Vaccines and immunization for monkeypox

Interim guidance
14 June 2022

Key points

The goal of the global outbreak response for monkeypox is to control the outbreak, and to effectively use public health measures to prevent onward spread of the disease. Judicious use of vaccines can support this response. This interim guidance provides the first WHO recommendations on use of vaccines for monkeypox. They 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, clinical data are limited.
- Most interim vaccination recommendations provided here concern off-label use.

Vaccines

- Some countries have maintained strategic supplies of older smallpox vaccines from the Smallpox Eradication Programme (SEP) which concluded in 1980. These first-generation vaccines held in national reserves 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 third-generation) vaccines for smallpox, some of which may be useful for monkeypox and one of which (MVA-BN) has been approved for prevention of monkeypox.
- The supply of newer vaccines is limited and access strategies are under discussion.

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 early case-finding, diagnosis and care, isolation and contact-tracing.
- 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.
- Post-exposure prophylaxis (PEP): For contacts of cases, PEP 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.
- Pre-exposure prophylaxis (PrEP): PrEP is recommended for 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 may be designated by national public health authorities.
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• Vaccination programmes should be accompanied by a strong information campaign, robust pharmacovigilance, and conduct of vaccine effectiveness studies.
• All efforts should be made to administer vaccines for monkeypox within a framework of collaborative research and randomized clinical trial (RCT) protocols with standardized data collection tools for clinical and outcome data.

Introduction

In April 2022, an Ad-hoc Strategic Advisory Group of Experts (SAGE) on Immunization Working Group on smallpox and monkeypox vaccines was established to advise the World Health Organization (WHO) Secretariat on the use of smallpox and monkeypox vaccines.

While monkeypox is a zoonotic disease, human monkeypox has been reported since 1970, with rising frequency in recent years. Since 2017, seven countries in the WHO Africa region have reported outbreaks and most have continued to occur in forested rural areas. However, countries are increasingly reporting monkeypox in previously unaffected regions; in Nigeria, of the more than 550 cases reported since the outbreak began in 2017 (West Africa clade), many have occurred in urban and peri-urban areas. The Democratic Republic of the Congo has reported over 1300 cases just from January to May 2022 (Congo Basin clade). Surveillance in all countries is expanding rapidly and WHO expects that more cases will be reported.

From 13 May to 9 June 2022, monkeypox has been reported to WHO from over 30 Member States that don’t usually or have never reported monkeypox. While epidemiological investigations are ongoing, the identification of over 1200 confirmed cases of monkeypox in just over three weeks is an unprecedented event. The virus may have been present for some time although for how long is not known. While in the current outbreak most but not all initially reported cases from four WHO regions are among persons who self-identify as men who have sex with men, it is expected that other cases will continue to occur in different population groups.

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

Principles

The experts of the SAGE Ad-hoc Working Group on smallpox and monkeypox vaccines have proposed 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. WHO recommendations should be inclusive of different risk groups, consider class of vaccine, and avoid being product specific.
• In 2013, WHO provided Recommendations on the use of smallpox vaccines. These additional interim recommendations from the WHO Secretariat apply for prevention and control of monkeypox only. They will be updated as more information becomes available.

WHO has also issued interim recommendations on Surveillance, investigation and contact tracing for monkeypox, on Laboratory testing for monkeypox virus (MPXV), and on Clinical management and infection prevention and control for monkeypox, as well as guidance on other measures to prevent onward transmission.
Recommendations

Topic 1 - Vaccination policy development

**Recommendation:**
The Member States of the World Health Organization (WHO) are strongly encouraged to consider the context of the current multi-country outbreak of monkeypox and convene their national immunization technical advisory groups (NITAGs) to review the evidence and develop policy recommendations for the use of vaccines as relevant to the national context.

