Vaccines and immunization for monkeypox

Interim guidance

24 August 2022

World Health Organization

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Abbreviations

GACVS	Global Advisory Committee on Vaccine Safety
ID	Intradermal
MEURI	Monitored Emergency Use of Unregistered and Investigational Interventions
MPX	Monkeypox
MPXV	Monkeypox virus
MSM	Men who have sex with men
NITAG	National immunization technical advisory groups
PEPV	Post-exposure vaccination
PPE	Personal protective equipment
PHEIC	Public health emergency of international concern
PLWH	People living with HIV
PPV	Primary preventive (pre-exposure) vaccination
RCT	Randomized controlled trial
SAGE	Strategic Advisory Group of Experts (SAGE) on Immunization
SEP	Smallpox Eradication Programme
WHO	World Health Organization

Executive Summary

The overarching goal of the global response for monkeypox, on 23 July 2022 declared a public health emergency of international concern, is to stop human-to-human transmission and to minimize zoonotic transmission of monkeypox virus where it occurs. Judicious use of vaccines can support this response. This interim guidance provides WHO recommendations on use of vaccines for monkeypox. It should be noted that there is significant uncertainty about the efficacy and effectiveness of vaccination in the context and characteristics of the current monkeypox outbreak. This guidance is for all countries, those with confirmed human-to-human transmission and to support preparedness and readiness in countries with no current or ongoing monkeypox outbreak in the human population. It will be updated as information becomes available.

General

- Monkeypox is an infectious disease caused by the monkeypox virus (MPXV). This double-stranded DNA virus is a member of the *Orthopoxvirus* genus in the *Poxviridae* family, related to the virus which caused smallpox (eradicated in 1980).
- Control of monkeypox outbreaks primarily relies on public health measures including surveillance, contact-tracing, isolation and care of patients. While smallpox vaccines are expected to provide some protection against monkeypox, efficacy data are limited.
- Most interim vaccination recommendations provided here concern off-label use.
- On 23 July 2022, WHO declared the global monkeypox outbreak as a public health emergency of international concern (PHEIC).

Summary of interim recommendations

- Based on currently assessed risks and benefits and regardless of vaccine supply, mass vaccination is not required nor recommended for monkeypox at this time.
- Human-to-human spread of monkeypox can be controlled by public health measures including surveillance, early case-finding, diagnosis and care, isolation and contact-tracing, and self-monitoring by contacts.
- In managing the response, vaccination should be considered an additional measure to complement primary public health interventions.
- All decisions around immunization with smallpox or monkeypox vaccines should be by shared clinical decision-making, based on a joint assessment of risks and benefits, between a health care provider and prospective vaccinee, on a case-by-case basis. At an individual level, vaccination should not replace other protective measures.
- Post-exposure vaccination (PEPV): For close contacts of cases (for definition, see *Recommendation 3 – Post-exposure vaccination (PEPV)*), PEPV with an appropriate second- or third-generation vaccine is recommended prior to onset of any symptoms, ideally within four days of first exposure (and up to 14 days in the absence of symptoms), to prevent onset of disease or mitigate disease severity.
- Primary preventive (pre-exposure) vaccination (PPV): PPV is recommended for individuals at high-risk of exposure including: individuals but not limited to those who self-identify as gay or bisexual or other men who have sex with men (MSM) or other individuals with multiple sexual partners; and health workers at high risk of exposure, laboratory personnel working with *orthopoxviruses*, clinical laboratory personnel performing diagnostic testing

for monkeypox, outbreak response team members (as designated by national public health authorities).

- Vaccination programmes should be accompanied by:
    - a strong information campaign to inform vaccinees that it takes approximately 2 weeks from finalizing a complete series of vaccination (1 or 2 doses depending on product) for immunity to develop and that the level of protection conferred by vaccination is currently unknown; and
    - robust pharmacovigilance.
- All efforts should be made to administer vaccines for monkeypox within a framework of collaborative research, including randomized controlled trials (RCT). Where observational study designs are considered, they should be carefully planned to minimize bias and include standardized data collection tools for clinical and outcome data.

Vaccines

- Some countries have maintained strategic supplies of smallpox vaccines procured for the Smallpox Eradication Programme (SEP) which concluded in 1980. These first-generation vaccines held in national reserves since that time are not recommended for monkeypox at this time, as they do not meet current safety and manufacturing standards.
- Many years of research have led to development of new and safer (second- and in particular third-generation) vaccines for smallpox, some of which may be useful for monkeypox. Two vaccines (MVA-BN and LC16) have been approved in several jurisdictions for prevention of monkeypox.
- The supply of the newer, especially third-generation, vaccines is limited at this time and approaches for enhancing vaccine access are under discussion.

Changes from earlier version

This is an updated version of the guidance published on 24 June 2022. The revision contains minor updates as outlined in the table of revisions at the end of this document, primarily to emphasize the groups at risk of monkeypox for consideration for preventive vaccination, and to update terminology used in the guidance.

