

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 preventive 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 preventive vaccination (PEPV): For close contacts of cases (for definition, see [Recommendation 3 – Post-exposure preventive 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 reported 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/WER8901<https://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](https://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-General, 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](#).

Recommendations

Recommendation 1 – Vaccination policy development

Recommendation:

The Member States of WHO are strongly encouraged to convene their national immunization technical advisory groups (NITAGs) to review the evidence and develop policy recommendations for the use of vaccines for monkeypox as relevant to the national context. In accordance with the WHO declaration of a public health emergency of international concern, it is particularly important that countries support early and timely efficacy/effectiveness studies and ensure readiness to implement vaccination as soon as it is needed.

Remarks:

Vaccine supply, regulatory authorization in countries, and vaccine dose demand are evolving as the scope and scale of the outbreak are being characterized and better understood. Vaccine efficacy/effectiveness against monkeypox in the current epidemic remains uncertain. While further clinical data are collected, countries should be prepared to consider the use of third-generation vaccines approved for monkeypox, as well as selected second-generation smallpox vaccines for monkeypox. Benefit-risk profiles vary by product. In light of current vaccine supply constraints, countries are considering or have approved⁹ an intradermal (ID) route of administration of one fifth of the volume of a full dose of MVA vaccine¹⁰ as an alternate dosing regimen and antigen-sparing measure. Countries should review the national regulatory actions that may be required to facilitate the use of these vaccines.

Implementation and monitoring considerations:

All countries are advised to strengthen the biological, ecological, and epidemiological understanding of monkeypox in their context. With more precise characterization of infection, transmission patterns and disease, as well as ascertainment of risk and needs assessments, countries can determine their clinical and public health needs regarding vaccines, along with operational requirements, as well as research and development regarding public health measures, vaccines, antivirals, diagnostics, materials and supplies, and research needs to support policy.

⁹ Monkeypox Update: FDA Authorizes Emergency Use of JYNNEOS Vaccine to Increase Vaccine Supply (<https://www.fda.gov/news-events/press-announcements/monkeypox-update-fda-authorizes-emergency-use-jynneos-vaccine-increase-vaccine-supply>, accessed 10 August 2022),

¹⁰ Frey SE, Wald A, Edupuganti S, et al. Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects. *Vaccine*. 2015;33(39):5225-5234. doi:10.1016/j.vaccine.2015.06.075

Recommendation 2 – Vaccination strategy and outbreak response

Recommendation:

Mass vaccination is not recommended for outbreaks of monkeypox. Vaccination is not recommended for the general population at this time.

Public health authorities should put in place a robust surveillance and containment strategy to ensure detailed case investigation, care and isolation, as well as thorough contact tracing and monitoring, as described in the WHO interim guidance on [Surveillance, case investigation and contact tracing for monkeypox](#). This will help identify those at highest risk of infection and therefore the priority if vaccination takes place.

To control the current outbreak, the public health measures needed include use of personal protective equipment (PPE) for caregivers, good hand hygiene, and isolation and supportive care of case patients for the duration of the infectious period, that is until the skin lesions dry up, become crusts and fall off or mucosal lesions have disappeared. This may take 2 to 4 weeks.

Where appropriate vaccines are available, PEPV is recommended for selected close contacts of monkeypox patients (see *Recommendation 3*).

Where appropriate vaccines are available, PPV is recommended for groups at high risk of exposure to monkeypox at this time (see *Recommendation 4*).

As the outbreak evolves and vaccine supply improves, broader use of vaccines for persons at risk may be warranted if justified by the evidence.

Remarks:

The above recommendations are based on surveillance-containment approaches for vaccine-preventable disease outbreaks. Identifying contacts requires sensitive yet essential public health collaboration locally and between countries. The identification of contacts requires carefully designed communication to be effective and to avoid stigmatization.

It is critical that national and local response be rapid, targeted and effective to stop onward transmission of monkeypox. Non-vaccine measures should be widely advised and emphasized.

Identifying contacts who may be at risk based on possible recent exposure (for example having recently had multiple sexual partners) may be challenging. Nonetheless, given ongoing monkeypox transmission, every effort must be made to identify and assess those who may be at risk of infection, ensure they know how to monitor for appearance of symptoms, and consider offering vaccine where feasible and appropriate. Beyond close contacts of a case the extent to which more indirect contacts should be included is unknown and will depend on epidemiology and risk behaviours. Even where vaccine cannot be offered for supply, regulatory, choice of product, programmatic, timeliness for PEPV, safety considerations or other reasons, contact-tracing is essential to identify those at risk and break chains of transmission. Symptom monitoring for contacts and isolation of newly diagnosed cases is critical to prevent onward spread of the disease, particularly given the atypical presentation of many cases.

Implementation and monitoring considerations:

Where vaccines are used, national authorities should make every effort to evaluate the vaccines using collaborative research protocols and data collection tools on efficacy/effectiveness and safety.

WHO is developing template protocols and data collection recommendations for emergency or investigational use.

Further, where vaccines are proposed, national health authorities must ensure that staff are fully informed and trained on the safe and proper use of replication-competent,¹¹ minimally replicating and/or non-replicating smallpox and monkeypox vaccines.

