TPPs and overview of data and SAGE recommendations on mpox vaccines

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Current smallpox and monkeypox vaccine options

There are additional candidate vaccines in the pipeline

https://www.who.int/publications/m/item/landscape-of-vaccines-licensed-or-under-development-for-mpox

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) (0.5ml). The USA has granted emergency use authorization for intradermal administration (0,1ml).
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

https://iris.who.int/bitstream/handle/10665/364528/WHO-MPX-Immunization-Background-2022.3-eng.pdf?sequence=1

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SAGE Recommendation 1: **mpox outbreak response**[1]

Vaccination is **recommended for persons at high risk of exposure to mpox in an outbreak**. The identification of populations at risk of exposure is limited in some settings by currently available epidemiological data. In studies involving **men who have sex with men, pre-exposure vaccination with one or two doses of smallpox/mpox vaccine was demonstrated to be effective** against mpox. Effectiveness of **post-exposure vaccination is less certain**, which may be linked to the predominantly sexual mode of transmission in available studies. To allow the greatest flexibility with respect to local risk assessment, varied modes of transmission and response options, populations to consider for vaccination may include:

- **based on local epidemiology**, members of a **geographically defined area or community** (e.g. village), **including children**, with a documented high risk of exposure to mpox;
- **sex workers; gay, bisexual or other men who have sex** with men (MSM) with multiple sexual partners; or other **individuals with multiple casual sexual partners**;
- **health workers at risk of repeated exposure**; clinical laboratory and health care personnel performing diagnostic testing for mpox or providing care, and outbreak response team members (as designated by national public health authorities).
- **contacts of persons with mpox**, **ideally within four days of first exposure**.[2] Contacts may include children, others in the household or in congregate settings (such as prisons, schools, health facilities or residential facilities)

1. Outbreak definition: occurrence of two or more laboratory confirmed (or one laboratory confirmed and one or more epidemiologically linked cases) of mpox in nationally or locally defined geographic areas

2. Criteria to define risk of exposure in this context include e.g. direct skin-to skin physical contact, contact with contaminated materials such as clothes or bedding. Vaccination ideally up to 14 days in the absence of symptoms.

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SAGE Recommendation 2: **preventive use of mpox vaccines (outside of an outbreak)**

Primary preventive vaccination is recommended for:

- Laboratory personnel working with orthopoxviruses

The duration of protection of mpox vaccines is not fully characterized. Therefore, **periodic revaccination should be considered** for individuals who are at high risk of exposure to more virulent orthopoxviruses (e.g. variola virus, monkeypox virus, cowpox virus, vaccinia virus and/or others as appropriate). This may be as often as every 2 to 5 years for laboratory workers at highest risk of exposure, as practiced in the two authorized WHO Collaborating Centres for variola virus research, or less frequently in other settings, according to the latest available information on duration of protection for the vaccines used.

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SAGE Recommendation 3: **choice of vaccines for immunocompetent non-pregnant individuals**

WHO recommends that for immunocompetent non-pregnant individuals, non-replicating vaccine (MVA-BN), minimally replicating vaccines (LC16-KMB), replicating cell-culture derived vaccinia-based vaccines (e.g. ACAM2000) or equivalent vaccines that meet WHO standards for quality, are appropriate for use.

Specific considerations, including potential off-label use, apply as to vaccine choice for special population groups (see recommendation on vaccine choice for special populations).

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SAGE Recommendation 4: **choice of vaccine for special populations - infants, children and adolescents**

For infants, children and adolescents, where consideration is given to vaccination, non-replicating (MVA-BN) or minimally replicating (LC16-KMB) vaccines may be used.

- LC16-KMB is approved for use in children in Japan. While MVA-BN is currently not licensed for persons under 18 years old, this vaccine may be used in infants, children and adolescents when the benefits of vaccination outweigh the potential risks in the context of an mpox outbreak. The use of MVA-BN in children constitutes an “off-label” product use.

Replicating vaccine (such as ACAM2000) should not be used in infants.

WHO recommends further collection of data on vaccine safety and effectiveness for these populations.

SAGE Recommendation 4: choice of vaccine for special populations – **immunocompromised persons and persons with other conditions**

For immunocompromised individuals for whom replicating (such as ACAM2000) or minimally replicating (LC16-KMB) vaccine is contraindicated, non-replicating vaccine (MVA-BN) should be used; likewise for individuals for whom there are warnings or precautions because of immunosuppressive therapies or proliferative skin conditions (e.g. atopic dermatitis), non-replicating (MVA-BN) vaccine should be used.

Immunocompromised persons include those with active cancer, transplant recipients, immunodeficiency, and active treatment with immunosuppressive agents. It also includes people living with HIV with a current CD4 cell count of <200 cells µl.

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SAGE Recommendation 4: **choice of vaccine for special populations – pregnancy**

During pregnancy, where consideration is given to vaccination, non-replicating vaccine (MVA-BN) may be used. Administration of MVA-BN in pregnancy constitutes “off-label” use.

There are no data available to assess the risk of minimally replicating (LC16-KMB) vaccines in pregnant women. No development and reproductive toxicology studies have been performed.

Replicating vaccine (such as ACAM2000) should not be used in pregnancy.

