AfricaCDC Centres for Disease Control and Prevention

CEPI

NIH National Institute of Allergy and Infectious Diseases

World Health Organization

A COORDINATED RESEARCH ROADMAP

MPOX VIRUS

Immediate Research Next Steps to Contribute to Control the Outbreak

SEPTEMBER 2024

This summary outlines the immediate next steps to contribute to control the outbreak. A full research roadmap will become available shortly.

There is broad consensus on the need for research to focus on studies that contribute to control the outbreak now; guide interventions so that those at highest risk of infection are protected, promptly diagnosed and receive op-timal care; and to catalyse the full integration of all research within each ar-ea of the outbreak response, in a collaborative manner and with researchers and Ministries of Health of the affected countries in the driving seat.

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ABOUT THIS DOCUMENT

A scientific conference was held on August 29-30, 2024. It focused on aligning mpox research with outbreak response goals. This meeting was part of a comprehensive effort to align research initiatives with the practical needs of mpox outbreak control, emphasizing collaboration, regulatory and ethical considerations, and the leadership of affected countries. Over 2500 participants from the affected countries and across the world came together at the meeting, including scientists, Member States' representatives, public health professionals, funders and private sector representatives, to accelerate the development of innovations to control the mpox epidemic.

The meeting aimed to develop an emergency mpox research response agenda, enhance collaboration and partnerships, and outline key steps and timelines for addressing research gaps. There was a strong emphasis on putting affected countries and their researchers at the forefront of shaping the research agenda.

Key principles guiding the meeting included collaboration, leadership from affected regions, alignment with outbreak response goals, and a people-centered focus.

MAIN TOPICS DISCUSSED DURING THE MEETING

The meeting covered several main topics including:

- **Current disease transmission dynamics and clinical characteristics of mpox and clinical care optimization**
- **Assessment of therapeutics, diagnostics, and vaccines**
- **Novel evaluation approaches for medical countermeasures**
- **Incorporation of good participatory practices in research**
- **Enhancement of scientific and ethical capacity**
- **Review of regulatory and ethics frameworks**
- **Identification of research priorities and opportunities**
- **Coordination of studies across sites and countries in Africa**
- **Promotion of multi-country trial collaboration**
- **Incorporation of good participatory practices and community engagement**
- **Identification of immediate research priorities and opportunities**
- **The meeting concluded with discussions on how governments can support national researchers and research institutions, followed by a summary of major conclusions and next steps.**

10 Immediate Next Steps for a Coordinated Mpox Research Roadmap

Obtain additional data on Mpox transmission and epidemiology, including clinical outcomes and risk factors for severe disease.

Evaluate and deploy new rapid and sensitive diagnostic tests (including unbiased tests) that detect all MPXV clades and help differential diagnosis of diseases that can mimic mpox.

Define and implement all elements of optimized clinical standard of care for all MPXV infected patients

Promote the development of new therapeutics and the evaluation of safety and efficacy of prioritized candidate therapeutics for mpox, in coordinated collaborative multicenter trials.

Conduct research on animal models and use animal models towards the determination of correlates of protection, and support research on immunoassays

Define regulatory pathway for "next generation" of medical countermeasures

Facilitate availability of vaccines in areas with sustained human to human transmission, as part of an integrated response, and promote generation of critical data regarding vaccines safety, effects, and delivery strategies.

Use existing tools to incorporate Good Participatory Practices and community engagement in research including public health research.

Integrate research into the outbreak response activities.

Embrace and expand opportunities for coordination and collaboration of all research initiatives with local authorities and research institutions, with researchers from affected countries and the MoH at the centre of the response.

1

Obtain additional data on Mpox transmission and epidemiology, including clinical outcomes and risk factors for severe disease

A better understanding of the clade-specific disease transmission dynamics and modes of transmission in different population risk groups, including among children is important.

This will enable improved understanding of how different outbreak control strate-gies can be most efficiently deployed and is also important for embedding infec-tion control measures at healthcare facilities, at home, and other settings.

2

Evaluate and deploy new rapid and sensitive diagnostic tests (including unbiased tests) that detect all MPXV clades and help differential diagnosis of diseases that can mimic mpox

A specific focus on evaluation and access high performing to point of care diag-nostics, including RDTs is critical. It is also important to facilitate establishment of reference laboratories that can perform tests with high sensitivity and specificity and built capacity to implement and assess unbiased methods for diagnostics and smart surveillance.

Access to these tests will enable appropriate care of Mpox patients and im-proved outbreak tracking for deployment and evaluation of countermeasures. Research will also help address diagnostic challenges in the context of multi-pathogen outbreaks in one location.

3

Define and implement all elements of optimized clinical standard of care for all MPXV infected patients

Optimizing the clinical standard of care is essential for treatment of patients, and inclusion of optimized standard of care is a key element to make possible therapeutics trials.

Studies to help understanding of the optimized clinical standard of care for mpox infected patients – with candidate therapeutics or alone - is therefore im-portant, including the assessment in various age-groups including children, in-fants, and in various contexts.