¹¹ Replication-competent smallpox vaccines consist of live vaccinia virus (an orthopoxvirus) that offer cross-protection when administered for the prevention of infectious disease due to other orthopoxviruses (such as smallpox, monkeypox and cowpox). ACAM2000 currently produced by Emergent BioSolutions is a replication-competent vaccine. Vaccines that are minimally replicating (e.g. LC16 from KM Biologics) and non-replicating (e.g. MVA-BN by Bavarian Nordic) consist of live vaccinia virus that has been greatly attenuated, resulting in vaccine products that are immunogenic against orthopoxviruses with improved safety profiles. More information is available here: <https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/smallpox-vaccines>, accessed 3 August 2022.

Recommendation 3 – Post-exposure preventive vaccination (PEPV)

Recommendation:

For close contacts of cases at high or medium risk of exposure ([Table 1](#)), post-exposure preventive vaccination (PEPV) is recommended with an appropriate second- or third-generation vaccine, ideally within four days of first exposure (and up to 14 days in the absence of symptoms), to prevent onset of disease or to attenuate its severity. PEPV can be offered with any of the vaccines listed in [Table 1](#), as appropriate and available. Immunization schedules vary by product.

Vaccine recipients must be informed that the level and duration of protective efficacy is currently unknown, and also that it takes approximately 2 weeks from time of finalizing a complete series of vaccination (1 or 2 doses, depending on product) for immunity to develop.

Remarks:

Recommendations for PEPV vaccination against monkeypox should be considered in light of the potential risk of monkeypox to the person exposed, the presence of contraindications or precautions with respect to the choice of vaccines available, priorities set at national level for the use of limited vaccine supplies and inclusion or exclusion criteria for clinical trial protocols or compassionate use.

Exposure risk for contacts of persons with confirmed, probable or suspected monkeypox is classified by the nature of the potential exposure.

Definition of a contact

A contact is defined as a person who, in the period beginning with the onset of the source case's first symptoms and ending when all scabs have fallen off, has had one or more of the following exposures with a probable or confirmed case of monkeypox:

- direct skin-to-skin physical contact (such as touching, hugging, kissing, intimate or sexual contact)
- contact with contaminated materials such as clothing or bedding, including material dislodged from bedding or surfaces during handling of laundry or cleaning of contaminated rooms
- prolonged face-to-face respiratory exposure in close proximity
- respiratory exposure (i.e., possible inhalation of) or eye mucosal exposure to lesion material (e.g., scabs/crusts) from an infected person
- the above also apply for health workers potentially exposed in the absence of proper use of appropriate PPE

[Table 1](#) provides a summary of recommendations on post-exposure vaccination in light of the assessed level of risk of possible types of exposure. Where indicated, PEPV is recommended with second- or third-generation vaccines as outlined in *Recommendation 5* and *Recommendation 6* below.

Table 1: Description of exposure risk and recommendation for post-exposure preventive vaccination (PEPV) of contacts for prevention of monkeypox (19 August 2022)

Exposure risk	Description of exposure	Post-exposure preventive vaccine (PEPV)	Vaccine
High	<p>Direct exposure of skin or mucous membranes to skin or respiratory secretions of a person with confirmed, probable or suspected monkeypox, their body fluids (e.g., lesion vesicular or pustular fluid) or potentially infectious material (including clothing or bedding) if not wearing appropriate PPE. This includes:</p> <ul style="list-style-type: none"> • inhalation of droplets or dust from cleaning contaminated rooms • mucosal exposure due to splashes from body fluids • physical contact with someone who has monkeypox, including direct contact during sexual activities. This includes face-to-face, skin-to-skin or mouth-to-skin contact or exposure to body fluids or contaminated materials or objects (fomites) • normally sharing a residence (permanently or occasionally) during the presumed incubation period with a person who has been diagnosed with monkeypox, or • a penetrating sharps injury from a contaminated device or through contaminated gloves. 	PEPV is recommended with vaccine appropriate for each individual Table 1	ACAM2000 LC16 MVA-BN
Medium	<ul style="list-style-type: none"> • No direct contact but close proximity in the same room or indoor physical space as a symptomatic patient with confirmed monkeypox, if not wearing appropriate PPE (see interim guidance on Clinical management of monkeypox and infection prevention and control). 	PEPV is recommended with vaccine appropriate for each individual Table 1	ACAM2000 LC16 MVA-BN
Low / Minimal	<ul style="list-style-type: none"> • Contact with a person with confirmed, probable or suspected monkeypox or an environment that may be contaminated with monkeypox virus, while wearing appropriate PPE and without any known breaches of PPE or of donning and doffing procedures. • Community contact, such as being in an outdoor setting with a symptomatic case without any close proximity or physical contact. • No known contact with a symptomatic monkeypox case in the last 21 days, or • Laboratory personnel handling routine clinical blood samples or other specimens not directly related to monkeypox diagnostic testing. 	PEPV is not recommended	Not applicable

Persons who have had primary preventive (pre-exposure) vaccination (e.g. health workers, laboratory personnel or other persons who may be at occupational or personal risk) who become exposed (contacts) are not recommended to receive PEPV but should monitor for any symptoms up to 21 days after the last exposure.