**Remarks:**
Vaccine supply, regulatory authorization in countries, and vaccine dose demand are evolving as the scope of the outbreak is being characterized and better understood. In the context of the interim guidance, global supply is being assessed with manufacturers and partners to support sufficient supply, and mechanisms for access are being developed. While further clinical data are collected, countries should be prepared to consider use of selected smallpox vaccines off-label for monkeypox, as well as vaccines approved monkeypox, for groups at risk, and consider the national regulatory actions that may be required. Benefit-risk profiles vary by product.

**Justification:**
Monkeypox can present clinically in the manner classically described or with less typical features, such as less severe illness, fewer or less widely disseminated lesions, appearance of lesions before constitutional symptoms such as fever, or appearance of lesions in different stages of development. Such atypical features are being observed in the outbreak and possible transmission mechanisms in different contexts are not fully understood.

**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 — to include operational requirements, as well as research and development regarding public health measures, vaccines, antivirals, diagnostics, materials and supplies, and research needs to support policy.
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, investigation and contact tracing for monkeypox. This will help identify those at highest risk of infection and therefore the priority if vaccination takes place.

Where appropriate vaccines are available, post-exposure prophylaxis is recommended for selected close contacts of monkeypox patients (see Topic 3).

Where appropriate vaccines are available, pre-exposure vaccination is recommended for groups at risk of occupational exposure to monkeypox at this time (see Topic 4).

Remarks:
To control the current outbreak, the public health measures needed include strict 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. This may take 2 to 4 weeks. Where available, offering vaccines to contacts may be an adjunct to this strategy but not a replacement.

Persons who may be at risk in this outbreak include personnel working in health facilities and laboratory personnel who work with orthopoxviruses or perform diagnostic testing for orthopoxvirus infections. Also at risk in the current outbreak, in the context of possible exposure to monkeypox, are persons living in the same household or otherwise in close or intimate contact with a case, including but not limited to persons in social and sexual networks of men who have sex with men, as well as other persons connected through high frequency close or intimate physical contact.

The above recommendations are based on surveillance-containment approaches for vaccine-preventable disease outbreaks. In the past, ring vaccination as described for the eradication of smallpox generally referred to vaccination of persons in the family, household or local community of a case. Similar strategies have been applied for other infectious diseases (such as for Ebola Virus Disease) through vaccination of household members and other persons at risk, including contacts and contacts-of-contacts, regardless of the geographic location of contacts exposed during the infectious period of the case. Identifying contacts requires sensitive yet essential public health collaboration locally and between countries.

Identifying contacts, and contacts-of-contacts, who may be at risk based on possible recent exposure (for example having recently had multiple sexual partners) may be challenging. However, even where vaccine cannot be offered for supply, regulatory, choice of product, programmatic, timeliness for PEP, 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. 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. Variations of these strategies merit consideration and applied research in the local context to bring this outbreak under control. As the outbreak evolves and vaccine supply improves, broader use of vaccines for persons at risk may be warranted if justified by the evidence. Vaccines and
treatments for monkeypox should be administered within a collaborative research framework with standardized shared data collection tools, including implementation of clinical trial protocols.

Regardless of response strategies adopted, 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, minimally replicating and/or non-replicating smallpox and monkeypox vaccines, as required, and their associated vaccination or injection techniques, materials and supplies.

**Justification:**

At this time, the general risk to the public from monkeypox is considered to be low. This may change if the outbreak is not controlled.

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. Such exposure can occur in a range of settings including at home, in social or sexual networks, or in the health care setting. Modes of transmission in current and recent outbreaks are not yet fully understood.

All countries are encouraged to respond quickly; rapid response is essential to prevent onward spread and slow person-to-person transmission in the context of a lack of immunity to orthopoxviruses since the eradication of smallpox, and to monkeypox in particular.

**Implementation and monitoring considerations:**

It is critical that despite apparently small numbers of cases in many locations, national and local response be rapid, targeted and effective to stop onward transmission of monkeypox. Outbreak response policy and strategies must include guidance for essential public health measures which include contact-tracing, including contacts-of-contacts wherever possible, and isolation of ill persons until skin lesions have fully healed, the practice of good hand hygiene, the use of personal protective equipment by health care or home care providers and by the patient as required. Non vaccine measures should be widely advised and emphasized. These elements are further detailed below and in related published WHO guidance and other information products.

