

Treatment Update

PrEP4All's M-Pox Alert is a bimonthly 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 now issue our alerts every two weeks—please follow us on Twitter (@PrEP4AllNow) for more regular information and urgent action alerts.

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In this issue:

- ▶ Epidemic Update
 - ▶ *Time to act, not step back*
- ▶ Treatment Update
 - ▶ *Decoding the FDA and CDC communication on TPOXX resistance*

Epidemic Update

Time to act, not step back

In recent weeks, many states and jurisdictions in the United States, and many countries across Europe have reported declines in the daily rates of monkeypox diagnosis and the growth of the epidemic. In its [most recent technical update](#), for example, the CDC reported that the estimated outbreak doubling time (how long it takes for the cumulative number of diagnoses to double) is approximately 25 days. For much of July, the outbreak doubled in size every eight days. In late September, the European Center for Disease Control and Prevention [reported](#) that twenty countries saw decreases in the number of cases, compared to the previous reporting period.

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.

In the United States and other high-income settings, these reports, combined with a more reliable supply of vaccines, have led to a sense that the outbreak is under control and does not require additional action on the part of the World Health Organization, which has not yet taken key steps such as pre-qualification and emergency use authorization that would make it much easier for low- and lower-middle income countries to obtain vaccines and treatments.

Recently, [US officials have suggested that the “eradication” and “elimination” are possible](#) in the United States. This statement followed President Biden’s declaration that the COVID-19 pandemic is ‘over.’

PrEP4All advocates for and wholeheartedly pursues a cessation of suffering, illness and death from monkeypox, COVID-19 and HIV/AIDS. We welcome declining case numbers and expanding vaccine access—but we condemn the public health establishment’s decision to, yet again, choose complacency over urgency at the first sign that an outbreak is waning.

Here are three reasons to call for urgency and action even, and especially, when the monkeypox threat seems to be waning in the United States.

▶ **We haven’t learned anything from this epidemic.**

This is true on a lot of levels. Here, we are talking about the scientific lessons. Cases may be dropping but there is no clear explanation for why, and no system in place to track factors like drug resistance that could compromise the public health response. If we don’t understand how and why cases drop, how and for how long vaccines delivered intradermally or intramuscularly and treatments work, and what the barriers and enablers are to people getting the care we need, then the next outbreak of monkeypox (or something else) will be just as much of an experiment with people’s lives, defined by dose-sparing, treatment rationing and racial disparities. PrEP4All recently joined a range of advocates and scientists in calling for a coordinated, prioritized USG research agenda that has strong community engagement. You can read the letter we sent to leading USG scientists [here](#).

▶ **Monkeypox is global—as is injustice.**

There is also absolutely no coordinated global action to secure affordable, equitable access to vaccines and treatments in regions of the world including Latin America and sub-Saharan Africa, where monkeypox is endemic. Access to testing is limited so reports of cases in LMICs are unreliable. Even if these factors were not the case, monkeypox is endemic in parts of the world which should, in the wake of this globalized outbreak, be assured of access to tests, treatment with TPOXX and painkillers and JYNNEOS vaccines at affordable costs. A recent deal between Bavarian Nordic and the Pan-American Health Organization (PAHO, the regional arm of the WHO), for 100,000 doses brings too few vaccines into the region at too high a cost.

▶ **Outbreak response is pandemic preparedness.**

Even as the United States government comes up empty with funds for monkeypox and COVID-19, it is pushing forward a new Pandemic Preparedness and Response fund at the World Bank. The US is fast-tracking this fund so it can be sure its USD\$750 million contribution is banked before the end of the fiscal year. Putting money aside to prevent future pandemics is a wasted effort if the US does not also fund the research and programs that address current outbreaks and ongoing pandemics. Providing medical countermeasures today is among the best ways to figure out how to do better, faster in the future.

Action Step:

- ▶ Tweet, email or call your elected officials in Congress to let them know that funding for monkeypox and SARS CoV2 MUST be included in the FY2023 budget. This week, a group of US activist and advocacy groups recently sent this [public letter](#) with demands and a call to action. Your tweet or call say: **Congress needs to fund monkeypox and COVID now, authorizing \$26.9 billion as requested by the White House, including \$4.6 billion for the US global response and \$9.5 billion for research and development of lifesaving medical tools to treat and prevent these diseases. We're still at risk and still fighting—and we will be until there is money, urgency and political action to end pandemics now.**
- ▶ Demand that CDC (@cdcgov) and NIAID (@NIAIDnews) expand and systematize the research agenda needed to answer questions about monkeypox that are of urgent importance for the present epidemic—and for a scenario where smallpox re-emerged. These questions, which must specifically look at PLHIV, include:
 - ▶ **How long and how well monkeypox vaccines work,**
 - ▶ **How best to use treatments, including as pre- and post-exposure prophylaxis**
 - ▶ **If and where an animal reservoir of monkeypox is established as a result of the current outbreak**