4

Promote the development of new therapeutics and the evaluation of safety and efficacy of prioritized candidate therapeutics for mpox, in coordinated collaborative multicenter trials

Only trials that allow combination of data across sites are likely to promptly have sufficient power to reach clear conclusions regarding therapeutic safety and efficacy (pre-exposure and post-exposure), including at different times af-ter infection and in special populations.

Factorial design will enable improvement of optimized standard of care, which is critical given uncertainties regarding antiviral efficacy. Independent assessment of which therapeutics to evaluate is critical. Evaluation of new therapeutics will help to expand supply of key countermeasures and potentially lead to improved outcomes.

5 

Conduct research on animal models and use animal models towards the determination of correlates of protection, and support research on immuno-assays

Continue to develop animal models of MPXV Clades and support investiga-tion into host range and susceptibility of animals to form an infectious reser-voir.

Sero-surveillance studies to determine the natural reservoir for MPXV should be conducted and the feasibility of various animal species to be susceptible to infections and able to transmit virus should be determined.

Specific correlates of protection for vaccine and natural infection should be identified and animal models of co-infections be developed.

The development of standardized comparable binding and neutralizing antibody assays and assays technology transfer is important.

6 

Define regulatory pathway for "next generation" of medical countermeasures

Foster deliberations among scientists, developers and regulatory authorities, and encourage convergence on the package of data required for the assessment of new mpox vaccines and therapeutics, including but not limited to use immuno-bridging of humans to animal efficacy data as pathway for licensure of next generation vaccines.

7 

Facilitate availability of vaccines in areas with sustained human to human transmission, as part of an integrated response, and promote generation of critical data regarding vaccines safety, effects, and delivery strategies

Vaccines are only one additional tool in the outbreak control response. Vac-cines delivery should be part of an integrated package of interventions.

Generation of additional evidence requires Immediate attention to be given to regulatory, ethics and procurement frameworks and will enable targeted vac-cination of people at high risk of infection It is a priority to understand the effect of different outbreak response and vaccination strategies and their impact on achieving the set objectives.

For example, assessing the impact of different targeted vaccination strategies on reducing/interrupting transmission and reducing severe mpox disease (e.g. targeting of contacts of cases plus HCW/FLW in areas with recent cases; special populations including infants, children and adolescents, pregnant women and immunocompromised.

Moreover, the collection of critical safety data, using standardized adverse event definitions will enhance confidence in deployed vaccines. Lastly, im-proved understanding of vaccine efficacy, including for different clades and in the context of modifiers (e.g, HIV, malnutrition), modified dosing (e.g., fractional, intradermal), or single doses will aid in vaccine deployment decisions and may enable stretching of limited vaccine supplies.

Given the initial limitations in number of doses versus target populations, pub-lic health research during deployment is a fair way to distribute vaccine dos-es.

Evaluating new vaccines will help to expand supply of key countermeasures and potentially lead to improved outcomes.

8

Use existing tools to incorporate Good Participatory Practices and community engagement in research including public health research

Support research on non-pharmaceutical areas (e.g. anthropological, so-cio- behavioral science) to assess their contribution to the outbreak re-sponse activities.

Understanding the health seeking behaviors that influence mpox health risk as well as vaccine confidence can help to inform the response.

This is acknowledged as an ethical imperative and population engagement is at the heart of all successful research initiatives.

9

Embrace and expand opportunities for coordination and collaboration of all research initiatives with local authorities and research institutions, with research-ers from affected countries and the MoH at the centre of the response.

A myriad of stakeholders play important roles in research and innovation dur-ing outbreaks. Each stakeholder brings with it different and, at times, conflicting values, perspectives and priorities, adding yet a further layer of complexity.

Benefiting from the facilitation of the Research pillar, this will improve quality of scientific outcomes, speed of availability of robust results, trust in research re-sults, and enhance sustainable and collaborative scientific, regulatory and eth-ical capacity as well as joint decision-making procedures.

Leverage cooperative/joint regulatory and ethical reviews via AVAREF and existing ethical framework and network to accelerate protocol approval us-ing existing mechanisms.

10

Integrate research into the outbreak response activities

The Incident Management Team of the response at a continental level includes a Research pillar. This pillar's aim is to ensure research is integrated into the re-sponse, is collaborative and addresses the critical knowledge gaps.

Isolated research initiatives can interfere with response efforts if not integrated.

On the other hand, including research as part of a comprehensive imple-mentation package of all outbreak response actions, can help improve community engagement, quality of surveillance and contact tracing and enhance quality and implementation of standard of care for patients and ef-ficient access to vaccines to people at highest risk of infection everywhere.

FINAL REFLECTIONS

The strategic response plans are initially designed to limit the impact of the outbreak, re-search needs to be an integral part of the outbreak response structure and contribute to appropriately update these plans based on accumulated data. Research outcomes have the potential to provide the evidence base for established decision-making forums to ad-just strategic plans to potentially achieve better health outcomes through more effective deployment of outbreak response interventions. Using the Research pillar structure is critical to ensure priority response objectives remain people focused, are transparent, collabora-tive and leverage limited resources, and focus on harmonized tools, as appropriate.

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