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1 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.
**Recommendation:**

For contacts of cases, post-exposure prophylaxis (PEP) 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.

PEP can be offered with any of the vaccines listed in Table 1, as appropriate. While PEP is likely to be most effective if given within four days of exposure, there is provision to offer PEP for up to within 14 days, particularly for those at high risk of ongoing exposure.

**Remarks:**

Exposure risk for contacts of persons with confirmed or probable/suspected monkeypox is classified by the nature of the potential exposure. The risk to the individual concerned (that is, the likelihood of exposure, existing medical conditions that may put a person at higher risk for severe disease, and the risk profile for the individual and their household members of the specific vaccine proposed) must also be considered in any decision to offer vaccination.

A contact is defined as outlined in the interim guidance on surveillance, investigation and contact-tracing provided by WHO. This section offers more detail to assist in determining the level of risk of a person who has had one or more exposures to a probable or confirmed case of monkeypox, in the period beginning with the onset of the source case’s first symptoms, and ending when all scabs have fallen off, as follows:

- inhalation of respiratory droplets from infected people or lesion material (e.g., scabs) dislodged from surfaces (e.g., while shaking bedding during cleaning of contaminated rooms) without appropriate personal protective equipment (PPE)
- contact with contaminated materials such as clothing or bedding without appropriate PPE
- face-to-face exposure, including for health workers without appropriate PPE
- direct skin-to-skin physical contact, including sexual contact

**Table 1** provides a summary of recommendations on post-exposure vaccination in light of the assessed level of risk of the possible types of exposure. These include the following.

**High risk** - Post-exposure prophylaxis (PEP) vaccine is recommended:

For contacts of cases, PEP is recommended with second- or third-generation vaccines as outlined in Topics 5 and 6 below.

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:

- 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.
Medium risk – Post-exposure prophylaxis is also recommended for a person with

- no direct contact but close proximity in the same room or indoor physical space as a symptomatic monkeypox patient, if not wearing appropriate PPE (see interim guidance on Clinical management of monkeypox and infection prevention and control).

Lower or minimal risk - Post-exposure prophylaxis is not recommended for a person with:

- 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 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.

Persons who have had pre-exposure vaccination (e.g. health workers, laboratory personnel or other persons who may be at occupational or personal risk) who become exposed (contacts), should also continue with monitoring for 21 days after the last exposure.

Monitoring of contacts, regardless of vaccination status, should be applied rigorously and preferably within the context of agreed clinical trial or other study or data collection protocols.

Justification:

Recommendations for post-exposure vaccination against monkeypox are considered in the light of 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.

While the frequency of occurrence of secondary cases among contacts (the secondary attack rate) is not yet known in the current context, given the importance of timely vaccine administration, household or sexual contacts who may be at particular risk of severe disease (e.g., pregnant women, immunosuppressed persons, or infants or young children) may be considered priority for post-exposure vaccination where appropriate vaccine is available.
Implementation and monitoring 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 that takes into consideration need, risk factors for exposure, existing medical conditions that may put a person at higher risk, and the appropriate choice of vaccine, where available, as well as inclusion or exclusion criteria established for clinical studies where applicable.

For persons for whom replicating vaccines may be considered a precaution or are contraindicated, non- or minimally replicating vaccine should be used (such as MVA-BN or LC16). This concerns persons with immune deficiencies, immunosuppression therapies or atopic dermatitis, as well as children and pregnant or breastfeeding women.

