

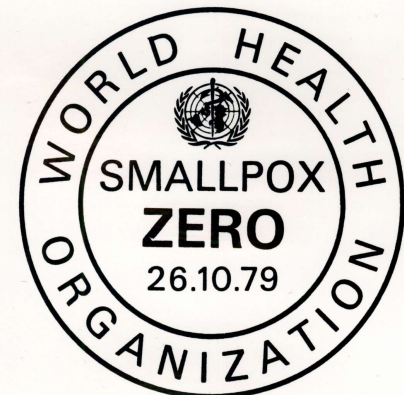
Committee on the current state of Research, Development, and Stockpiling of Smallpox Medical Countermeasures

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**World Health
Organization**



Outline

- **Research programme using variola virus for 2020-2023**
 - **Genome sequencing and diagnostics**
 - **Antivirals**
 - **Vaccines**
 - **Animal models**
- **WHO smallpox vaccine emergency reserves**
- **WHO preparedness planning for a smallpox event: Health Emergency Preparedness, Response & Resilience (HEPR)**
- **WHO Standing recommendations for mpox (August 2023)**
- **WHO Strategic framework for elimination of human-to-human transmission of mpox**

Research programme using variola virus for 2020-2023

Genome sequencing and diagnostics

Objectives: Development of smallpox countermeasures of public health benefit for humanity

Programme overseen by WHO with recommendations from Advisory Committee on Variola Virus Research

Area of work	US CDC	VECTOR
Genome sequencing	Complete genomic sequencing of 40 isolates. Updated to include isolates samples from the long-term repository vault in 2022.	Complete the genome sequencing of 50 of the remaining 88 isolates.
Diagnostics	- Adapt and optimize multiplex nucleic acid tests for new platforms and field settings. - Continue development and optimization of protein-based tests.	Optimize the design of the immunochemistry test kit and its accessories using orthopoxviruses, including variola and monkeypox viruses.

Research programme using variola virus for 2020-2023

Antivirals

Area of work	US CDC	VECTOR
Antivirals	Tecovirimat Complete testing in vitro against variola virus strains with F13L gene mutations. For F13 variants no longer available, use surrogate orthopoxviruses or create cell lines expressing F13 protein to evaluate tecovirimat against vaccinia virus lacking the F13L gene. ST-357 Continue to study in vitro activity (EC50s) of candidate ST-357 and optimized analogues to select preclinical candidates. (Study on hold) Monoclonal antibodies and antibody mixes Complete screens of individual and mixes of mAbs to neutralize variola virus within optimized IMV and EV assays. Assist in creating a new universal poxvirus monoclonal mix and evaluate final products in variola virus PRNTs by 2021. <i>Amended to include new work with a commercial entity, to evaluate mAbs and cocktails in vitro against variola virus</i>	NIOCH-14 oral formulation Assessing the oral formulation of NIOCH-14: Complete Phase 1 clinical trials in 2020. (Done) Complete Phase 2 and 3 trials for 2021–2022. (Done) Licensure obtained on 4 October 2022. New compounds Test 15 compounds found to be highly active against orthopoxviruses against live variola virus. Complete testing in cell culture in 2020 Complete testing in vivo in 2021–2022. Monoclonal antibodies and antibody mixes Evaluate antivirals against variola virus based on monoclonal antibodies.

Research programme using variola virus for 2020-2023

Vaccines, Animal models

Area of work	US CDC	VECTOR
Vaccine	MVA-BN, LC16m8 and mRNA Finalize efficacy testing on long-term titer samples from MVA-BN and/or LC16m8 vaccine trials (as samples are available).	VACdelta6 - Complete Phase 1 clinical trials (adults 18–40 years) by December 2019. (Done) - Undertake Phase 2 and 3 clinical trials in 2020-2021 and assess variola virus neutralizing antibody titres from sera of participants. (Done) - Licensure obtained on 11 November 2022 as OrthopoxVac for smallpox, mpox and other OPXV.
Animal models	Humanized mouse models Complete remaining in vitro work on HU-BLT model. Continue to assess Hu-BLT and Hu- CD34 models using tecovirimat.	