Introduction

In April 2022, a Strategic Advisory Group of Experts (SAGE) on Immunization Working Group on smallpox and monkeypox vaccines was established to advise the World Health Organization (WHO) on the use of monkeypox vaccines and update the 2013 recommendations on the use of smallpox vaccines.[1]

While monkeypox is a zoonotic disease, human monkeypox has been reported since 1970, with rising frequency in recent years. Two clades of monkeypox virus have been identified, Clade I and Clade II.[2] Since 2017, seven countries in the WHO Africa region have reported outbreaks, many in forested rural areas. However, countries are increasingly reporting monkeypox in previously unaffected regions. The Democratic Republic of the Congo, where Clade I has previously been identified, has reported over 2266 suspected cases from January to July 2022.[3] In Nigeria where Clade II has been identified, of the more than 550 cases reported since the outbreak began in 2017, many have occurred in urban and peri-urban areas with increasing human-to-human transmission.[4]

On 23 July 2022, the Director-General of the World Health Organization declared the multi-country outbreak of monkeypox to be a public health emergency of international concern (PHEIC).[5] Surveillance in all countries is expanding rapidly and WHO expects that more cases will be reported.

From 1 January to 23 August 2022, over 41000 cases of monkeypox have been reported to WHO from 96 Member States, with more than 60% of cases reporter from the Region of the Americas and 38% of cases reported from the European Region. Currently, most cases reported are MSM in connected social and sexual networks. It is expected that cases will also continue to occur in the other population groups.

Spread of monkeypox from person to person has been known in the past to generally require prolonged close contact, such as face-to-face contact in close proximity, or skin-to-skin physical contact.[6] Such exposure can occur in a range of settings including at home, in social or sexual networks, or in the health care setting.

Monkeypox can present clinically in the manner classically described or with fewer typical features, such as less severe illness, fewer or less widely disseminated lesions, appearance of lesions before

[1] Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization. November 2013: Conclusions and recommendations. Available at: www.who.int/publications/i/item/WER8901https://www.who.int/publications/i/item/WER8901, accessed 3 August 2022.

[2] Clade I of monkeypox virus was previously known as the Congo Basin or Central African clade and Clade II was previously known as the West African clade.

[3] Outbreaks and Emergencies Bulletin, Week 31: 25 - 31 July 2022. (www.afro.who.int/health-topics/disease-outbreaks/outbreaks-and-other-emergencies-updates, accessed 9 August 2022).

[4] Yinka-Ogunleye A et al. Monkeypox Risk and Mortality Associated with HIV Infection: A National Case Control Study in Nigeria. Lancet Preprint. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4172063, accessed 9 August 2022.

[5] Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox. (www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox, accessed 9 August 2022).

[6] While it is also possible that transmission through other body fluids such as semen or vaginal fluids might occur, this has not yet been confirmed and is not necessary for exposure to occur during sex.

constitutional symptoms such as fever, or appearance of lesions in different stages of development. Such atypical features are being observed in the current outbreak and transmission mechanisms in different contexts are not fully understood.

This interim guidance for vaccination is provided to support the global response to help stop the monkeypox outbreak in an evolving situation.[7] For information on different vaccines that may be available, consult the background section which follows these recommendations. Smallpox and monkeypox vaccines have been procured nearly exclusively by national governments and are not available on the private market. In this context, any decisions to use smallpox or monkeypox vaccines should occur in consultation with national health authorities.

Principles

In consultation with the experts of the SAGE Working Group on smallpox and monkeypox vaccines and further to the Temporary Recommendations**Error! Bookmark not defined.** issued by the Director-G eneral, WHO proposes the following principles to underpin the recommendations:

- The WHO interim guidance should be broad to guide national authorities in development of their own monkeypox vaccination policies and strategies to support readiness and response.
- In 2013, WHO provided recommendations on the use of smallpox vaccines. These additional updated interim recommendations from WHO apply for prevention and control of monkeypox only. They will be updated as more information becomes available.
- This guidance is provided to support the strategic imperatives of the response, which include information and communication, public health action, and evidence-based programming.[8]
- Established principles of human rights, inclusion and the dignity of all individuals and communities should support the planning for and implementation of these recommendations.

Additional WHO guidance

WHO has also issued the following monkeypox-related guidance:

- Surveillance, case investigation and contact tracing for monkeypox;
- Laboratory testing for monkeypox virus (MPXV);
- Clinical management and infection prevention and control for monkeypox;
- Risk Communication and Community Engagement (RCCE) for monkeypox outbreaks;
- Monkeypox: public health advice for gay, bisexual and other men who have sex with men;
- Advice for gatherings during the current monkeypox outbreak;

[7] The recommendations contained in this publication are based on the advice of independent experts who have considered the best available evidence, a risk–benefit analysis and other factors, as appropriate. This publication may include recommendations on the use of medicinal products for an indication, in a dosage form, dose regimen, population or other use parameters that are not included in the approved labelling. Relevant stakeholders should familiarize themselves with applicable national legal and ethical requirements. WHO does not accept any liability for the procurement, distribution and/or administration of any product for any use.

[8] WHO Monkeypox Research - What study designs can be used to address the remaining knowledge gaps for monkeypox vaccines? (https://www.who.int/news-room/events/detail/2022/08/02/default-calendar/who-monkeypox-research---what-study-designs-can-be-used-to-address-the-remaining-knowledge-gaps-for-monkeypox-vaccines, accessed 9 August 2022)

More information, including for the general public on monkeypox is available in the form of Questions and Answers (Q&As) as well as on the respective WHO website.