National health authorities must ensure that information is provided to health personnel on administration of MVA-BN monkeypox vaccine via sub-cutaneous injection, and on the use of bifurcated needles for administration of ACAM2000, LC16 or other similar smallpox vaccines. Instructions for smallpox vaccination with a bifurcated needle are provided here.²

The third-generation vaccine MVA-BN is characterized by its lower reactogenicity, and as a consequence the vaccine is differentiated from other products by its recommended schedule of two doses to be administered 4 weeks apart. While some authorities may consider offering PEP as a single dose, there is as yet little data on the relative effectiveness of this approach.

Hand hygiene should be performed with soap and water or an alcohol-based hand rub before and after vaccine administration. In addition, there are specific infection prevention and control measures to be implemented during administration of smallpox vaccines and care of the vaccination site. Replicating smallpox vaccines such as ACAM2000 consist of live vaccinia virus; it is therefore important to follow special care instructions for the vaccination site including covering the site with a light bandage. 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 pregnant or breastfeeding women as well as infants or young children. Further guidance on disposal of bandages and care and laundry of clothing can be found here.

² WHO. Instructions for smallpox vaccine with bifurcated needle. 1968. Available here: https://apps.who.int/iris/handle/10665/67962
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Topic 4 - Vaccination for pre-exposure prophylaxis - (PrEP) (Table 2)

**Recommendation:**
Pre-exposure vaccination / prophylaxis (PrEP): PrEP is recommended for health workers at high risk of exposure, laboratory personnel working with orthopoxviruses; and clinical laboratory personnel performing diagnostic testing for monkeypox; and outbreak response team members as may be designated by national public health authorities. See Table 2.
Pre-exposure vaccination against monkeypox, in clinical settings where monkeypox may be encountered, may be recommended for laboratory personnel performing diagnostic testing or research for monkeypox and for health workers who may be at risk exposure.

**Remarks:**
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 such as cleaners. In the context of limited vaccine supply, in assessing eligibility for pre-exposure preventive vaccination, national authorities should consider whether health workers 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.

As vaccine supply improves, national authorities should consider strategies for vaccinating all persons at high risk of exposure, as determined by the epidemiology of monkeypox.

**Justification:**
A high-risk exposure is defined as a direct exposure of skin or mucous membranes to the skin or respiratory secretions of a person with monkeypox, their body fluids or potentially infectious material (including clothing or bedding), without appropriate PPE. This includes:

- inhalation of droplets or dust from cleaning contaminated rooms
- mucosal exposure to splashes
- direct physical contact with someone who has monkeypox, such as face-to-face, skin-to-skin or mouth-to-skin contact, including contact during sexual activities
- normally sharing a residence (permanently or occasionally) with a person who has been diagnosed with monkeypox
- a penetrating sharps injury from a contaminated device or through contaminated gloves.

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3 Health workers are health service providers, such as doctors, nurses, midwives, public health professionals, laboratory technicians, health technicians, medical and non-medical technicians, personal care workers, environmental cleaning staff, community health workers, healers and 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. (WHO SAGE roadmap for prioritizing use of Covid-19 vaccines in the context of limited supply (July 2021): https://apps.who.int/iris/handle/10665/342917)
Implementation and monitoring considerations:

Table 2 provides a summary of recommendations on 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 that takes into consideration need, risk factors for exposure, existing medical conditions that may put a person at higher risk, and the appropriate choice of vaccine, where available.

For persons for whom replicating vaccines may be considered a precaution or are contraindicated, non-replicating (such as MVA-BN) or minimally replicating (such as LC16) vaccine should be used. This concerns persons with immune deficiencies, immunosuppression therapies or atopic dermatitis, as well as children and pregnant or breastfeeding women.

National health authorities must ensure that information is provided to health personnel on administration of the MVA-BN monkeypox vaccine via sub-cutaneous injection and on the use of bifurcated needles for administration of ACAM2000, LC16 or other similar smallpox vaccines. Instructions for smallpox vaccination with a bifurcated needle are provided here.