In case of limited vaccine supply, close contacts at risk of developing severe disease, such as children, pregnant women and immunocompromised people, such as those on immunosuppressive therapy or living with poorly controlled HIV, should be prioritized for receipt of vaccine following analysis of risks and benefits on a case-by-case basis according to vaccine(s) available (see *Recommendation 5*).

In the case of supply shortages, some authorities may consider offering PEPV with MVA-BN as a single dose or with a delayed second dose, however there is as yet no data on the effectiveness of this approach.

Implementation and monitoring considerations:

National health authorities must ensure that information is provided to health personnel on administration of MVA-BN monkeypox vaccine via sub-cutaneous or ID injection, and on the use of bifurcated needles for administration of ACAM2000 or LC16. Instructions for smallpox vaccination with a bifurcated needle are provided [here](#). Replicating smallpox vaccines such as ACAM2000 consist of live vaccinia virus; it is therefore important to follow special care instructions¹² for the vaccination site (available also in video form¹³) including covering the site with a light bandage.

[Hand hygiene](#) should be performed with soap and water or an alcohol-based hand rub before and after vaccine administration. The vaccination site must not be touched before it has healed and care must be taken so that others do not touch the vaccination site, particularly infants or young children. Further guidance on disposal of bandages and care and laundry of clothing can be found [here](#).

¹² Written instructions on care of the smallpox injection site. USCDC. Available here :

<https://www.cdc.gov/smallpox/vaccine-basics/who-gets-vaccination.html#care-for>, accessed 3 August 2022.

¹³ Video instructions for the care of the vaccination site for replicating smallpox vaccines. USCDC. Available here: [Chapter 3: How to Care for the Smallpox Vaccination Site and Prevent the Spread of Vaccinia Virus - YouTube](#), accessed 3 August 2022.

Recommendation 4 – Primary preventive (pre-exposure) vaccination (PPV)

Recommendation:

Primary preventive (pre-exposure) vaccination (PPV): PPV is recommended for high risk groups 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; and outbreak response team members (as designated by national public health authorities), see Table 1.

Remarks:

As vaccine supply improves, national authorities should consider strategies for vaccinating all persons at high risk of exposure, and consider appropriate inclusion of individuals with high risk of severe outcomes based on their risk of exposure as determined by the epidemiology of monkeypox.

Health workers are all people engaged in work whose primary intent is to improve human health particularly in the clinical setting, including health service providers and support workers.¹⁴ In the context of limited vaccine supply, in assessing eligibility for primary preventive (pre-exposure) vaccination, national authorities should consider who may be at risk of repeated exposure and the possible nature of the exposure.

Clinical laboratory personnel who perform routine chemistry, hematology, and urinalysis testing, including for patients with suspected or confirmed monkeypox, are not included in this recommendation as their risk of exposure is low.

Implementation and monitoring considerations:

Table 1 provides a summary of recommendations on primary preventive (pre-exposure) vaccination according to the assessed level of risk and vaccine indications and precautions. These include the following considerations.

Where vaccination is considered for any individual, it should be the result of shared clinical decision-making between the individual and their health care provider or public health officer.

As for PEPV, national health authorities must ensure that information is provided to health personnel on the routes of administration and interval of doses, as applicable (see Implementation considerations in *Recommendation 3*).

¹⁴ Health workers are all people engaged in work actions whose primary intent is to improve health. This includes health service providers, such as doctors, nurses, midwives, public health professionals, lab-, health- and medical and non-medical technicians, personal care workers, community health workers, healers and some practitioners of traditional medicine. It also includes health management and support workers, such as cleaners, drivers, hospital administrators, district health managers and social workers, and other occupational groups in health-related activities. Health workers include not only those who work in acute care facilities but also those employed in long-term care, public health, community-based care, social care and home care and other occupations in the health and social work sectors as defined by the International Standard Industrial Classification of All Economic Activities (ISIC), revision 4, section Q: Human health and social work activities (https://unstats.un.org/unsd/publication/seriesm/seriesm_4rev4e.pdf, accessed 3 August 2022).

Table 1: Use of vaccines for primary preventive (pre-exposure) vaccination (PPV) for prevention of monkeypox: WHO interim recommendations (19 August 2022)

Population group	Interim recommendations for vaccination
General population	Not recommended
Individuals at high risk of exposure, importantly but not exclusively gay, bisexual and other men who have sex with men (MSM) or individuals with multiple sexual partners	Recommended <i>Vaccines to be used:</i> <ul style="list-style-type: none"> • ACAM2000 • LC16 • MVA-BN
Health workers at risk of exposure, research laboratory personnel,* clinical laboratory personnel performing diagnostic testing for <i>orthopoxviruses</i> ,** and designated response team members at risk for occupational exposure to monkeypox	Recommended <i>Vaccines to be used:</i> <ul style="list-style-type: none"> • ACAM2000 • LC16 • MVA-BN
Individuals for whom replicating vaccine is not recommended because of young age (children), pregnancy, immune deficiencies, immunosuppression therapies*** or atopic dermatitis****	Recommended <i>Vaccines to be used:</i> <ul style="list-style-type: none"> • LC16 • MVA-BN

*Research laboratory personnel are those who handle 1) cultures or 2) animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent strains that can cause clinical infection and produce infectious virus in humans, or other orthopoxviruses that infect humans (e.g., *Monkeypox virus*, *Cowpox virus*, and *Variola virus*).