Treatment Update

Deciphering the US Government Messages on Drug Resistance

On September 12, the US Food and Drug Administration publicly posted data on the risk of drug resistance emerging in people receiving tecovirimat (US brand name TPOXX, manufactured by SIGA Technologies) as a treatment for orthopoxviruses, including smallpox and monkeypox. When viruses copy themselves, they introduce errors and changes into the genetic code. Some of these changes can make the virus less susceptible, or resistant, to the medication. The FDA's update presented information from *in vitro* studies, in which the medication was added to the virus and cells grown in laboratories, a study in non-human primates, and anecdotal information from one human. The conclusion from these studies, according to the FDA and the CDC, which also issued an update, is that tecovirimat resistance is a concern, and that health providers should take the risk of resistance into consideration when prescribing the medication.

In the case of tecovirimat, it appears that a change in one amino acid (a protein building block) in an orthopoxvirus protein called VP37 can lead to what the DFA calls a “substantial reduction” in tecovirimat activity against the virus.

Drug-resistance is a huge risk to individual health and health systems and it must be taken seriously.

However, the US government actions simply don’t add up:

- ▶ There is no systematic approach to or federal funding for sample collection and genomic sequencing of monkeypox viruses. Without genomic sequencing, it is simply impossible to track or gauge the risk and/or emergence of tecovirimat resistance.

As of September 21, fewer than 400 full length monkeypox virus genomes from the United States have been collected and shared with the [NIH NCBI Virus Database](#). 459 US viruses have been shared with [GISAID](#). This is roughly 1.6 percent of the 24,000 cases recorded in the United States to date. The sequences are not geographically distributed and representative—they come from a handful of states with researchers and capacity to collect sequence and share samples.

Monkeypox is more genetically stable than a virus like SARS CoV-2. It has a lower mutation rate, and so a considerable amount of mutation isn’t likely to occur. However, if genetic resistance is going to be used by the FDA and the CDC as a rationale for potentially restricting access to tecovirimat, then the US must fund and act on a robust sequencing effort to substantiate or alleviate these concerns.

The easiest way to do this is by expanding the sequencing planned as part of the [Study of Tecovirimat for Human Monkeypox Virus \(STOMP\)](#) study which aims to enroll more than 500 adults and children in the United States. Right now, STOMP is only funded to do deep sequencing (full length viral sequences from blood, mucosal tissue and other ‘compartments’ in the body) in 100 participants. PrEP4All calls for all participants’ virus to be sequenced. In addition, the CDC should explore and transparently share its assessment of the cost and potential for sequencing a representative sample of the viral material it receives from commercial laboratories. All commercial labs except for Quest Diagnostics send samples that test positive for orthopox virus to CDC for confirmation that the virus is monkeypox.

An efficient, humane and rights-based approach to initiating monkeypox treatment can’t be—and is not—linked to a positive test. Many people receiving tecovirimat are being diagnosed based on symptoms, not via laboratory tests. The CDC [recently reported](#) on the data from 549 people who received tecovirimat in the United States. Approximately half of these people did not have a laboratory diagnosis at the time of treatment initiation. This is efficient, humane and reflective of the reality that confirmatory laboratory diagnosis is not free to all Americans, regardless of insurance status.

This is the same high-risk approach that the US government has taken to collection, sequencing and sharing of representative samples of SARS CoV-2. Flying blind puts everyone at risk. The CDC and FDA have identified a concern, but neither clinicians nor people with monkeypox have a way to take action. This is one of many areas where the lack of funding, federal planning and strategy is putting communities at risk.

Action Step:

- ▶ NIAID must fund more extensive sequencing of every participant in the STOMP trial who do (and do not) receive tecovirimat to understand if and when resistance is happening
- ▶ CDC with support from other federal, state and jurisdictional agencies must establish a system for tracking emergence of tecovirimat resistance. This must include steps to make it easy to submit samples and get genotypic information, assurance that people with resistant virus will receive appropriate alternative care, and attention to approaches that do not delay treatment initiation where indicated.
- ▶ Remove the Expanded Access Investigational New Drug (EA IND) classification of tecovirimat. As described in previous Mpox Alerts, tecovirimat is approved for use against both of these viruses by the European Medicines Agency (EMA); in the United States, TPOXX access is restricted due to the US Food and Drug Administration's classification of the medication as an Expanded Access Investigational New Drug (EA IND). This classification is clearly not leading to better surveillance of drug resistance; it is merely restricting access and ensuring racial disparities.