Monkeypox Evidence Brief

for NITAGs

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PIVI Partnership for International Vaccine Initiatives

TASK FORCE

CDC U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

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Abbreviations

AFRO	WHO Regional Office for Africa
ACIP	Advisory Committee on Immunization Practices
AEFI	Adverse Events Following Immunization
BeSD	Behavioral and Social Drivers of Vaccination Study
CAR	Central African Republic
CD4	Cluster of DIfferentiation 4
CE	Cost Effectiveness
DRC	Democratic Republic of the Congo
EPI	Expanded Program on Immunization
EtR	Evidence to Recommendation Framework
EUL	Emergency Use Licensure
EURO	WHO European Regional Office
GAVI	The Global Vaccine Alliance
GNN	Global NITAG Network
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
ID	Intradermal
IMST	Incident Management Support Team
HIV	Human Immunodeficiency Virus
KAP	Knowledge Attitudes and Practice Study
LIC	Low Income Country
LMIC	Low and Middle Income Country
MOH	Ministry of Health
MVA-BN	Modified Vaccinia Ankara-Bavarian Nordic
NISH	National Immunization Technical Advisory Groups Support Hub
NITAG	National Immunization Technical Advisory Group
PHEIC	Public Health Emergency of International Concern
PICO	Population Intervention Comparison Outcome
RoC	Republic of the Congo
SAGE	Strategic Advisory Group of Experts
SEARO	WHO South East Regional Office
SITREP	Situation Report
SOP	Standard Operating Procedures
SQ	Subcutaneous
U.K. JCVI	United Kingdom Joint Committee on Vaccines and Immunization
U.S. CDC	United States Centers for Disease Control and Prevention
U.S. FDA	United States Food and Drug Administration
UNICEF	United Nations Children's Fund
WHO	World Health Organization
WPRO	WHO Western Pacific Regional Office

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Purpose and Intended Use of this Brief

Monkeypox (mpox) reemerged in 2022 as a global health concern, with cases spreading through close human-to-human contact in non-endemic regions across 115 countries. The outbreak in non-endemic countries resulted in much wider use of monkeypox vaccines, and helped provide clearer evidence of safety and effectiveness of the available vaccines.

The World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC) in July 2022, which lasted until May 2023. Following a rapid surge in cases in Central Africa, WHO declared a second PHEIC in August 2024, which ended in September 2025 (Acosta-España, 2024). Africa CDC announced in September 2025 that monkeypox remains a Public Health Emergency of Continental Security. Since that second declaration, countries and international partners have been working to plan and implement vaccination campaigns. As of Novmeber 2025, Burundi, Democratic Republic of the Congo, Kenya, Malawi, Rwanda, Sierra Leone, South Sudan, Tanzania, Uganda, and Zambia continue to experience sustained human-to-human transmission of the virus (Berias, C et al., 2025).

National Immunization Technical Advisory Groups (NITAGs) play a crucial role in outbreak response as they gather and organize available evidence to provide timely vaccine policy recommendations to their Ministries of Health (MoH) on vaccine policy. Under an emergency response posture, NITAGs may adapt their processes to operate more rapidly — holding ad hoc meetings, relying on preliminary data (including from other countries), coordinating closely with national emergency response teams, and issuing interim recommendations to address urgent public health needs while awaiting more robust evidence. This flexible approach enables NITAGs to support timely decision-making during fast-evolving outbreaks like monkeypox.

At the beginning of the current 2024 monkeypox outbreak in Africa, vaccines were donated to affected countries. Supply has since become very limited, however, and as of November 2025 does not meet the growing demand as outbreaks continue to spread. This has made the work of NITAGs in Africa increasingly difficult. Some of the challenges that NITAGs face during this outbreak include:

1. Vaccine availability: NITAGs should issue recommendations for currently available vaccines

2. Target population decisions: Due to limited vaccine supply and operational funding, NITAGs are tasked with recommending which target populations should be prioritized.
3. Dosing strategies: NITAGs are considering both single-dose and fractional-dose use of MVA-BN, which constitutes off-label use of the vaccine.

The purpose of this evidence brief is to summarize and catalogue key findings of existing evidence for the most common monkeypox vaccines through the lens of Population, Intervention, Comparison, Outcomes (PICO) questions and the Evidence to Recommendation Framework (EtR).

This document can be used as a starting point for NITAGs to develop context-specific recommendations in their countries. The vaccines considered in this document are:

1. MVA-BN
2. LC16m8
3. ACAM2000

The PICO questions covered in the document will focus on evidence required for:

1. Full series, broad policy question
2. Single dose of MVA-BN
3. Fractional dose of MVA-BN
4. Target groups

The PICO question is used to structure and focus a broad policy question into specific elements guiding the systematic collection and assessment of evidence used to inform evidence-based decisions. It is now commonly used by NITAGs.

This policy brief has been produced in response to the multi-country outbreak in Africa, but can be used by NITAGs globally to inform their decision-making around which monkeypox vaccine to choose and when or how to select a target population.

Each section includes a selection of specific references, scientific articles, and resources for NITAGs to consider for the topic. The end of the evidence brief includes references organized by topic for NITAGs to consider when gathering evidence to make recommendations.

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Background

MONKEYPOX CLINICAL PRESENTATION

Monkeypox disease typically presents with cutaneous lesions and widespread systemic clinical manifestations. Common symptoms are cutaneous and mucosal lesions.

There are three typical clinical phases (Table 1):

1. **Latent phase** is the period when the infected person is asymptomatic and non-contagious. The virus enters the body through damaged skin, or nearby mucous membranes (such as oral, respiratory, and ocular) after direct or close contact to infected fomites, droplets, aerosols, or infected bodily fluids through scratches, bites, or sexual contact. Monkeypox disease has an incubation period between 1 and 21 days. During this latency, the virus spreads throughout the body and into the lymph nodes.
2. **Prodromal phase** is the period when the index case presents with non-specific flu-like symptoms following the latent phase. The prodromal phase occurs within 21 days of being infected and usually lasts 1 to 5 days. During this stage, the individual becomes contagious. Monkeypox has a reported reproduction number ranging from 0.8 to 2.1. The common prodromal symptoms include fever, headache, widespread muscle aches, fatigue, lethargy, and painful, enlarged lymph nodes—typically in the cervical, axillary, and inguinal regions — which is the distinguishing symptom that differentiates the illness from smallpox.
3. **Eruptive phase** is the period when the individual develops painful skin lesions, either as a sore single lesion or widespread lesions, within 1 to 3 days after the fever subsides (if fever occurred). This stage lasts for 14 to 21 days. The monkeypox rash typically begins on the face before spreading across the body, including the palms of the hands; soles of the feet; face, mouth, and throat; groin and genital areas; and the area around the anus. If the individual aquired monkeypox through sexual contact, the rash usually begins in the anal and gential area. More than 90%

of patients develop characteristic skin lesions. The typical monkeypox rash progresses through several sequential stages: macules, papules, vesicles, pustules, umbilications, necrotic crusts, and scabs, which finally fall off, leaving varioliform scars. The number of lesions varies significantly between individuals; some may have only a few, while others develop hundreds (Chenchula, S., et al. 2025).