** Clinical laboratory personnel who perform routine chemistry, hematology, and urinalysis testing, including for suspected or confirmed patients with monkeypox, are not included as their risk for exposure is very low.

*** Persons with immunocompromise (e.g., HIV/AIDS, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumour necrosis factor inhibitors, high-dose corticosteroids, hematopoietic stem cell transplant recipient <24 months post-transplant (or ≥24 months with graft-versus-host disease or disease relapse, or having autoimmune disease with immune deficiency) <https://www.cdc.gov/poxvirus/monkeypox/treatment.html>, accessed 3 August 2022

**** Persons who have these conditions (e.g., atopic dermatitis, immunosuppression, pregnancy) can safely receive the vaccines recommended following consideration of risks and benefits for each individual; a risk of serious illness due to monkeypox may remain should infection occur despite PPV. For this reason, consideration should be given to avoidance of diagnostic laboratory work or provision of care for monkeypox patients.

Recommendation 5 – Vaccination for special population groups

Recommendation:

Children, pregnant women¹⁵ and immunocompromised persons may be at risk of more severe disease with monkeypox and/or a worse outcome than other persons.¹⁶ Vaccination against monkeypox as a primary preventive (pre-exposure) vaccination (PPV) measure is not currently recommended for these population groups solely on the basis of their higher risk of severe disease. For persons in these groups who may be at increased risk of exposure, PPV may be warranted. The choice and timing of vaccination must be considered in light of a detailed joint risk-benefit analysis and shared clinical decision-making with respect to the person's individual circumstances, in accordance with the risk criteria and implementation and monitoring considerations detailed in this interim guidance.

Vaccination against monkeypox as post-exposure preventive vaccination (PEPV) may be considered for individuals in special population groups, i.e. during pregnancy, for children, or for persons with immune suppression,¹⁷ including people living with HIV (PLWH), if a vaccine appropriate for these groups is available, following a careful evaluation of risks and benefits.

Remarks:

Of the second- and third-generation vaccines, LC16 has been licensed for use in children in Japan and MVA has obtained emergency use authorization in children in the USA.¹⁸ On the choice of vaccine for specific population groups see *Recommendation 6*.

Implementation and monitoring considerations:

Provision of monkeypox or smallpox vaccines to special population groups such as young children or pregnant women should be done under emergency investigation protocols to ensure proper monitoring of vaccine recipients and sufficient collection of critically important information to inform the ongoing and future responses.

¹⁵ Pittman PR, et al. Clinical characterization of human monkeypox infections in the Democratic Republic of the Congo. medRxiv 2022. <https://doi.org/10.1101/2022.05.26.22273379>, accessed 9 August 2022.

¹⁶ Human Monkeypox. Jezek, Z.; Fenner, F., 1988. DOI: 10.1159/isbn.978-3-318-04039-5

¹⁷ Persons with immune compromise who could develop severe monkeypox include the following: human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumour necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component). www.cdc.gov/poxvirus/monkeypox/treatment.html, accessed 3 August 2022

¹⁸ Subcutaneous injection only, 2 doses, 4 weeks apart. FDA Fact Sheet: <https://www.fda.gov/media/160773/download>, accessed 11 August 2022)

Recommendation 6 – Choice of vaccines for monkeypox

Recommendation:

National authorities should consider approved monkeypox and/or smallpox vaccines in the response to monkeypox outbreaks.

Vaccine options that can be considered for approved, off-label or compassionate use for primary preventive (pre-exposure) or post-exposure preventive vaccination of monkeypox include MVA-BN, LC16 or ACAM2000. The safety and reactogenicity of available vaccines and the risk of vaccine-related adverse events should be considered in the benefit-risk analysis for choice of vaccine as there are significant differences between the vaccines.

For healthy adults, replicating vaccinia-based vaccines (ACAM2000), minimally replicating vaccines (LC16), or non-replicating vaccine (MVA-BN) may be considered, while preference should be given to non or minimally replicating vaccines, if available.

For individuals for whom replicating vaccine (such as ACAM2000) is contraindicated (severe immune deficiency according to package leaflet) or for which there are warnings or precautions because of e.g. immunosuppression therapies, atopic dermatitis, the non-replicating monkeypox vaccine MVA-BN would be preferred, where available.

During pregnancy, where consideration is given to primary or post-exposure vaccination, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred, and ACAM 2000 should not be used. For women who are breast-feeding, where consideration is given to primary or post-exposure vaccination, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred, and ACAM 2000 should not be used.

For children, where consideration is given to vaccination for post-exposure vaccination, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred. As in most countries MVA-BN is approved for 18 years and above, any use in children in those countries would be off-label use.

Shared clinical decision-making is recommended for all persons mentioned above.