WHO Smallpox vaccine reserves (as of Nov 2023)

• Physical stockpile

- Held by WHO in Switzerland.
- 2.8 million doses
 - 2.5 million (88%) is 1st gen.
 - 0.3 million (12%) is 2nd gen (ACAM-2000, provided by a donation from the UK)
- Inventory done January 2022
- Potency test in Oct./Nov. 2022 by WHO CC RIVM (Netherlands)

• Pledged stockpile

Held by donor countries

– France, Germany

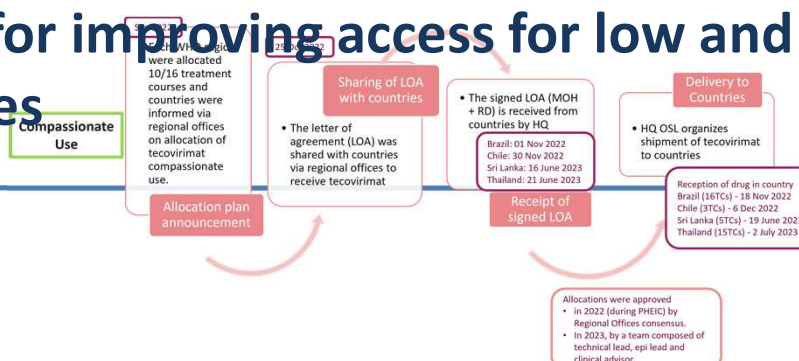
The United States of America

- US pledged stock to vaccinate 20 million people – vaccine are mixed products based on SNS composition
- Discussions re-opened to update agreements and include antivirals

WHO preparedness planning for smallpox event

Countermeasures support

- WHO emergency vaccine reserve
 - Working group to review potency testing protocols for 1st, 2nd and 3rd generation vaccines (began April 2023)
- WHO support for therapeutics during mpox outbreak
 - Compassionate use reserve
 - MEURI framework –
 - RCTs –
- Coordination support for LC16 vaccine research (Japan)
- External evaluation of access to countermeasures commissioned by WHO
- Discussions underway for improving access for low and middle-income countries



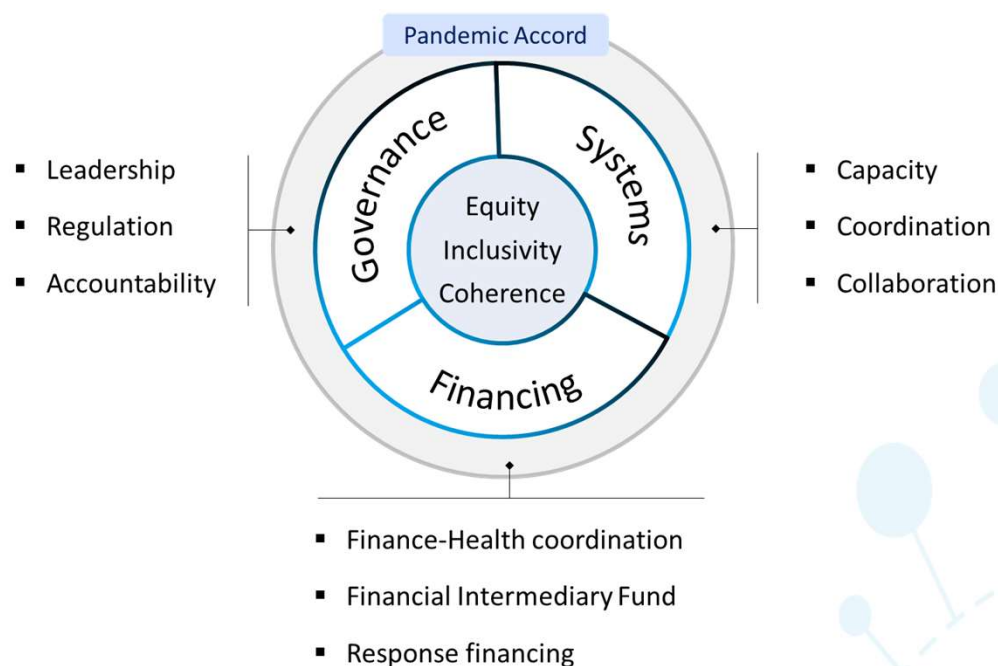
Director General presented 10 proposals to build a safer world together