Not all monkeypox cases present with the typical sequence of clinical phases — prodromal, rash, and recovery. Emerging evidence indicates that some individuals may develop skin lesions without experiencing early systemic symptoms such as fever, headache, or lymphadenopathy. These atypical presentations, particularly in the context of the 2022 to 2025 outbreaks, challenge traditional case definitions and complicate detection and containment strategies. However, current data on such presentations remain limited, highlighting a critical need for further investigation and systematic reporting (Tanasov, A., et al. 2025).

Table 1: Clinical Progression and Symptomatology of monkeypox Infection

Phase	Time Frame	Key Characteristics	Symptoms / Signs	References
Latent / Incubation	~1 – 21 days post-exposure	Virus enters via damaged skin or mucous membranes; asymptomatic and non-contagious	No symptoms; virus spreads systemically and accumulates in lymph nodes	(Lu et al., 2023; WHO, 2024b)
Prodromal	Begins after incubation; lasts ~1 – 5 days when present	Onset of non-specific flu-like symptoms; individual becomes contagious	Fever, headache, myalgia, fatigue, lethargy, painful lymphadenopathy (cervical, axillary, inguinal) which is a symptom to be distinct from smallpox	(N. Atceken et al., 2025; CDC, 2024b; Lu et al., 2023; WHO, 2024e)
Eruptive	Follows prodrome; duration varies ~ 14 – 21 days	Development of skin lesions; highly contagious phase	Rash (initially face or contact site, incl. genitals); lesions evolve from flat spots to scabs; may include proctitis, dysuria, dysphagia	(CDC, 2024b; WHO, 2024b, 2024e)

Monkeypox Virus Clades

It is important for NITAGs to consider their local epidemiological context when developing vaccine policy recommendations. The populations affected must be taken into account when comparing vaccines and programmatic interventions.

Epidemiologic surveillance and genomic analysis show two distinct monkeypox genetic clades with two subclades within each: Clade I (with subclades Ia and Ib) and Clade II (with subclades IIa and IIb) (Table 2).

Table 2: Summary of MPXV Clades – Distribution, Transmission, and Epidemiological Characteristics (WHO, 2025c)

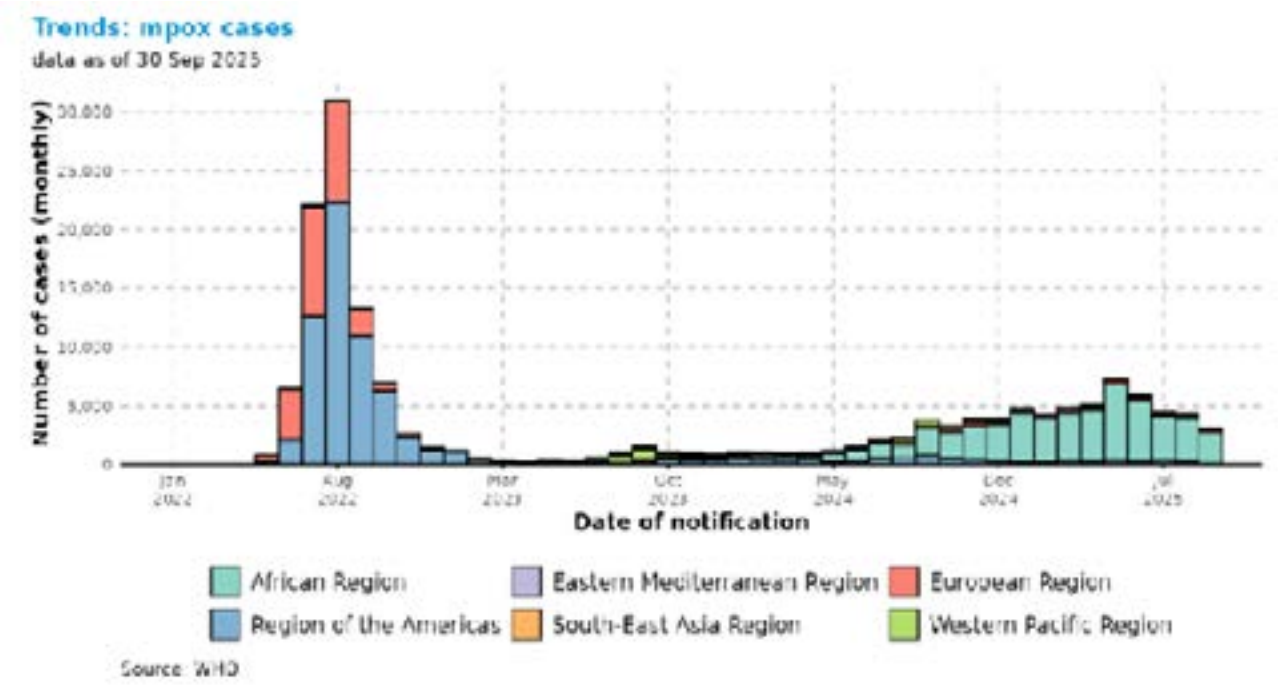
Clade	Geographic Location	Transmission Characteristics	Notable Features	Mortality Rate
Clade Ia	Central Africa (e.g., DRC, CAR, RoC)	Regular zoonotic spillover from animals with human-to-human transmission	Cross-border movement observed through phylogenetic analysis	1-12%
Clade Ib	Eastern Democratic Republic of the Congo, spreading to East Africa	Sustained human-to-human transmission	Recently emerged and rapidly expanding across regions like Burundi and Uganda	0.6%.
Clade IIa	West Africa (e.g., Côte d'Ivoire, Guinea, Liberia)	Historically rare in humans; recent reports suggest human-to-human transmission	Previously mostly found in animals	3.6%
Clade IIb	Initially Nigeria; global spread since 2022	Long-standing sustained human transmission, especially via sexual contact	Caused the 2022 global outbreak; peaked in August 2022	<.1%

GLOBAL SITUATION

Monkeypox virus is endemic to West and Central Africa and has caused sporadic outbreaks in humans since the first human case was detected in 1970 in the DRC. Since 2018, travel-associated cases have been found outside Africa; a global outbreak began in 2022. That outbreak saw hundreds of thousands of cases in 118 countries across five WHO regions, including Africa, Europe, the Americas, the Eastern Mediterranean, and Western Pacific (Acosta-España, J. D., 2024). The rapid rise in global cases led WHO to declare a PHEIC in 2022, which was lifted in May 2023 as case numbers declined.