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SAGE Recommendation 5: **vaccination in previously vaccinated individuals**

The duration of protection of vaccinia-based mpox vaccines is not fully characterized and may vary between vaccine products. WHO recommends that individuals, should they be **eligible for vaccination**, be vaccinated **irrespective of documented previous smallpox vaccination** and/or visible smallpox vaccine scar. For individuals previously vaccinated with mpox vaccines, an individual benefit-risk assessment should be done.

SAGE Recommendation 6: **“off label” use of vaccine schedules and doses**

Based on the risk profile and the available vaccine data, WHO recommends “off-label” use of a single dose or fractional dosing of MVA-BN in supply constrained outbreak situations.

WHO emphasizes the need to collect further data on vaccine safety and effectiveness in these circumstances.

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Research priorities & call to action

Research priorities:

- In regions with endemic disease, there is an urgent need for better understanding of modes of transmission; age-specific cases (incidence), deaths and seroprevalence; and characterization of risk factors for MPXV infection and severity of disease.
- In particular, the reported high morbidity and mortality in children requires a dedicated effort to understand the epidemiology and vaccine effectiveness, safety and immunogenicity in this group.
- Duration of vaccine protection based on route of administration and number of doses received must be defined.

Call to action:

- SAGE emphasizes the importance of **availability and access to vaccines** in mitigating the impact of mpox in regions with endemic disease and promoting equity
- SAGE requests that immediate **attention be given to regulatory and procurement processes** that facilitate equitable vaccine access and deployment in low-and-middle income countries
- SAGE strongly recommends **systematic on-going data collection during deployment of vaccines** to evaluate the effectiveness, safety and impact of vaccination strategies.
- SAGE recommends **sustainable investment in research** institutions, research capacity and regulatory authorities **in the African region**

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WHO Target Product Profiles for mpox Vaccines
Version 1, 16 August 2024

Purpose of the document

Target product profile development followed evidence of increasing monkeypox transmission and need to make one or more vaccines available under WHO's emergency use listing (EUL) procedure. This target product profile is intended to convey, based on the most recently available data, WHO's current priorities for vaccine development, regardless of regimen (including whether they are intended as primary vaccination or as boosters), and whether they are intended to address currently circulating clades or future clades.

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WHO Target Product Profiles for mpox Vaccines
Version 1, 16 August 2024

This DRAFT Target Product Profile (TPP) was developed through a consultation process with key stakeholders in human and animal health, scientific, funding and manufacturing communities. Open for comments on the WHO webpages.

It is intended to guide and prioritize the development of vaccines and decisions about need for boosters, based on available data on mpox.

As new evidence is generated, this TPP may again require further review and revision.

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WHO DRAFT Target Product Profiles for mpox Vaccines Version 1, 16 August 2024

Vaccine characteristic	Preferred	Critical or Minimal
Indication for use	People at risk of exposure to monkeypox virus in an outbreak: Prevention of mpox disease People exposed to monkeypox virus: Prevention of mpox disease and reduction of severe mpox disease. Prevention of mpox disease transmission	People at risk of exposure to monkeypox virus in an outbreak: Prevention of mpox disease People exposed to monkeypox virus: Prevention of mpox disease and/or reduction of severe mpox disease
Contraindication	Minor (e.g., hypersensitivity or linked to specific adverse events)	Limited contraindications may include severely immunocompromised patients
Target population	Adults, children, and infants Data to support administration to special populations such as those who are pregnant, lactating, or immunocompromised	Adults

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WHO DRAFT Target Product Profiles for mpox Vaccines Version 1, 16 August 2024

Vaccine characteristic	Preferred	Critical or Minimal
Safety/Reactogenicity	Minimal reactogenicity No serious ADRs	Up to mild-moderate reactogenicity Serious adverse events occurring only in rare circumstances
Measures of Efficacy	Efficacy point estimate >90% Direct evidence of efficacy against disease caused by relevant monkeypox clades, preferably generated through randomized clinical trials	Efficacy point estimate >60% Animal studies, immune responses, and/or observational data supporting efficacy against mpox Additionally strong evidence of efficacy against smallpox if available would be supportive

Immune response data against monkeypox virus could be adequate if supported by other relevant evidence

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WHO DRAFT Target Product Profiles for mpox Vaccines Version 1, 16 August 2024

Vaccine characteristic	Preferred	Critical or Minimal
Dose regimen	Single dose	Two or fewer doses for primary regimen Boosters are acceptable
Durability of protection	≥3 years	≥6 months after the primary series
Deployability		
Route of Administration	Not requiring specialized equipment or supplies	Any route of administration is acceptable, including IM, subcutaneous, or ID via bifurcated needle
Product Stability and Storage	Shelf life ≥ 2 years at ambient temperature	Shelf life ≥ 1 year at -20°C
Co-administration with other products	No interactions with other vaccines Able to be administered with antivirals	Some interactions expected but not impacting use in outbreak response
Presentation	Multidose and single dose vials are both available	Single or multi-dose vials suitable for outbreak response
	Barcodes on secondary packaging. Including serialization, GTIN, expiry and lot number	
	For parenteral, dose volume of 0.5 mL preferred, with AD syringes that are WHO prequalified	
Registration and Prequalification	Prequalification In addition, relevant NRA approval	EUL

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