Remarks:

Approval of MVA-BN and LC16 for the prevention of monkeypox has been granted on the basis of human safety and animal efficacy data as well as human and animal immunogenicity studies compared to other smallpox vaccines. Efficacy of these vaccines in humans, particularly in the context of human-to-human transmission during an outbreak of monkeypox, remains to be quantified.

Implementation and monitoring considerations:

National authorities should convene their NITAGs to review vaccine choices and availability in their jurisdiction and discuss the implications of vaccination with smallpox/monkeypox vaccines including off-label use, protocols for compassionate use or emergency listing, and investigational protocols for robust data collection in line with WHO recommendations.

Recommendation 7 – Global coordination and vaccine supply

Recommendation:

All Member States are strongly encouraged to make information on their smallpox/monkeypox vaccine reserves available to WHO to support global coordination efforts.

Vaccine supply currently remains very constrained. Strong collaboration between all Member States is essential to ensure supply is made available adequately, equitably and according to public health need. Member States are encouraged to share vaccine doses with countries that face supply constraints.

All current and future vaccine manufacturers are strongly encouraged to make information on their smallpox and monkeypox vaccine research plans, existing stocks, current production capacity and emergency surge planning available to WHO.

Remarks:

Manufacturers are also encouraged to consider smallpox/monkeypox vaccine presentation and packaging to optimize operational features and reduce cold-chain requirements (e.g. small size multi-dose vials), as appropriate to the circumstances and vaccination strategies implemented, and to ensure provision of bundled injection materials and safety boxes where appropriate, with instructions for their use.

Implementation and monitoring considerations:

Training materials should be developed and made available on accessible platforms for the use of bifurcated needles where required, based on [WHO's guidance](#).

The WHO is establishing coordination mechanisms to maximise the timeliness and efficiency in making vaccines available where they are needed.

Background

Vaccines and vaccine development

Smallpox vaccines produced and successfully used during the intensified SEP are called first-generation vaccines in contrast to smallpox vaccines developed at the end of the eradication phase or thereafter and produced by modern cell culture techniques. Second-generation smallpox vaccines use the same vaccinia virus vaccine strains employed for manufacture of first-generation vaccines or clonal virus variants plaque-purified from traditional vaccine stocks and manufactured on defined cell lines. The term third-generation refers to more attenuated smallpox vaccine strains specifically developed as safer vaccines towards (LC16) or after (MVA-BN) the end of the eradication phase by further passage in cell culture or animals. In 2019, MVA-BN¹⁹ was approved for prevention of monkeypox by national regulatory authorities. LC16 vaccine was approved for the prevention of monkeypox in August 2022 in Japan. Table 2 outlines the vaccines currently available and their regulatory status. First generation smallpox vaccines are not included in the table below.

Table 2: Smallpox and monkeypox vaccine options (19 August 2022)

Vaccine (Manufacturer)	Licensed for smallpox (country, type, date)	Licensed for monkeypox (country, type, date)	Considerations	Presentation	Injection materials
MVA-BN (Bavarian Nordic) Third generation	EU (Imvanex): has been authorised under exceptional circumstances (2013) Canada (Imvamune): Full MA (2013) USA (Jynneos): Full MA (2019)	USA (Jynneos): Full MA (2019) Canada (Imvamune): Full MA (2019) EU (Imvanex): has been authorized under exceptional circumstances (2022)	Two doses four weeks apart. Liquid-frozen formulation, approved for use in the general adult population. The USA has granted emergency authorization for use in individuals 18 years and below (August 2022).	Liquid frozen or lyophilized (freeze-dried) Single dose vials (Multidose vials possible)	Needle and syringe (sub-cutaneous administration)
LC16 (KM Biologics) Third generation	Japan - Full MA (1975)	Japan: MA (August 2022)	Single dose. Approved for use in infants and children (all ages) as well as adults	Freeze-dried Multidose vials	Bifurcated needle
ACAM2000 (Emergent BioSolutions) Second generation	Multiple countries - Approved	USA - EIND for PEPV	Single dose. Approved for use in adults aged 18 – 64 years of age.	Freeze-dried Multidose vials	Bifurcated needle

EU: European Union (European Medicines Agency). USA: United States of America (Food and Drug Administration). Canada: Health Canada. MA: market authorization. EIND: Emergency investigational new drug programme of the US Food and Drug Administration. PEPV: post-exposure preventive vaccination. SEP: Smallpox eradication program. **For example: Wetvax/APSv; Lister/Elstree or Lancy-Vaxina.

¹⁹ MVA-BN is the modified Ankara strain of vaccinia virus developed by Bavarian Nordic and marketed as Imvanex™, Imvamune™ or Jynneos™ in the European Union, Canada and the United States of America, respectively.