The global monkeypox indicator-based surveillance system, established in 2022, continuously collects data on confirmed and probable monkeypox cases and deaths reported by Member States to WHO or publicly by Member States (see Figures 1-3). Since this data is regularly updated, please visit the WHO monkeypox dashboard for the most current information.

Figure 1. Global Monkeypox Cases January 2022 - September 2025 (WHO, 2025a)



In 2024, there was a significant increase in cases and deaths in the African Region, starting in the Democratic Republic of Congo, which led to a joint PHEIC declaration from WHO and Africa CDC.

Figure 2. Global Monkeypox Cases by clade, October - September 2025 (WHO, 2025b)

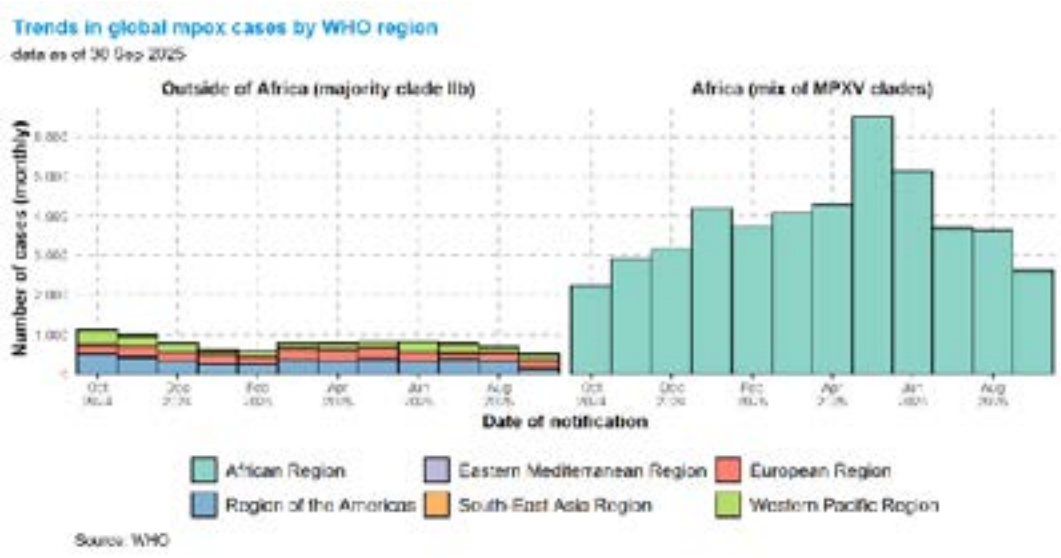
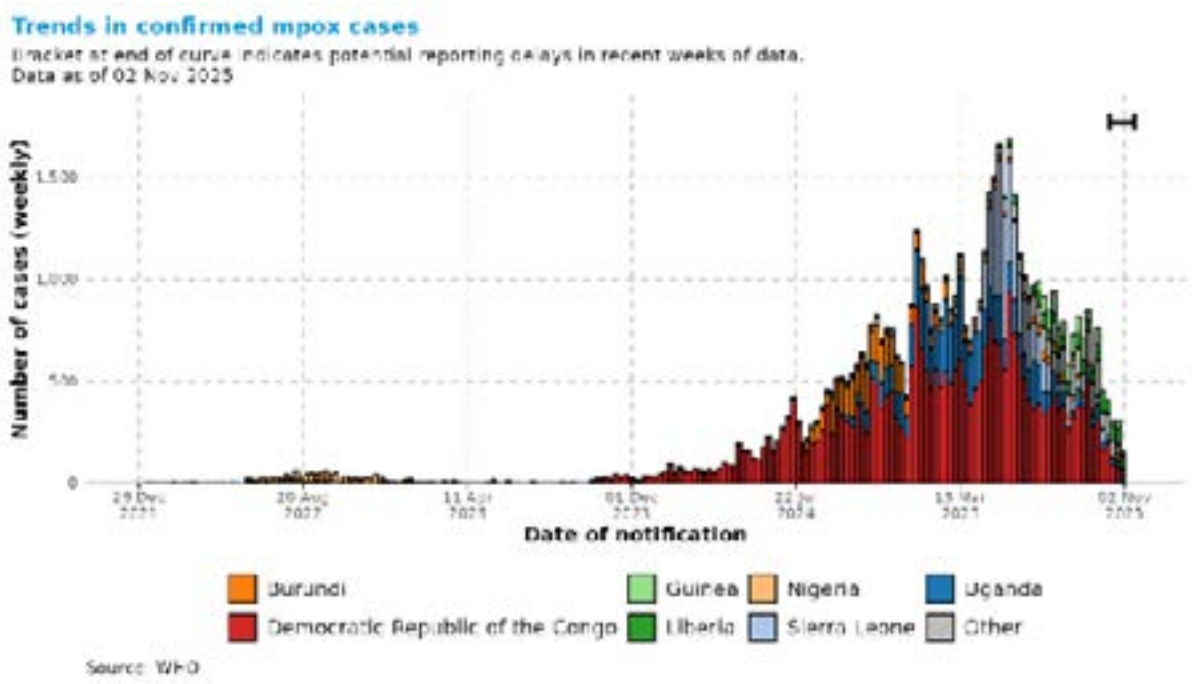
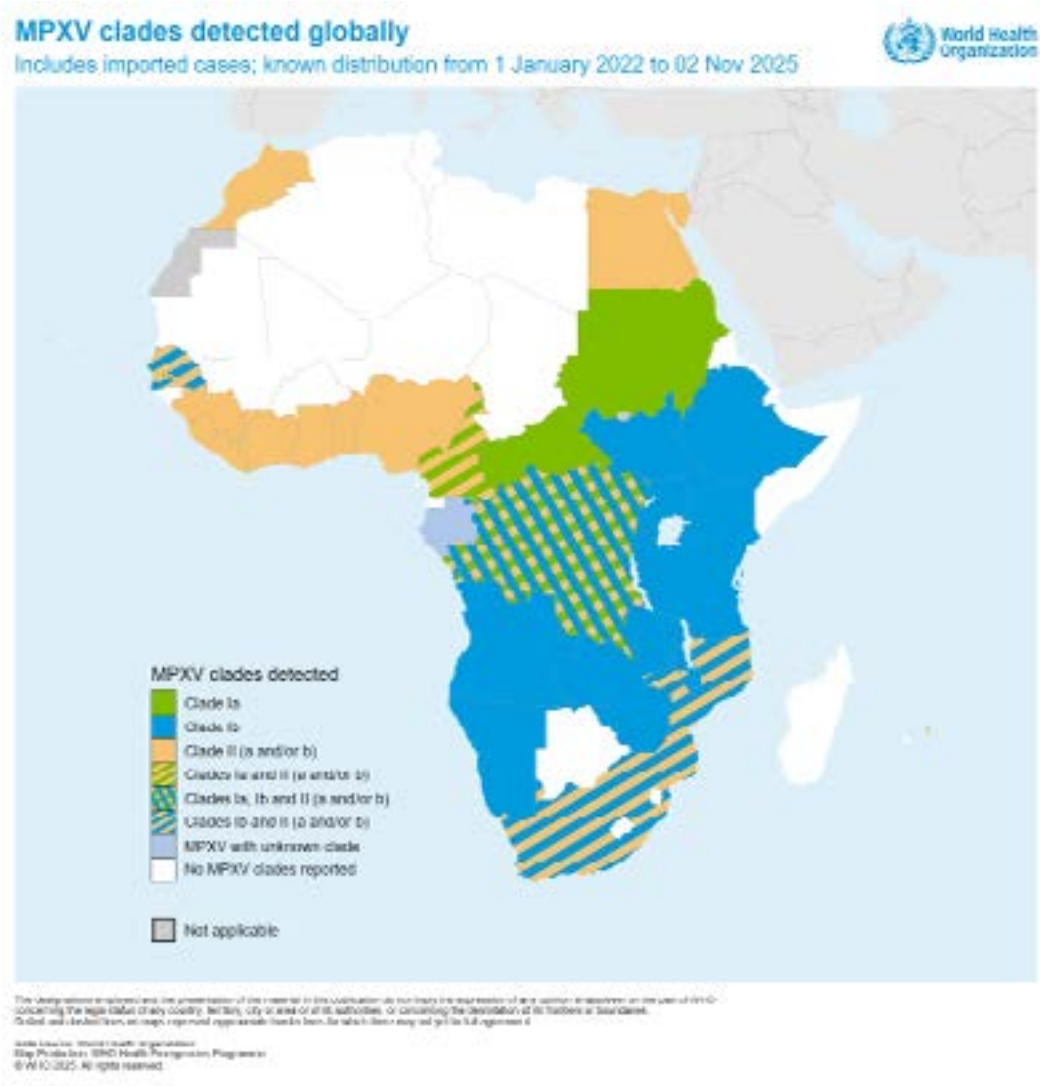