Hand hygiene should be performed with soap and water or an alcohol-based hand rub before and after vaccine administration. In addition, there are specific infection prevention and control measures to be implemented during administration of smallpox vaccines and care of the vaccination site. Replicating smallpox vaccines such as ACAM2000 consist of live vaccinia virus; it is therefore important to follow special care instructions for the vaccination site (available also in video form) including covering the site with a light bandage. 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.

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5 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
Topic 5 – Vaccination for special population groups

Recommendation:
Vaccination against monkeypox as post-exposure prophylaxis may be considered for special population groups, i.e. during pregnancy, for children, or for persons with immune suppression, including persons living with HIV, if a vaccine appropriate for these groups is available, following a careful evaluation of risks and benefits. 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 a pre-exposure measure is not generally recommended for special population groups i.e. for children, in the context of pregnancy or breastfeeding, or in persons with immune suppression. For persons who may be at risk of exposure, 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.

Remarks:
Children, pregnant women and immunocompromised persons may be at risk of more severe disease with monkeypox and/or a worse outcome than other persons. In the context of post-exposure prophylaxis, they may be considered priority for timely vaccination after a careful evaluation of risks and benefits, particularly with respect to choice of vaccine product.

Justification:
Of the second- and third-generation vaccines, only LC16 (Japan) has been licensed for use in children. On the choice of vaccine for specific population groups, see below (Topic 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.
Topic 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 or off-label use for pre-exposure or post-exposure prophylaxis 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 need-risk-benefit analysis for choice of vaccine.

For healthy adults, replicating vaccinia-based vaccines (such as ACAM2000, or other vaccines developed through cell culture techniques), minimally replicating vaccines (such as LC16), or non-replicating vaccine (such as MVA-BN) may all be considered.

For individuals for whom standard replicating vaccine (such as ACAM2000) is contraindicated because of immune deficiencies, immunosuppression therapies, atopic dermatitis, specific non-replicating monkeypox vaccine such as MVA-BN would be preferred, where available. Shared clinical decision-making is recommended for immunocompromised persons.

During pregnancy, where consideration is given to pre- or post-exposure vaccination, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred.

For women who are breast-feeding, where consideration is given to pre- or post-exposure vaccination, non-replicating (MVA-BN) or minimally replicating (LC16) vaccines are preferred.

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

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

**Remarks:**

Approval of MVA-BN for the prevention of monkeypox has been granted on the basis of human safety and animal efficacy data as well as non-inferiority immunogenicity studies with other smallpox vaccines. First-generation vaccines from the Smallpox Eradication Programme (SEP) held in national or WHO reserves are not recommended for use. National authorities should nonetheless ensure that smallpox vaccines are appropriately stored, monitored and periodically tested for potency. WHO has provided recommendations on the production and quality control of smallpox vaccines (2003).

**Justification:**

Currently available smallpox and monkeypox vaccines are developed from well-characterized live vaccinia virus strains using different attenuation protocols and manufactured on different cell substrates, resulting in distinct safety and reactogenicity profiles for each.

**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 or 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.
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National authorities should ensure that robust pharmacovigilance is in place along with standard investigational protocols for the use of any smallpox or monkeypox vaccines selected, to ensure full data collection on effectiveness and safety.

WHO is developing template protocols and data collection recommendations for emergency or investigational use. Research on response vaccination strategies is strongly encouraged.

**Topic 7 – Global coordination and vaccine supply**

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

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 the WHO Secretariat.

Vaccine supply remains very constrained. It is essential for all Member States to work together to ensure supply is made available adequately and equitably. Member States are encouraged to make available vaccine doses to countries with limited/no vaccine supply.

**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.

Modern training materials should be developed and made available on accessible platforms for the use of bifurcated needles where required.

**Justification:**
Strong collaboration between all Member States is essential to ensure supply is made available adequately, equitably and according to public health need.