***Based on independent reviews,
synthesizing +300 recommendations***



***... developed in consultation with
Member States & partners,
presented at the World Health
Assembly May 2022***

Strengthening the Global Architecture for Health Emergency Preparedness, Response & Resilience (HEPR)



The ability to prepare for, prevent, detect and respond effectively to health emergencies depends on the operational readiness and capacities in five subsystems



- Integrated disease surveillance
- Laboratories & diagnostics
- Public health intelligence

- Fast-tracked research and development
- Scalable manufacturing
- Coordinated supply chains & equitable access

Ecosystem of partners & networks across the systems capacities and inter-connected capabilities



- Risk communication & infodemic management
- Environmental & population interventions
- Social welfare & economic protection

- Emergency clinical care
- Health workers & patient protection
- Maintained essential health services

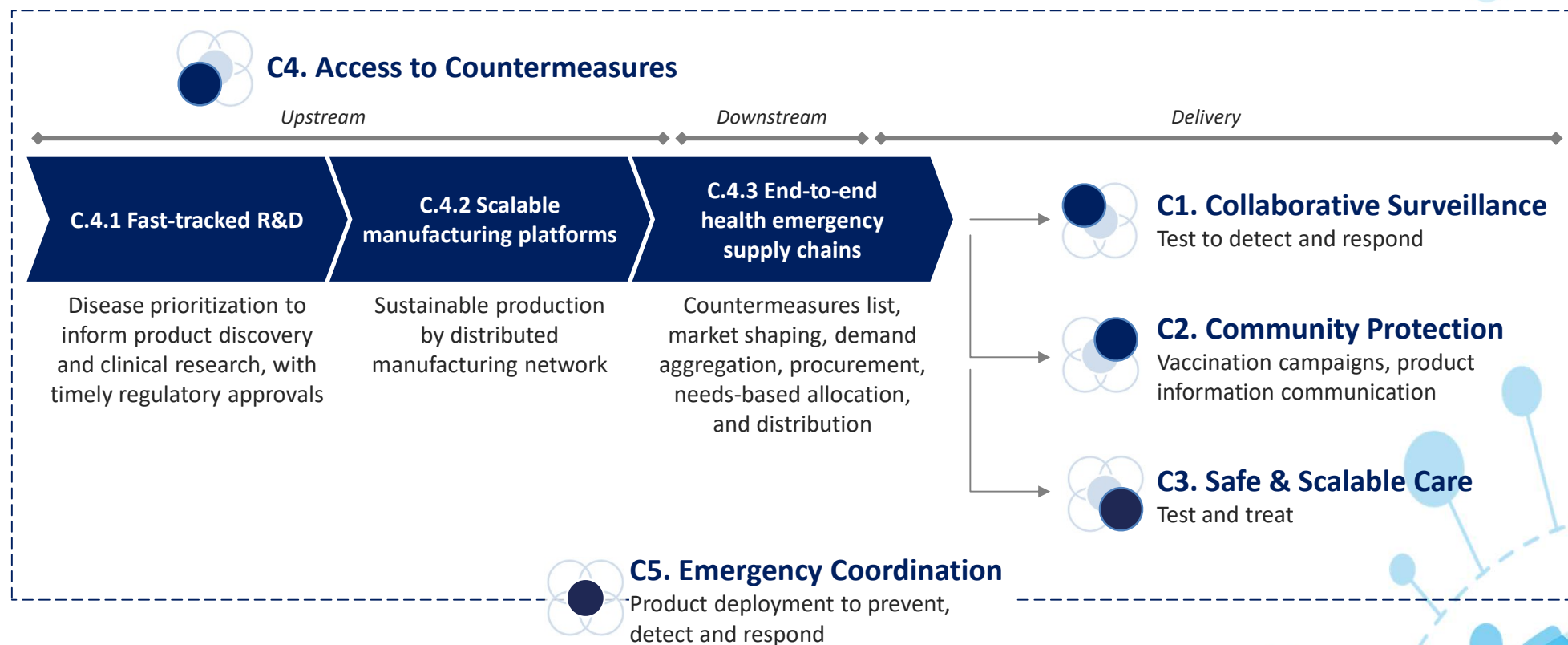
- Health emergency workforce
- National action plans for prevention, preparedness & readiness
- Rapid alert & response coordination



World Health Organization

HEALTH EMERGENCY

Access to Countermeasures value chain is integrated within health emergency preparedness and response



WHO Standing recommendations for mpox issued by Director-General in accordance with the IHR (2005) – August 2023 – August 2024

Recommendations directed to all countries:

A. Have national mpox plans integrated into broader health systems. Capacities that have been built in resource-limited settings and among marginalized groups should be sustained.