Figure 3. Confirmed Monkeypox Cases by Country, December 2021 - November 2025 (WHO, 2025b)



Since January 2022, the WHO Regional Office for Africa (AFRO) has reported monkeypox cases by every clade from 30 countries (Figure 4); From January to October 19, 2025 27 countries in Africa reported 39,799 confirmed cases and 178 deaths (CFR 0.4%). Seventeen countries have reported active transmission of monkeypox since August 2025. Existing counts likely underestimate the true scale of the outbreak, as countries lack the surveillance and laboratory capacity to confirm cases (WHO, 2025b).

Figure 4. Monkeypox Clades by Country, November 2025 (WHO, 2025a)



OVERVIEW OF MONKEYPOX VACCINES

Three vaccines are currently available globally to prevent monkeypox. These vaccines were initially developed to prevent smallpox, and are now recommended by WHO SAGE to prevent smallpox and monkeypox disease (Lu et al., 2023). The vaccines differ in terms of vaccinia-strain used for development, presentation, storage, recommended dosing, and age and risk groups for which they are recommended or contraindicated.

One of these vaccines (MVA-BN) has been used widely in response to both the global monkeypox epidemics from 2022 to 2025 and the current epidemic in sub-Saharan Africa. The following section summarizes and compares the characteristics, experience in use, and safety and effectiveness of each, as well as guidance for potential use in monkeypox epidemic and endemic settings.

Vaccines Descriptions

- MVA-BN (Modified Vaccinia Ankara Bavarian Nordic) is a third-generation, non-replicating, vaccinia-based vaccine developed by Bavarian Nordic and first licensed in 2013 for prevention of smallpox and monkeypox in adults >18 yrs in Canada and the U.S. FDA in 2019. In response to the global epidemic, licensure for adults was expanded by many countries by July 2022, and an Emergency Use Licensure (EUL) granted for persons <18 yrs in the US.

  MVA-BN is currently approved and prequalified as a two-dose series administered subcutaneously, for use in persons >12 years by WHO SAGE. Immunogenicity and safety are currently being studied in children >4 m-11 yrs and in pregnant women; the vaccine may be used off-label in both groups currently. As it is non-replicating, MVA-BN can be safely used in immunocompromised persons. This vaccine has been widely used globally since 2022 in response to the monkeypox epidemics.
- LC16m8 is a third-generation, minimally replicating, vaccinia-based vaccine developed and licensed in Japan in 1975 to prevent smallpox. Licensure was extended to include monkeypox in August 2022. It is administered using a bifurcated needle, and is recommended for persons >1 yr in Japan.

  LC16m8 vaccine was granted an EUL for this age group by WHO in November 2024, as well as in one African country (DRC). As this vaccine is minimally replicating, it is contraindicated for pregnant women, immunocompromised persons, and those with certain skin conditions.

  Use outside Japan has been limited to date, but as of July 2025, DRC has initiated use in Kinshasa with active follow-up for adverse events following immunization (AEFI), and additional use planned.
- ACAM2000 is a second-generation, replicating, vaccinia-based vaccine approved by U.S. FDA and recommended by U.S. Advisory Committee on Immunization Practices (ACIP) in 2015 to prevent orthopoxvirus infections including smallpox and monkeypox in all age groups.

  It has many contraindications and precautions, and requires a bifurcated needle for administration. As such, it has not been used to prevent monkeypox outbreaks in civilian populations since the availability of MVA-BN vaccine.

03

The Role and Functions of NITAGs in Emergency Response Settings

National Immunization Technical Advisory Groups (NITAGs) are multi-disciplinary, independent expert bodies that provide evidence-based recommendations on immunization policy and strategy to national governments, Ministries of Health (MoH), policymakers, and immunization program managers (Henaff, L et al. 2024).

During public health emergencies, NITAGs play a critical role in rapidly assessing risks, reviewing available evidence, and formulating timely vaccination recommendations. Developing vaccine policy in emergencies requires NITAGs to adjust their standard operating procedures (SOPs) to prioritize agility without compromising scientific rigor. During such emergencies, there are several factors that can complicate the NITAGs decision-making process.