**Implementation and monitoring considerations:**
The WHO is establishing coordination mechanisms to maximise rapidity and efficiency in making vaccines available where they are needed.
Background

Vaccines and vaccine development

Smallpox vaccines produced and successfully used during the intensified smallpox eradication program (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, one of these third-generation vaccines, MVA-BN\(^7\) was approved for prevention of monkeypox by national regulatory authorities. Table 3 outlines the vaccines currently available and their regulatory status.

In 2013, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization made a series of recommendations\(^8\) for the use of smallpox vaccines based on a comprehensive assessment of smallpox vaccine effectiveness and safety, included GRADEing of evidence.\(^9\) In the 2013 guidance focussed on preparedness for a re-emergence of smallpox through natural, accidental or deliberate causes, monkeypox was not specifically included. The WHO SAGE did recommend that preventive vaccination be reserved for laboratory personnel working with orthopoxviruses.\(^10\) 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).\(^11\) 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 Smallpox Eradication Programme (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). There may be other products commercialized in some countries and smallpox vaccine development continues. 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 or LC16.

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\(^7\) 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.

\(^8\) Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization. November 2013: conclusions and recommendations. Available at: https://www.who.int/publications/i/item/WER8901.


\(^10\) 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.

\(^11\) 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.
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,\(^{12}\) and in Canada the indication was also extended to monkeypox the same year.\(^{13}\) Pre-exposure phase III trials have demonstrated positive results for immunogenicity and efficacy and a favourable safety profile was confirmed for healthy population groups, as well as for people with HIV, atopic dermatitis and haematopoietic stem cell transplants (see references below). No cases of myocarditis were reported but data evaluating this 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 and efficacy data from pre-clinical studies in comparison 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).\(^{14}\) 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 (RSV). 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.\(^{15}\)

In 2015, the WHO Global Advisory Committee on Vaccine Safety (GACVS) reviewed the evidence on the safety of replicating and non-replicating smallpox vaccines.\(^{16}\) 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 replicating\(^{17}\) 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. Following summarizes current information on smallpox vaccine safety.

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\(^{12}\) 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.

\(^{13}\) 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.

\(^{14}\) Mvabea is given as a single injection about 8 weeks after an injection of Zabdeno.

\(^{15}\) 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)


\(^{17}\) Replicating viral vectors retain the ability to make new viral particles alongside delivering the vaccine antigen when used as a vaccine delivery platform.
The vaccine LC16 is the only smallpox vaccine licensed for use in children of all ages. 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. 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 exposures to, other orthopoxviruses may occur and adequate screening procedures may minimize any risks associated with vaccination.

ACAM2000 (USA)

ACAM2000 is contraindicated in persons with a weakened immune system (e.g., leukemia, HIV, AIDS, transplant recipients, people with cancer that has spread, and those undergoing treatment with medicines that suppress the immune system such as steroids, prednisone, and cancer drugs). Individuals with skin conditions such as eczema, dermatitis or psoriasis who are at increased risk of complications can be vaccinated with caution.

ACAM2000 should not be used in pregnant women, or in infants or young children. Use of ACAM2000 should also be avoided in women who are breastfeeding.

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 (PV), generalized vaccinia (GV), skin infections, erythema multiforme including Stevens-Johnson syndrome, and eczema vaccinatum (EV). Cardiac manifestations such as myocarditis and pericarditis and neurological manifestations like post-vaccinial encephalitis (PVE), encephalomyelitis (PVEM), 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 vulnerable person, 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. 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)

The LC16 vaccine should be used with caution in any person who is immunosuppressed or has atopic dermatitis as outlined above, or during pregnancy, or 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 LC16.
Minor side effects seen following administration of LC16\textsuperscript{18} 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 and are 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 randomized clinical trial (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, vaccines may be used under expanded access protocols such as Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI)\textsuperscript{19}.

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, 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.

**Information for the public**

Information for the general public on vaccines for monkeypox is available in the form of Q&A on the WHO website.