Smallpox vaccine policy

In 2013, WHO made a series of recommendations¹ for the use of smallpox vaccines based on a comprehensive assessment of smallpox vaccine effectiveness and safety, included GRADEing of evidence.²⁰ The 2013 guidance focussed on preparedness for a re-emergence of smallpox through natural, accidental or deliberate causes; monkeypox was not specifically included. WHO did recommend that preventive vaccination be reserved for laboratory personnel working with *orthopoxviruses*.²¹ To date, smallpox vaccines have been developed using live replicating, minimally replicating, or non-replicating strains of vaccinia virus which are known to confer cross-protection against human disease due to other *orthopoxviruses*, including monkeypox, cowpox, and smallpox (caused by the variola virus).²² Over 30 years, research has continued under the oversight of WHO to develop newer and safer vaccines in the event of a re-emergence of smallpox.

Smallpox vaccines held in national reserves and vaccines more recently developed would likely provide protection against monkeypox. This statement is based on experience with their use during the SEP as well as available pre-clinical and clinical studies for the newer products. These products included ACAM2000 (developed and produced through cell culture techniques in France and the United States of America) and LC16 (attenuated strain developed in Japan and licensed in 1975). Along with the MVA-BN vaccine described below, there may be other products available in some countries. ACAM2000 and LC16 have been shown to be protective against monkeypox in animal models and immunogenic in human studies. Licensure for the prevention of monkeypox has not been sought to date for ACAM2000, however, Japan's national regulatory authority has authorized LC16 for monkeypox.

In 2013, MVA-BN was approved for prevention of smallpox (in Canada and in the European Union). In 2019, MVA-BN was approved for the prevention of smallpox and monkeypox in the USA,²³ and in Canada the indication was also extended to monkeypox the same year.²⁴ On 22 July 2022 the European Union recommended extending the indication to include protecting adults from monkeypox disease. Pre-exposure phase III trials have demonstrated positive results for immunogenicity and indirect measures of efficacy and a favourable safety profile was confirmed for healthy population groups, as well as PLWH, atopic dermatitis and haematopoietic stem cell transplants (see references below). No cases of myocarditis were reported but data evaluating this

²⁰GRADE tables available at:

https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Nov2013/8_session_smallpox/Nov2013_session_8_GRADE_tables.pdf, accessed 3 August 2022.

²¹ Orthopoxvirus is a genus of viruses in the Poxviridae family several of which can be pathogen to humans, including variola, monkeypox, cowpox and vaccinia viruses.

²² Exploration in the 1700s of the use of animal lymph or human lesion fluid from cowpox sores to prevent smallpox was based on the premise that infection with the milder form of disease would prevent the dreaded smallpox. This culminated in the demonstration by Dr Jenner in 1796 that 'vaccination', as the practice was named, was protective against smallpox. In 1980, WHO declared the eradication of smallpox.

²³ In the USA, MVA-BN, commercialized as JYNNEOS, is a vaccine Indicated for prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection

²⁴ Health Canada expanded the approval of MVA-BN, commercialized as IMVAMUNE®, to include additional indications – specifically, monkeypox and related orthopoxvirus infections and disease in adults 18 years of age and older determined to be at high risk for exposure. The European Medicines Agency has approved MVA-BN, commercialized as IMVAMEX®, for the prevention of smallpox.

outcome were limited. While there is limited clinical data on the use of vaccines to prevent monkeypox, the effectiveness of MVA-BN against monkeypox was extrapolated from human immunogenicity trials, from animal studies (including those comparing MVA-BN with ACAM2000) and from clinical studies of reduction of the size of the vaccine ‘take’ following vaccination with ACAM2000. Further information is provided later in the references to this document.

While MVA-BN has not been specifically studied in a clinical trial in pregnant women or children, the same non-replicating MVA viral vector is used as a platform for other vaccines including MVA-filo (marketed as Mvabea™) against Ebola virus disease (EVD).²⁵ This EVD vaccine is approved in the European Union for adults and children aged one year and older. The MVA viral vector platform is also being used to develop a vaccine against infection with respiratory syncytial virus. Data from nine published studies on MVA-BN as a viral vector platform for prevention of Ebola or RSV support the favourable safety profile of the product and some data suggest that immune response to MVA is not altered by serving as a vector. In addition, animal models have shown no evidence of fetal harm.

Vaccine safety

Expected vaccine-related common reactions following use of smallpox vaccines are usually mild to moderate in severity and include local reactions such as pain, redness or inflammation of the injection site, and systemic reactions such as fever, malaise, headache, chills, nausea, fatigue, and lymphadenopathy. The frequency and severity of such reactions vary by vaccine and individual characteristics of the vaccinee. Serious adverse events are rare. Guidance for countries on smallpox vaccine safety surveillance was published by WHO in 2018.²⁶

In 2015, the WHO Global Advisory Committee on Vaccine Safety (GACVS) reviewed the evidence on the safety of replicating and non-replicating smallpox vaccines.²⁷ The Committee was provided with safety information on several smallpox vaccines to make informed decisions regarding emergency reserves and future use. The safety update also included an overview of the safety of smallpox vaccines used by the SEP. Detailed safety information was provided for the replicating²⁸ vaccine ACAM2000 and the non-replicating MVA-BN smallpox vaccines. The GACVS noted that no new safety concerns had been observed with the ACAM2000 (USA), LC16 (Japan) or MVA-BN (Denmark) vaccines. The following summarizes current information on smallpox vaccine safety.