In order for NITAGs to be effective during public health emergencies or large outbreaks of vaccine-preventable diseases, they must make recommendations quickly with fewer data points and possibly weaker evidence. NITAGs are strongly encouraged to collaborate with global partners, local non-governmental organizations (NGO), and other organizations to collect and review evidence, taking into account both their national context and the broader international response, including vaccine supply.

NITAGs should update their SOPs to include a section specifically oultining how to function during a public health emergency. The SOPs should include information on:

1. **Formation of an Emergency Workgroup**
   In emergency settings, NITAGs should establish a specialized workgroup composed of members of the NITAG and its secretariat, and include relevant experts to provide timely, evidence-based recommendations, such as:
   a. **Disease experts:** Epidemiologists, infectious disease specialists, microbiologists, and laboratorians
   b. **Policy experts:** Vaccine regulators, legal advisors, and health policy specialists

c. **Programmatic experts:** EPI (Expanded Program on Immunization) managers, community health workers, logistics and cold chain specialists
d. **Technical partners:** Representatives from WHO, CDC, UNICEF, and other relevant response partners
e. **RCCE experts:** Risk Communication and Community Engagement specialists who address vaccine hesitancy and misinformation, providing critical insights into community perceptions and behaviors. Their input helps ensure that recommendations are practical, culturally appropriate, and effective in building public trust and encouraging vaccine acceptance.

2. **Meeting Cadence**
   The SOPs should define a meeting cadence for the NITAG emergency workgroup during an emergency. This could include regular (e.g., weekly or biweekly) meetings to review emerging evidence, discuss updated guidance, and respond to urgent issues. The NITAG should use an established, tested mode and platform for communication that would be ready to be stood up when there is an emergency.
3. **Coordination with Emergency Response Partners**
   NITAGs should work in coordination with relevant emergency response partners, both local and international, particularly those partners that are generating early data and information that can inform policy decisions (vaccine pillar, research pillar, surveillance, etc).
4. **Coordination with International Partners and Regulatory Organizations**
   Clear mechanisms should be outlined for ongoing coordination with international partners such as WHO, UNICEF, and CDC, as well as with national and regional regulatory authorities. This ensures alignment with global guidance, supports access to timely data, and facilitates decision-making on vaccine approval, importation, and use under emergency provisions (e.g., technical pillars such as vaccine, research and surveillance within the WHO Incident Management Support Team (IMST)).

During an emergency, NITAGs need to collect and organize data and evidence across the seven EtR domains, often making decisions based on incomplete information. Using the EtR framework as an organizational tool during emergencies can allow NITAGs to rapidly understand the evidence that exists, identify evidence gaps, and adjust interventions as new evidence emerges.

To do so, the NITAG will need to be connected early to an appropriate response structure and be appraised of changes in the context to make the strongest possible evidence-based recommendation with available data. Ideally, the EPI manager would be in communication with the NITAG, connected to the response infrastructure, and able to share information with the NITAG.

High-quality, context-specific data is essential for guiding vaccine policy. However, many NITAGs face challenges in data availability due to under-resourced surveillance systems, limited laboratory and genomic sequencing capacity, and inconsistent case reporting.

For monkeypox, data gaps currently exist in areas such as:

1. True incidence and prevalence, particularly in rural or forested regions;
2. Vaccine effectiveness in African settings, especially for newer vaccines like MVA-BN;
3. Adverse event reporting post-vaccination;
4. Population immunity levels post-smallpox vaccination cessation.

To compensate, NITAGs may rely on:

- **Global evidence summaries,** including reviews from WHO's SAGE, regional updates from entities such as Africa CDC, and other relevant public health organizations;
- **Rapid reviews or modeling studies** from peer-reviewed literature (e.g., Lu et al., 2023; Zinnah, 2024);
- **Regional data sharing** mechanisms through, Regional Technical Advisory Groups (RITAGs), AFRO, WHO collaborating centers, The National Immunization Technical Advisory Groups Support Hub (NISH), or academic consortia.

NITAGs should clearly communicate the level of certainty in recommendations when data is incomplete. Use of the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluations) and the WHO EtR framework helps in documenting assumptions and limitations transparently (GNN, 2025).

As the outbreak continues, both the quantity and quality of data will improve, enabling NITAGs to refine their recommendations, which will ultimately help to save lives and conserve resources by directing guidance and limited supplies to the areas most in need.

KEY INFORMATION SOURCES AND REFERENCES

1. Current trends and epidemiological data by WHO Member Country:
   - WHO. (2025a) Global Monkeypox Trends
   - WHO. (2025b) Mpox Multi-country external situation report no. 60 published December 2025.
2. Background on Current Global Outbreak
   - Acosta-España, J. D., et al. (2024). The Resurgence of Monkeypox: A New Global Health Crisis. Le Infezioni in Medicina, 32(3), 267. pmc.ncbi.nlm.nih.gov/articles/PMC11392552/
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04

Evidence-to-Recommendation Process (EtR)

EtR RATIONALE

In addition to assessing the certainty of scientific evidence regarding vaccine safety and effectiveness, expert advisory committees such as NITAGs must consider other domains when making a recommendation — e.g., the resource use, patient's values and preferences, etc. During the process of recommendation formulation, panels consider a range of factors in addition to evidence certainty.

Elucidation of these factors and the judgments behind them facilitates transparency, consistency, and communication of recommendations to healthcare providers, partner organizations, and the public. To structure the discussion of these additional factors to make judgments transparent, an evidence to recommendation (EtR) framework is used.

The EtR structures decision-making by:

- Informing panel members' judgments about the pros and cons of each intervention under consideration;
- Ensuring the important factors that determine a decision (criteria) are considered;
- Providing a concise summary of the best available evidence to inform judgements about each criterion;
- Helping structure discussions and identify reasons for disagreements when they occur;
- Making the basis for decisions transparent to guideline users or those affected by a policy decision.

The following sections present the information that should be considered when formulating a vaccine recommendation, as well as important sources of information for each of the "domains" of evidence being considered for the monkeypox vaccine. Specific types of documents should include SAGE/WHO recommendations as well as those of other monkeypox recommending bodies (such as U.S. ACIP or United Kingdom Joint Committee on Vaccines and Immunization (U.K. JCVI)); clinical trial reports and vaccine manufacturers information; global surveillance and WHO situation reports,

national and regional surveillance reports; national records such as hospitalization, immunization records and surveys; scientific literatures, etc.