\textsuperscript{18} LC16 package insert unofficially translated here:  https://www-info-pmda-go-jp.translate.goog/go/pack/631340KD1037_2_04/?x_tr_sl=ja&x_tr_tl=en&x_tr_hl=en&x_tr_pto=sc

Other considerations and next steps

Along with this Interim guidance on Vaccines and immunization for monkeypox, WHO will also publish operational guidance for immunization programmes and an updated safety review.

WHO has published the following interim guidance to support countries to respond to the multi-country outbreak of monkeypox. These are provided here for reference.

WHO interim guidance on surveillance and contact-tracing.
WHO interim guidance on laboratory testing for monkeypoxvirus.
Clinical management and infection prevention and control for monkeypox
Monkeypox: public health advice for gay, bisexual and other men who have sex with men.

WHO is also publishing:
Interim guidance on Community protection, risk communication and community engagement.
Table 1. Use of vaccines for post-exposure prophylaxis (PEP) for prevention of monkeypox according to exposure risk: WHO interim recommendations (June 2022)

<table>
<thead>
<tr>
<th>Exposure risk</th>
<th>Description of exposure</th>
<th>Post-exposure prophylaxis (PEP)</th>
<th>Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>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: • 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.</td>
<td>Post-exposure prophylaxis (PEP) is recommended with vaccine appropriate for each individual*</td>
<td>ACAM2000 LC16 MVA-BN</td>
</tr>
<tr>
<td>Medium</td>
<td>• no direct contact but close proximity in the same room or indoor physical space as a symptomatic monkeypox patient, if not wearing appropriate PPE (see interim guidance on Clinical management of monkeypox and infection prevention and control).</td>
<td>Post-exposure prophylaxis (PEP) is recommended with vaccine appropriate for each individual*</td>
<td>ACAM2000 LC16 MVA-BN</td>
</tr>
<tr>
<td>Low / Minimal</td>
<td>• 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 or contact in an outdoor setting with a symptomatic case • 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.</td>
<td>Post-exposure prophylaxis (PEP) is not recommended</td>
<td>N/A</td>
</tr>
</tbody>
</table>

PPE: personal protective equipment. N/A: not applicable. *See text or Table 2 of interim guidance
Table 2. Use of vaccines for pre-exposure prophylaxis (PrEP) for prevention of monkeypox: WHO interim recommendations (June 2022)

For reference to principles underpinning the recommendations, see the introduction to this guidance.

<table>
<thead>
<tr>
<th>Population group</th>
<th>Recommendations for vaccination (WHO SAGE, 2013)</th>
<th>Interim recommendations for vaccination (WHO Health Emergency Programme, 2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Health workers at risk of exposure, research laboratory personnel,* clinical laboratory personnel performing diagnostic testing for orthopoxviruses,** and designated response team members at risk for occupational exposure to monkeypox</td>
<td>Recommended ACAM2000 LC16</td>
<td>Recommended ACAM2000 LC16 MVA-BN</td>
</tr>
<tr>
<td>As above — Individuals for whom standard replicating vaccine is contraindicated because of young age (children), pregnancy, immune deficiencies, immunosuppression therapies*** or atopic dermatitis****</td>
<td>Recommended MVA-BN</td>
<td>Recommended LC16 MVA-BN</td>
</tr>
</tbody>
</table>

*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]

****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 PrEP. For this reason, consideration should be given to avoidance of diagnostic laboratory work or provision of care for monkeypox patients.
### Table 3. Smallpox and monkeypox vaccine options (June 2022)