B. Strengthen and sustain testing and surveillance capacity and ensure that new cases of mpox are notified nationally and to WHO.

C. Protect communities through communication and engagement; continue to build trust and fight stigma and discrimination.

D. Invest in research to better understand mpox disease and transmission patterns, and to develop improved vaccines, tests, and treatments.

E. Provide travelers with information to protect themselves and others before, during and after travel and refrain from implementing travel-related health measures, including mpox screening and testing for travelers.

F. Deliver optimal clinical care for mpox patients, integrated within HIV and STI programmes, with access to treatments and measures to protect health workers and caregivers.

G. Work towards equitable access to safe, effective and quality-assured vaccines, tests and treatments for mpox.

WHO actions to support Member States on testing capacity during global mpox outbreak and PHEIC

WHO is working on ensuring **rapid access to testing** for monkeypox globally

In addition to the procurement and international referral network, WHO is supporting Member States through the following:

- Publication of guidance for laboratory testing for the current mpox outbreak
- Support on biosafety issues for mpox
- Provision of protocols, diagnostics materials and reagents to >100 countries
- Development of target product profiles (TPPs) for MPXV rapid diagnostics
- Support for trainings in diagnostics
- Rollout of global EQA programme for MPXV testing
- Monitoring virus evolution
- Addition of MPXV to WHO BioHub

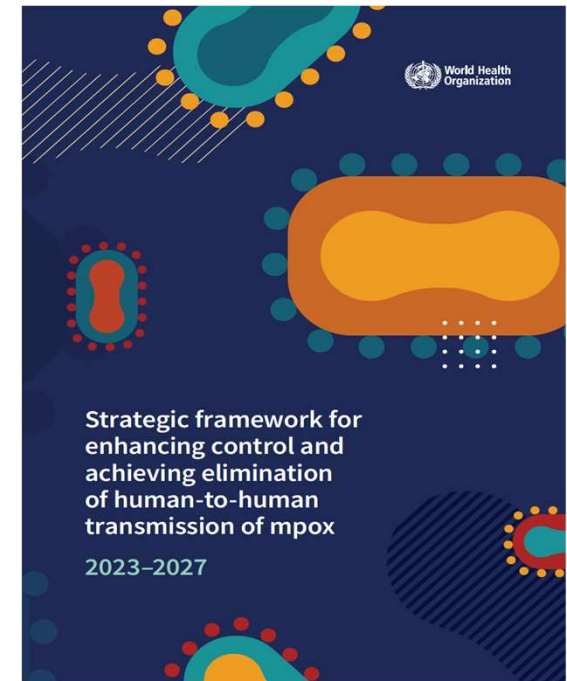
WHO Strategic framework for mpox elimination

Goal

Sustained elimination of human-to-human transmission of mpox

Objectives

1. Achieve control of mpox in every context
2. Advance mpox research and access to countermeasures
3. Minimize zoonotic transmission



Elimination of human-to-human transmission is the absence of new cases (without defined travel history or zoonotic exposure) for $\geq$ three months in the presence of adequate surveillance. **This goal applies to all countries and contexts.**

Reflections on lessons learned

- The importance of preparedness and readiness cannot be overstated
- WHO platforms for COVID-19 supported rapid and effective mpox response
- Not everything is countermeasures:
 - Surveillance and diagnostics
 - Risk communication and community engagement
 - Clear communication on public health and social measures
- The next outbreak or pandemic will still manage to surprise us
- Be ready to embrace new technology
- Equity Equity Equity must be integral to countermeasures development from the project concept and design phase
 - Offering vaccine donations after the crisis is over is too late for public health
 - Low and middle-income settings may need upstream support on regulatory procedures for product registration in country

Discussion

Thank-you!



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