Evidence to Recommendations Resources and Tools

- WHO. (2022b). Guidance on an adapted Evidence to Recommendation Process for National Immunization Technical Advisory Groups. iris.who.int/bitstream/handle/10665/356896/WHO-EURO-2022-5497-45262-64756-eng.pdf?sequence=1&isAllowed=y
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DEVELOPING PICO QUESTIONS FOR USE OF MONKEYPOX VACCINE

As mentioned above, the PICO question is used to structure and focus a broad policy question into specific elements guiding the systematic collection and assessment of evidence used to inform evidence-based decisions. It is now commonly used by NITAGs.

Specification of the PICO elements (Population, Intervention, Comparison, and Outcome) can ensure that research questions are framed effectively for systematically reviewing literature, searching for evidence on the effects of the intervention, checking whether studies are relevant or useful, and conducting the analysis of evidence gathered.

As NITAGs consider the use of monkeypox vaccination to protect populations in their countries, specific considerations should be clearly defined and incorporated into the development of the broad PICO policy question(s). These issues may evolve during the course of an epidemic, and may necessitate a clinical guidance section of recommendations, or even a new PICO question. Specific considerations that should be defined are:

1. **Is this response to an outbreak or an endemic disease?** Risk and age groups to be considered will likely differ depending on the context.
2. **Populations at risk.** These should be identified based on local or national epidemiology at the time the recommendation is being considered. Risk groups may vary during an outbreak versus in an endemic situation. Age groups—such as adults, adolescents, and children under 12 years—may be considered together or separately, since specific risk factors and the vaccines licensed and available differ by age.
3. **Vaccines available and licensed for use in the country.** This should be defined by the country's National Regulatory Agency (NRA) in coordination with the development of NITAG recommenda-

tions. Considerations should include the status of WHO recommendations, prequalification, and national licensing.

As of May 2025:

- **MVA-BN** is licensed and WHO-prequalified for individuals over 12 years and may be used off-label in infants and children < 12 years (studies ongoing).
- **LC16m8** has WHO Emergency Use Listing (EUL) for all age groups over 1 year.
- During the current epidemic in Africa, some countries have expanded Emergency Use Authorizations (EUAs) (e.g., DRC expanded EUA for MVA-BN to include individuals over 1 year).

4. **Vaccine-specific recommendations (PICO questions).** Monkeypox vaccines differ significantly in properties such as method of administration, target risk groups, and safety profiles.
   - Each PICO question used to guide vaccine recommendations should initially consider **only one type of vaccine** (e.g., MVA-BN or LC16m8).
   - Once a vaccine is in use, subsequent PICO questions may compare another vaccine to the one currently in use.
5. **Expectations for vaccine supply.** Ideally, vaccines should be administered according to the full licensed and recommended series.
   - In times of limited supply, prioritizing first doses or using fractional dosing of MVA-BN has been shown to be effective and can expand coverage.
   - If supply constraints ease, a second dose may be offered to those who initially received only one dose, to provide enhanced protection.

These issues should be considered in developing one (or more) PICO questions to guide monkeypox vaccination recommendations. As the epidemic/outbreak evolves, additional PICO questions may be developed and considered by the NITAG. Examples of four possible monkeypox PICO questions are included below.

EXAMPLES OF BROAD PICO-BASED POLICY QUESTIONS

Early in the current Africa focused outbreak (2024-2025), NITAGs primarily focused on broad policy questions 1 and 2 outlined below, which have since become standard components of most monkeypox vaccine recommendations. Broad policy question 3 focuses specifically on children under 12 years, given its relevance to ensuring coverage across all recommended age groups, and the differing licensure status and availability of vaccines for this age group.

Additionally, as the vaccine landscape has evolved due to changes in supply and availability, broad policy question 4 may be relevant for countries not allocated sufficient doses or in need of strategies to stretch their available supply. In this situation, different PICO questions could be considered, with the Intervention: (1) Single full dose MVA-BN; (2) Fractional dose (FD) MVA-BN as a single dose, or (3) FD MVA-BN as a 2-dose series.

The following examples of broad PICO-based policy questions focus on the use of the MVA-BN monkeypox vaccine, which has been the only widely available monkeypox vaccine during the current epidemic. Other monkeypox vaccines (e.g. LC16m8, ACAM2000), if available, can be considered in separate PICO questions as appropriate for the country context.

Broad policy question 1: Should country X recommend monkeypox vaccine for populations in the community at high risk* of being exposed to monkeypox during an outbreak?

Population	Populations in the community at high risk* of exposure to monkeypox in an outbreak setting (e.g. close contacts or members of "key" populations) in outbreak regions
Intervention	Administration of the licensed^ or WHO pre-qualified monkeypox vaccine (2 doses of MVA-BN)
Comparison	No vaccination
Outcomes	Reduction in incidence of monkeypox and complications (hospitalization or death)
PICO Question	In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that MVA-BN monkeypox vaccine is safe and can reduce the incidence of monkeypox, and monkeypox-associated hospitalization and death?

*Populations in the community at high risk: To be defined based on epidemiology of monkeypox in the outbreak setting (e.g., household contacts of cases and contacts of contacts, other members of the local community, contact with live or dead wild animals, persons with multiple casual sexual contacts, etc.).
^ - licensed by country NRA.

Broad policy question 2: Should country X recommend monkeypox vaccine for healthcare workers and frontline workers at high risk of being exposed during outbreaks?

Population	Healthcare workers and frontline workers (e.g., lab workers) at high risk of exposure to monkeypox virus.
Intervention	Administration of the licensed^ or WHO pre-qualified monkeypox vaccine (2 doses of MVA-BN)
Comparison	No vaccination
Outcomes	Reduction in incidence of monkeypox and complications (hospitalization or death)
PICO Question	In healthcare and frontline workers at high risk of monkeypox during an outbreak, what is the evidence that monkeypox MVA-BN vaccine is safe and can reduce the incidence of monkeypox, and monkeypox-associated hospitalization and death?

^ - licensed by country NRA.

Broad policy question 3: Should country X recommend monkeypox vaccines for children (<12 yrs) in the community at high risk* of monkeypox (endemic or at risk of being exposed during the current outbreak)?

Population	Populations of children <12 yrs in the community at high risk* of exposure to monkeypox virus endemically or in an outbreak setting (e.g. close contacts or members of "key" populations) in outbreak regions
Intervention	Administration of the licensed^ or WHO pre-qualified monkeypox vaccine (MVA-BN - 2 doses) (not currently WHO pre-qualified for children <12 yrs)
Comparison	No vaccination
Outcomes	Reduction in incidence of monkeypox and complications (hospitalization or death)
PICO Question	In children <12 yrs at high risk of monkeypox in the community during an monkeypox outbreak or in endemic disease setting, what is the evidence that monkeypox vaccine is safe and can reduce the incidence of monkeypox infection, hospitalization, and death in this age group?

