

14 September 2022

To: Alondra Nelson, PhD, Director, Office of Science & Technology Policy
Demetre C. Daskalakis, MD, MPH, National Monkeypox Response Deputy
Coordinator
Rochelle Walensky, MD, MPH, Director, Centers for Disease Control
& Prevention
Anthony S. Fauci, MD, Director, National Institute for Allergy and Infectious
Diseases (NIAID), National Institutes of Health (NIH)
Robert Fenton, Regional Administrator for FEMA Region 9, National Monkeypox
Response Coordinator

Re: Toward an actionable and rigorous United States Monkeypox Research Agenda:

Dear Mr Fenton and Doctors Nelson, Daskalakis, Walensky, and Fauci:

The ongoing global Monkeypox virus (MPV) epidemic presents a unique opportunity to advance poxvirus biology, epidemiology, prevention and treatment, promote public health and, hopefully, improve preparedness and response to future infectious disease and other major health threats. Although researchers identified human MPV infection in 1970¹, the biology and epidemiology of the virus remain understudied. Basic questions about MPV persist, including the role of saliva, respiratory secretions, semen, and vaginal fluid in transmission, whether virus deposition on skin and mucus membranes results in different clinical features and outcomes, and the role of sexual contact in viral transmission. Biomedical countermeasures – the Jynneos non-replicating vaccinia vaccine² and TPOXX (tecovirimat) treatment³ – are both of unknown clinical efficacy for prevention of MPV transmission and mitigation of disease outcomes. Moreover, the use of novel approaches such as delaying the 2 dose of Jynneos by more than 4 weeks and the use of intradermal injections with 1/5th of the subcutaneous dose require additional study.

We propose that the US government, led by the White House Office of Science and Technology Policy (OSTP), the CDC, USAID, and the NIH/NIAID create, fund and implement a research agenda to prioritize and address the most pressing MPV research questions — both for management of the evolving global outbreak and to redress

¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2395797/>

² <https://www.cdc.gov/poxvirus/monkeypox/health-departments/vaccine-considerations.html>

³ <https://www.fda.gov/media/160480/download>

inequities that have precipitated it. In July, OSTP published an initial list of research areas,⁴ describing the fields of study needed in the MPV research response. We propose an update to this agenda with increased transparency and granularity, prioritizing the most essential gaps in knowledge, listing both ongoing and planned studies, indicating available new and existing funding for this agenda, as well as funding flow to support the agenda. A recent MPV research agenda by the UK Health Security Agency⁵ provides a useful template for such an analysis.

This research agenda should:

1. Be led by the federal government, but **build in community engagement with researchers, advocates, patients, and the most affected and at risk groups from its foundation**. To this end, we request regular meetings with federal officials building the research agenda, **culminating in a hybrid in-person/online meeting in the first quarter of 2023**.
 - Explicitly address the disparities in MPV cases, which are already disproportionately affecting Black, Hispanic/Latinx, and Native Americans, while access to countermeasures lag in these same communities.⁶ This must include research and implementation priorities to address racial and ethnic, class, gender, sexual orientation, and geographic disparities.
 - Continue to engage research and community experts (especially those from the most affected communities described above) with meaningful, demonstrable input at every stage of the research agenda's development and implementation.
2. **Integrate diverse fields of research** into granular, addressable questions with clear methodological pathways toward data output and analysis.
 - Ensure an integrated science agenda that includes essential behavioral, social, clinical and implementation questions relevant to MPV transmission (e.g., the role and operation of social and sexual networks), prevention approaches (e.g. vaccines and use of TPOXX for prevention), treatment (e.g., access to and uptake of available medications, including population disparities thereof), and mitigation (e.g., efficacy of targeted communications, community-driven behavioral change interventions).

⁴ <https://www.whitehouse.gov/ostp/news-updates/2022/07/21/u-s-monkeypox-research-priorities-speeding-science-for-impact/>

⁵ <https://www.gov.uk/government/publications/monkeypox-outbreak-technical-briefings/investigation-into-monkeypox-outbreak-in-england-technical-briefing-5#part-2-research-and-evidence-gaps-prioritisation-and-activity>

⁶ <https://www.ncdhhs.gov/media/17508/open>

- Coordinate across federal agencies, and explicitly list which agencies are responsible for research funding, which are actively doing research, and which are responsible for research implementation.
- Be clear about research priorities, both overall, and within each research area. This will describe explicitly which research questions are most pressing and therefore will receive funding in the event of ongoing limited federal resources for MPV research.
- Include not only broad research topics like “Transmission dynamics and modes” or “Clinical presentation and risk factors” but specific research questions and methodological pathways to address them, for example:

“What is the required infectious dose needed for productive MPV on skin and mucous membranes?” and/or “ranking of specific types of sex acts by level of transmission risk” and a variety of evidence needed to address these question such as animal studies with purified virus, including in non-human primates, and robust epidemiological studies to determine the risk of skin contact versus introduction to the mouth/throat, genitals, or rectum and the risks of various types of contact, familiar from decades of work on HIV.⁷

- Work with global and international partners to address global priorities to ensure access to biomedical, behavioral, social, and implementation research and MPV countermeasures everywhere MPV is a public health threat.
- Commit to investment in a diverse pool of early stage investigators (including the support for MPV-related F or K development awards).
- Coordinate ongoing research by cities, states, territories, private testing laboratories, and tribal nations to address MPV testing, transmission, vaccine and infection-induced immunity, and the immunological response to various Jynneos dosing regimes. Listing and coordinating city and state research will ensure essential questions get rapidly addressed while minimizing direct overlap that would waste vital resources.

3. **Communicate research resources, questions, ongoing studies, and findings** with a diverse group of partners, from clinicians and researchers to the public.

- Provide a public-facing dashboard listing ongoing and planned studies funded, including the institution and research question being addressed.

⁷ <https://www.aidsmap.com/about-hiv/estimated-hiv-risk-exposure>

- Provide a public-facing website where patients can easily determine where/if they can enroll in ongoing clinical research.
- Include a listing of funds available for additional studies, including pathways to funding for researchers, such as NIH grant supplements.
- Provide a public facing dashboard describing the roles of various federal agencies (NIH, NIAID, NIMH, NICHD, CDC, FDA, HRSA, Indian Health Service, etc.) in coordinating the research agenda and its implementation.
- Expedite clearance processes for CDC-supported research to ensure timely dissemination of scientific findings via conference presentations and peer-reviewed articles.
- Publicly disseminate essential scientific literature as it is released in pre-prints, presentations, and peer-reviewed articles. This list should be updated weekly to guide clinicians, researchers, and the public to the most essential MPV data.

We look forward to ongoing conversations with federal partners in the CDC, OSTP, and the NIH, and other agencies as this research agenda is drafted and finalized. **We request that the government sponsor an open meeting, inviting partners – academic scientists, clinicians, advocates, and patients – into the process.**

This United States MPV research agenda would present a major step forward in the multi-agency push to answer fundamental questions relating to MPV infection, treatment and prevention. Without this research, containing or eliminating the virus in the United States and contributing to the global response will likely remain out of reach. Even if MPV is contained in our country, global infections will ultimately reintroduce MPV here. In this increasingly interconnected world, infectious diseases anywhere on the planet are urgent national security and public health threats. With a push toward MPV research, and with urgency in implementing the biomedical tools, behavioral and social strategies, and epidemiological interventions it will create worldwide, we can ensure that MPV no longer presents a public health emergency in the United States and around the world.

Signed,

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