There is little safety information on ACAM2000 or LC16 among pregnant women, and no data on use of ACAM2000 in children. The GACVS recommended that any use of smallpox vaccines be guided by the anticipated risk versus benefit presented during various outbreak or exposure scenarios. The information needs here to be considered in the context of monkeypox. Known side effects, adverse events and contraindications for different smallpox vaccines are outlined below. The GACVS noted that while the risk of a smallpox outbreak remains low, outbreaks of, or

²⁵ Mvabea is given as a single injection about 8 weeks after an injection of Zabdeno.

²⁶ [Identifying and responding to serious adverse events following immunization, following use of smallpox vaccine during a public health emergency: a guidance document for smallpox vaccine safety surveillance \(who.int\), accessed 3 August 2022](#)

²⁷ Global Advisory Committee on Vaccine Safety, 2–3 December 2015. www.who.int/publications/i/item/who-wer9103-21-32<https://www.who.int/publications/i/item/who-wer9103-21-32>, accessed 3 August 2022.

²⁸ Replicating viral vectors retain the ability to make new viral particles alongside delivering the vaccine antigen when used as a vaccine delivery platform.

exposures to, other *orthopoxviruses* may occur and adequate screening procedures may minimize any risks associated with vaccination.

ACAM2000 (USA)

According to the package insert, ACAM2000 is [contraindicated](#) in severe immune deficiency. Warnings and precautions for certain population groups (e.g., in PLWH, children and in particular infants <12 months of age, or pregnant women, where it can cause fetal harm) apply. ACAM2000 live vaccinia virus may be transmitted from a lactating mother to her infant causing complications in the infant from inadvertent inoculation. It is important to note that the package insert reflects the indication of smallpox prevention.

Common side effects of ACAM2000 include inoculation site reactions, lymphadenitis, and constitutional symptoms, such as malaise, fatigue, fever, myalgia, and headache. Serious adverse events associated with ACAM2000 include rare, generalized reactions such as progressive vaccinia, generalized vaccinia, skin infections, erythema multiforme including Stevens-Johnson syndrome, and eczema vaccinatum. Cardiac manifestations such as myocarditis and pericarditis and neurological manifestations like post-vaccinial encephalitis, encephalomyelitis or encephalopathy have been reported.

It is very important for the ACAM2000 recipient to properly care for the vaccination site to prevent the virus in the vaccine from spreading and infecting another part of the body and other people as accidental infection can occur, most frequently through inoculation of the eyelids or conjunctiva, although accidental infection of other body sites such as mouth, lips, genitalia and anus is also possible. In most patients this occurred 5-12 days after vaccination.

If vaccination is being considered for someone who lives in the same household with or has close contact with a person contraindicated or with a warning/precaution according to the package leaflet, ACAM2000 should be avoided if possible; otherwise careful precautions must be taken by the vaccinee to avoid contact with infants, children, pregnant women or other persons in the household who may be at risk of severe outcomes. Although it is not known whether vaccine virus or antibodies are secreted in human milk, live vaccinia virus could be inadvertently transmitted from a mother to her infant through direct contact.

It should be noted that in unvaccinated persons who are accidentally infected by someone who has recently received the vaccine, serious health problems can also occur. Unvaccinated persons who are pregnant, or have problems with their heart or immune system, or have skin problems like eczema, dermatitis, psoriasis, and who have close contact with a vaccine recipient are at an increased risk for serious problems if they become infected with the vaccine virus, either by being vaccinated, or by being in close contact with a person who was vaccinated.

LC16 vaccination (Japan)

According to the package insert, LC16 vaccine is contraindicated in any person who is immunosuppressed or has atopic dermatitis, or during pregnancy, or who has experienced an

allergic reaction to any vaccine component.²⁹ Health care providers and vaccine administrators must be prepared to manage any anaphylactic reaction following administration of LC16.

Minor side effects seen following administration of LC16 vaccine include lymphadenopathy, fever, fatigue, rash, erythema at the inoculation site, joint pain, swelling at the inoculation site and autoinoculation as described above. The incidence of side effects for primary vaccinees is significantly higher than for re-vaccinees. No serious adverse events have been reported.

MVA-BN (Denmark)

The MVA-BN vaccine should be used with caution in any person who has experienced an allergic reaction to any vaccine component. Health care providers and vaccine administrators must be prepared to manage any anaphylactic reaction following administration of MVA-BN.

The most common side effects (in more than one in 10 vaccinees) associated with administration of [MVA-BN](#) were injection site reactions (pain, redness, swelling, induration, itching) and systemic reactions such as muscle pain, headache, fatigue, nausea, myalgia and chills. Persons with atopic dermatitis may experience more intense local skin reactions (such as redness, swelling and itching) and other general symptoms (such as headache, muscle pain, feeling sick or tired), as well as a flare-up or worsening of their skin condition.

Vaccine research

The targeted use of smallpox and monkeypox vaccines are expected to contribute to controlling and preventing the onward spread of monkeypox, in the context of a comprehensive public health response as outlined above. However, data on the effectiveness of these vaccines in the prevention of monkeypox in clinical practice and in field settings are very limited and many unknowns remain on their clinical effects and most appropriate use in different contexts.