*Children in the community at high risk in outbreaks or endemic disease setting: To be defined based on epidemiology of monkeypox in the outbreak or endemic setting (e.g., household contacts of cases and contacts of contacts, other children in the local community, contact with live or dead wild animals, etc.), including specific age groups of children at risk.
^ - licensed or in EUL by country NRA for this age group; WHO - may be used off-label in this age group.

Broad policy question 4: Should country X recommend monkeypox vaccines at reduced dose (single or fractional dose) for populations in the community at high risk* of being exposed to monkeypox during the current outbreak, in situations of limited vaccine supply?

Population	Populations in the community at high risk* of exposure to monkeypox in an outbreak setting (e.g. close contacts or members of "key" populations) in outbreak regions
Intervention	Administration of the licensed^ or WHO pre-qualified monkeypox vaccine (MVA-BN) as a single dose or fractional dose
Comparison	Administration of licensed or WHO pre-qualified monkeypox vaccine as a full 2 dose series
Outcomes	Reduction in incidence of monkeypox infection and complications (hospitalization or death)
PICO Question	In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that a single dose of MVA-BN monkeypox vaccine is safe and can reduce the incidence of monkeypox, hospitalization, and death?

*Populations in the community at high risk: To be defined based on epidemiology of monkeypox in the outbreak setting (e.g., household contacts of cases and contacts of contacts, other members of the local community, contact with live or dead wild animals, persons with multiple casual sexual contacts, etc.).
^ - The MVA-BN vaccine is the only WHO-prequalified monkeypox vaccine primarily recommended as a two-dose series, but it can also be administered as a single dose, or in fractional doses when vaccine supply is limited. Dose-sparing options are "off-label."

Evidence to Recommendation Domains for Monkeypox Vaccine: Evidence and Sources

05

DOMAIN 1: PROBLEM

Definition

Domain 1 of the EtR process, The Problem, is critical for NITAG to formulate recommendations for monkeypox vaccine use during or following a monkeypox outbreak or in the presence of endemic disease. Disease burden information that should be considered when making evidence-based recommendations for monkeypox vaccine, and some important sources of evidence for each EtR domain are summarized in the Table below, and Annex A – Monkeypox Criteria Evidence Tables.

The Problem domain is divided into five elements (Annex A), each with several categories of evidence:

1. **Burden of disease –** This includes monkeypox disease incidence, morbidity, and mortality; age specific incidence; risk groups for disease; disease occurrence over time; information on monkeypox clade.
   Key focuses should be:
   a. **Country data for disease burden -** current, with emphasis on the previous 4 months, and over the previous 1-2 years
   b. **Regional evidence on monkeypox burden -** particularly when considering risk for importation/cross border transmission. The most recent reported data is shown in Figures 1,2 (on pages 12, 13). (This data is updated frequently and NITAGs should refer to the WHO website for most current data. December 2025 WHO sit rep) (WHO, 2025a)
   c. **Information on national case reporting -** using standard WHO case definitions of suspected, probable, lab-confirmed cases , and should note any discrepancies with the country specific case definitions
   d. **Age distribution of cases -** case age distributions may reflect differing epidemiology and risk factors between and within countries

e. **Defining risk groups -** (persons at highest risk) in the current setting based on national/ local surveillance and case investigations, identification of geographic areas with highest incidence during the outbreak/epidemic (hotspots), and vaccine supply availability. A key task of the NITAG is to prioritize risk groups for vaccination (with MoH, EPI team):
   i. **Persons generally considered at high risk of infection and/or severe disease and death** are summarized by WHO (WHO definitions of risk groups (see Monkeypox SAGE or Technet Monkeypox Vx) (Figure 5))
   ii. **Hotspots are considered geographic areas where most new cases reported in previous four weeks**, or where highest disease incidence exists. Ideally, confirmed cases would inform this designation, but suspected cases can be included if surveillance is imperfect – from Technet Monkeypox (Figure 6)
   iii. **WHO and Africa CDC have developed guidance on how to use this information to develop the strategy for monkeypox vaccination** (Technet - Monkeypox vaccine, Vaccination strategies for outbreak response) (Figure 7)

f. **Defining persons as high risk of complications -** Persons recognized as high risk include immunocompromised (including HIV with CD4 counts <200), infants <1 yr, and pregnant women) (WHO SAGE)

g. **Monkeypox serotype distribution -** Identify serotypes causing disease locally. Current evidence suggests vaccines provide protection against all serotypes (best evidence for clade 2b).

h. **Change in epidemiology over time,** as this may evolve during epidemic

2. **Clinical characteristics -** Typical clinical characteristics of monkeypox and infection prevention and control strategies are well described globally (e.g., WHO SAGE, Sitreps, literature). These may vary somewhat by country.
3. **Use and costs of health care -** Country information should be used if available, particularly numbers of cases seeking treatment, hospitalized, treated in intensive care and costs where available.
4. **Alternative prevention measures -** What measures are currently being implemented to prevent disease spread? Recommended measures such as general prevention, infection control, surveillance, contact tracing and self monitoring are described in guidance documents provided by Africa CDC, WHO HQ and WHO AFRO.
5. **Regional and international considerations -**The NITAG should also consider information on cross-border transmission (neighboring countries) and relevant international travel (outside region). Always make sure to use the most recent publication on the topic.

Sources of Evidence

Primary sources of information for this domain are the country-level health information acquired through monkeypox surveillance and health systems (e.g., clinics, hospitalization, laboratories, prevention and vaccination programs, etc.). Regional information (e.g., Africa CDC, WHO AFRO, neighboring countries) may also be useful.

Global information from WHO monkeypox and surveillance websites, technical situation reports, and SAGE recommendations and from the WHO/UNICEF Monkeypox Technet resource package (Table 3, references below). Information from scientific articles may also provide useful guidance relative to global experience in monkeypox vaccination (Table 3).

