white gay men at vaccination centers in Black and Hispanic neighborhoods. BIPOC community members

may easily interpret this strategy as one that actually puts them in greater harm after the vast majority of full doses went to white gay men first. If the goal is to increase the number of people who can get vaccinated for monkeypox, this strategy to expand vaccination may have the opposite effect: Communities already showing disproportionate rates of monkeypox may be less inclined to seek the vaccine if it is perceived as being used in an experimental approach that is less than a full dose.

We reject and condemn the government's decision to introduce this strategy in the media and on calls with health advocates without a robust, honest and urgent engagement with community leaders from BIPOC LGBT groups about the resources needed, questions posed and risks presented by a shift from IM to ID dosing. **These communities must be engaged as architects, leaders and partners if there is any chance of preserving trust among communities who receive healthcare in the context of a white supremacy that preserves inequity.**

At the same time. Monkeypox is a painful, potentially fatal disease that can cause scarring, loss of work, income, intimacy and pleasure. People at risk of monkeypox should take any and all steps to protect themselves and reduce their risk. Vaccines are a risk-reducing strategy and the JYNNEOS vaccine is the most effective vaccine available. The data suggest that ID dosing will also provide protection. We fully support individuals and communities taking decisions that embody care for our bodies and our lives.

## Public Health Emergency Explainer

Both the United States and the World Health Organization have designated the ongoing monkeypox outbreak a public health emergency. The WHO announcement that monkeypox is a "public health emergency of international concern" or PHEIC came on July tk. On August 4, the United States Secretary for the Department of Health and Human Services, Xavier Becerra, announced the emergency in the US. These are the two such emergency designations to date, even as cases climb, including in Peru and India. An emergency designation is a signal and a statement that money, attention and coordination are needed. Concrete actions and commitments should follow. If they do not, then the emergency will continue and worsen. The emergency declarations are tools to compel action. It is important to note that the WHO called for manufacturing scale up to ensure equity (as mentioned earlier in this Update) and that it states that all countries, with and without cases, must engage community directly and actively work to reduce stigma and stigmatization of specific groups at high risk of monkeypox. All states must invest in groups trusted in and based in communities to counter homophobia, transphobia and the possible harms related to monkeypox infection in someone who is not openly living as LGBT and needs to seek care. Looking at the United States context, HHS has two declarations that it can invoke when it declares a public health emergency. It used a Section 319 Declaration for monkeypox. This paves the way for rapid mobilization of funding and other resources from tk. It does not, however, remove barriers to the FDA declaration of an EUA for the antiviral tecovimrat (TPOXX). Access to tecovimrat continues to be a major challenge, and the US FDA, which has shown itself willing to move ahead of evidence with its EUA for the ID vaccine dose, should take comparable action and issue an EUA for tecovimrat.