<table>
<thead>
<tr>
<th>Vaccine (Manufacturer)</th>
<th>Licensed for smallpox (country, type, date)</th>
<th>Licensed for monkeypox (country, type, date)</th>
<th>Considerations</th>
<th>Presentation</th>
<th>Injection materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC16 (KM Biologics) 3rd generation</td>
<td>Japan - Full MA (1975) USA - EIND (2014)</td>
<td>No</td>
<td>Approved for use in infants and children (all ages) as well as adults (all ages)</td>
<td>Freeze-dried Multidose vials</td>
<td>Bifurcated needle</td>
</tr>
<tr>
<td>ACAM20 (Emergent BioSolutions) 2nd generation</td>
<td>USA - Approved</td>
<td>USA - EIND for PEP</td>
<td>Approved for use in adults aged 18 – 64 years of age. Earlier production by Sanofi Pasteur approved in France.</td>
<td>Freeze-dried Multidose vials</td>
<td>Bifurcated needle</td>
</tr>
<tr>
<td>Vaccinia, various strains* from national production 1st generation</td>
<td>Various countries Various national production (SEP), held by various countries</td>
<td>No</td>
<td>Regular potency testing recommended</td>
<td>Liquid frozen or lyophilized vials or ampoules</td>
<td>Bifurcated needle</td>
</tr>
</tbody>
</table>

Vaccines and immunization for monkeypox: Interim guidance

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 the WHO Strategic Advisory Group of Experts (SAGE) on Immunization which had relied on GRADE methods. Also consulted were the *Summary report on first, second and third generation smallpox vaccines* (2013), the Report of the Global Advisory Committee on Vaccine Safety (GACVS) on *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 below), 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 May and on 31 May 2022 by the Ad-hoc SAGE Working Group on smallpox and monkeypox vaccines, which served as the Guideline Development Group for this interim guidance, and further also shared with SAGE members for comment. 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.

Plans for updating

WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue an update. A full review of evidence is planned for the WHO SAGE meeting in October 2022 which will lead to updated recommendations. In the absence of updates, this interim guidance will expire six months after the date of publication.
Contributors

**WHO core team:** Madhava Ram Balakrishnan (Pharmacovigilance, Access to Medicines and Health Products), Tracey Goodman (Essential Programme on Immunization), Alexandra Hill (Epidemic and Pandemic Preparedness, Health Emergencies Programme), Joachim Hombach (Agenda, Policy and Strategy, Immunization, Vaccines and Biologicals), Rosamund Lewis (Smallpox Secretariat, Emerging Diseases and Zoonoses, Health Emergencies Programme), Melanie Marti (Agenda, Policy and Strategy, Immunization, Vaccines and Biologicals), Elisabeth Pluut (Vaccines and Immunization Devices Assessment, Access to Medicines and Health Products).


**Members of the ad hoc SAGE Working Group on smallpox and monkeypox vaccines:** Kathleen M. Neuzil (Chair, University of Maryland, United States of America, Member of WHO SAGE). Joel Breman (Fogarty International Centre, United States), Clarissa Damaso (Federal University of Rio de Janeiro, Brazil), Poh Lian Lim (National Centre for Infectious Diseases, Singapore, Member WHO Health and Security Interface Technical Advisory Group), Raina Macintyre (University of New South Wales, Australia); Heidi Meyer (Paul Ehrlich Institute, Germany), Andreas Nitsche (Robert Koch Institute, Germany, Member WHO Advisory Committee on Variola Virus Research), Adesola Ogunleye, Gregory Poland, Agam Rao (US Centers for Disease Control and Prevention, United States), Anne Rimoin (University of California, United States), Tomoya Saito (National Institute of Infectious Diseases, Japan), Oyewale Tomori (Redeemer’s University, Nigeria).

**External advisors:** Larry Brilliant, Richard B Kennedy, Brett Peterson.

**Declaration of interests**

The composition of the technical advisory groups and their declared interests can be found on the SAGE website [https://www.who.int/news-room/events/detail/2022/04/04/default-calendar/sage_meeting_april_2022](https://www.who.int/news-room/events/detail/2022/04/04/default-calendar/sage_meeting_april_2022)

The membership of the Ad-hoc Working Group on Smallpox and monkeypox vaccines: [https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/working-groups/smallpox-and-monkeypox-vaccines](https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/working-groups/smallpox-and-monkeypox-vaccines)

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Selected WHO Member State documents, reports and recommendations


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Recently published studies and reviews


ACAM2000


**MVA-BN**


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