All efforts should be made to administer vaccines for monkeypox within a framework of collaborative research and RCT protocols with standardized data collection tools for clinical and outcome data. This will allow the rapid generation of safety and effectiveness data for the use of vaccines for different purposes, in different at-risk groups and in different settings, and document their performance. When an RCT design is not possible, observational studies should be considered. Vaccines may be used under expanded access protocols such as Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI).³⁰

Such field- and practice-based research using standard protocols will also provide much needed information on transmission dynamics of monkeypox and clinical features of the disease.

Vaccine reserves

WHO and some Member States hold strategic reserves of first-generation smallpox vaccines for health security preparedness in the event of a re-emergence of smallpox through natural,

²⁹ Package insert of the LC16m8 vaccine:

(www.info.pmda.go.jp/go/pack/631340KD1037_2_06/?view=frame&style=SGML&lang=ja, accessed 9 August 2022)

³⁰ World Health Organization. (2016). Guidance for managing ethical issues in infectious disease outbreaks. World Health Organization. <https://apps.who.int/iris/handle/10665/250580>, accessed 3 August 2022

accidental or deliberate causes. These first-generation vaccines are not recommended for use for monkeypox. Further information will be provided on vaccine reserves as required.

Guidance development

Process and methods

This rapid response interim guidance was developed in line with the methods described in the [WHO Handbook for guideline development](#) and led by the WHO Secretariat. Where possible, initial content and recommendations were drawn from published WHO recommendations and reports. The [WHO Recommendations on Smallpox vaccine](#) (2014) were published following consultation of SAGE which had relied on GRADE methods. Also consulted were the [Summary report on first, second and third generation smallpox vaccines](#) (2013), the Report of GACVS on the [Safety of Smallpox vaccines](#) (2015), the [Operational framework](#) for deployment of WHO smallpox vaccine reserves for a smallpox event (2017) and WHO guidance on [Identifying and responding to serious adverse events following immunization](#) (2018) for smallpox vaccine safety surveillance. Information on monkeypox was drawn from a draft version of the *Monkeypox field guide* (unpublished) as reflected in the OpenWHO training [Monkeypox: Epidemiology, preparedness and response](#) for African outbreak contexts. A rapid scoping review of the literature was also carried out.

Drawing on these and other documents published by WHO Member States (see Annex 1), and with support of WHO staff with expertise in smallpox and monkeypox, vaccines and immunization, vaccine safety monitoring, regulatory standards, and vaccine research and development, draft interim recommendations were discussed on 22 and 31 May 2022 by the [SAGE Working Group on smallpox and monkeypox vaccines](#) and further also shared with [SAGE](#) members for comment. The revised, second version of this guidance was discussed by the SAGE Working Group on 29 July 2022. All feedback received was addressed in this document.

Limitations

Information on optimal control strategies for monkeypox remains limited. While existing smallpox vaccines are considered to provide protection against monkeypox, in general, there is limited clinical data on the use of vaccines for this purpose. These evidence-informed interim recommendations take into consideration these limitations and initial vaccine supply constraints. An updated systematic review of the literature is underway and will inform future iterations of these recommendations.

Declaration of interests

The [composition](#) of SAGE and the [declared interests](#) of members can be found on the SAGE website.

The membership and their declared interests of the Working Group on Smallpox and monkeypox vaccines can be found [here](#).

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Table of updates

24 August 2022

Section	Rationale for update
Executive summary	Key points reflected in renamed section. Declaration of PHEIC; added emphasis on groups at risk, including MSM and persons with multiple sex partners; added language about time for immunity to develop after vaccination; added footnote with standard text about off label use.
Introduction	Reflect the recent epidemiology; Working Group no longer called “Ad Hoc”; added principle reflecting strategic imperatives of the response including information and communication, public health action, and strengthening reference to evidence-based programming (recommendation for research)
Recommendation 1 – Vaccination policy development	Light editing to improve flow. Added sentence about VE not known
Recommendation 2 – Vaccination Strategy and outbreak response	Moved relevant text from Remarks section to Recommendation section; Reordered para in Justification section to improve flow; deleted repetition
Recommendation 3 – Post-exposure preventive vaccination (PEPV)	Changed terminology from post-exposure prophylaxis (PEP) to post-exposure preventive vaccination (PEPV)
Recommendation 5 – Primary preventive (pre-exposure) vaccination (PPV)	Added men who have sex with men (MSM) to groups at risk of exposure Changed terminology from pre-exposure prophylaxis (PrEP) to primary preventive (pre-exposure) vaccination (PPV)
Tables 1 and 2	Updated info on number of dose and products

Plans for updating

WHO continues to review the evidence and monitor the situation closely for any changes that may affect this interim guidance. A systematic assessment and quality appraisal of the available literature on efficacy, effectiveness and safety of smallpox and monkeypox vaccines is currently ongoing and will lead to the development of evidence-based recommendations to be discussed by SAGE at its plenary meeting from 4-7 October 2022 and proposed to WHO thereafter.

In the absence of further updates, this interim guidance will expire one year after the date of publication.

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Annex: Additional smallpox and monkeypox resources

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