Table 3: Suggested Key Sources of Evidence for Domain 1 (Problem)

Element	Categories of Evidence	Sources of Evidence
Burden of disease	• Country data for disease burden • Regional evidence on monkeypox burden • Distribution of cases by sex and age group • High-risk groups • Geographic hotspots of exposure • Persons at risk of complications • Monkeypox serotypes in circulation • Changes in epidemiological trends over time	Surveillance (country) – emphasis last 4 weeks WHO websites – monkeypox data, situation reports (see below) AFR CDC WHO AFRO Rapid review (NISH/UCT)
Clinical characteristics of the disease	• Typical clinical characteristics, severity, complications and management of monkeypox • These may vary somewhat by country, based on differences in care seeking behaviors, prevalence of immunocompromised persons, etc.	WHO SAGE, website; AFR CDC, WHO AFRO, U.S. CDC, Medical literature, Country information on clinical cases, medical management
Use and costs of health care	• Primary/secondary/tertiary care use • Use of healthcare (e.g., treatments, hospitalization)	Country information from MoH, health system Clinical management and infection prevention and control for monkeypox: living guideline, May 2025
Alternative preventive and control measures	• Alternative preventive and control measures (e.g., health education, hygiene) and their effectiveness, costs, practicality	Country information on prevention WHO Strategic Framework for Enhancing Prevention and Control of Monkeypox Clinical management and infection prevention and control for monkeypox: living guideline, May 2025

Element	Categories of Evidence	Sources of Evidence
Regional and international considerations	• Global and regional recommendations • Disease potential for international spread and pandemic risk	WHO SAGE (2024, March 2025) Africa CDC, WHO AFRO GACVS Vaccine safety Technet Resource Package (Figures 5-7)

Figure 5. Risk groups for monkeypox (Technet Resource package)

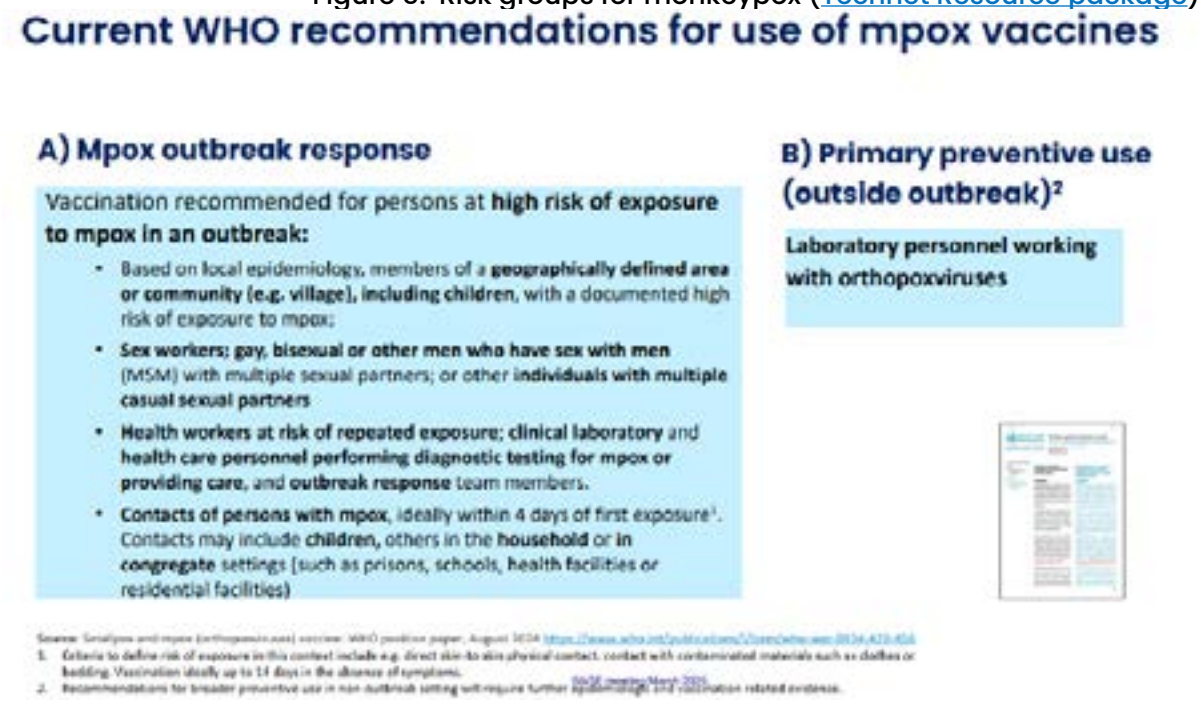


Figure 6. Monkeypox Vaccine, vaccination strategies (Technet Resource Package)

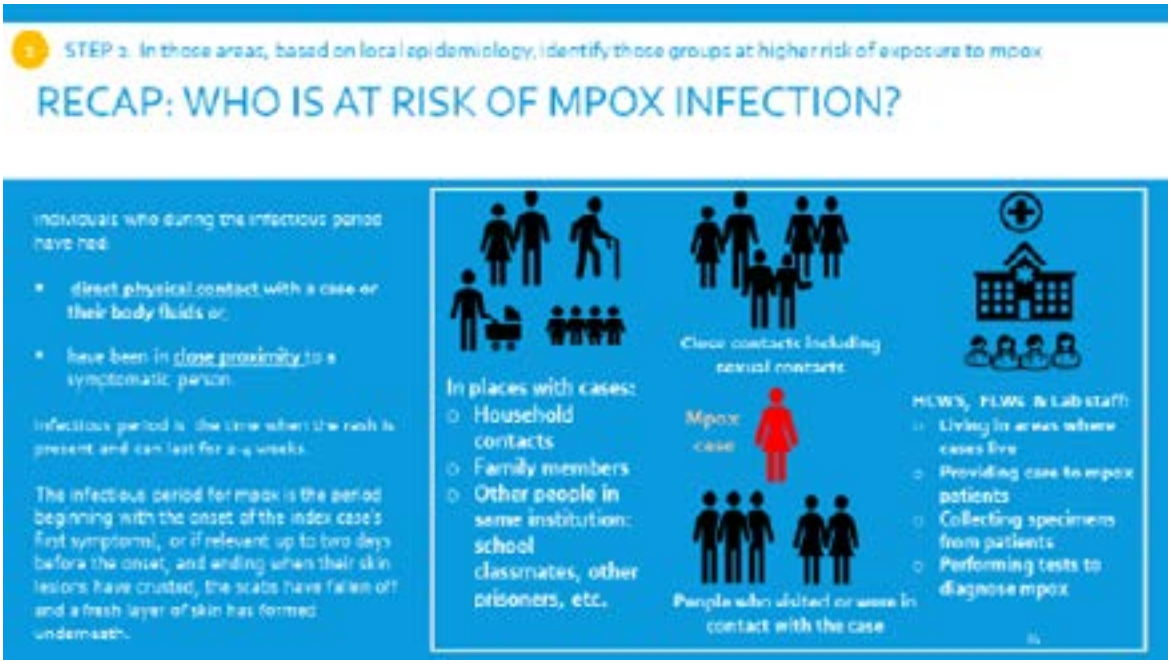
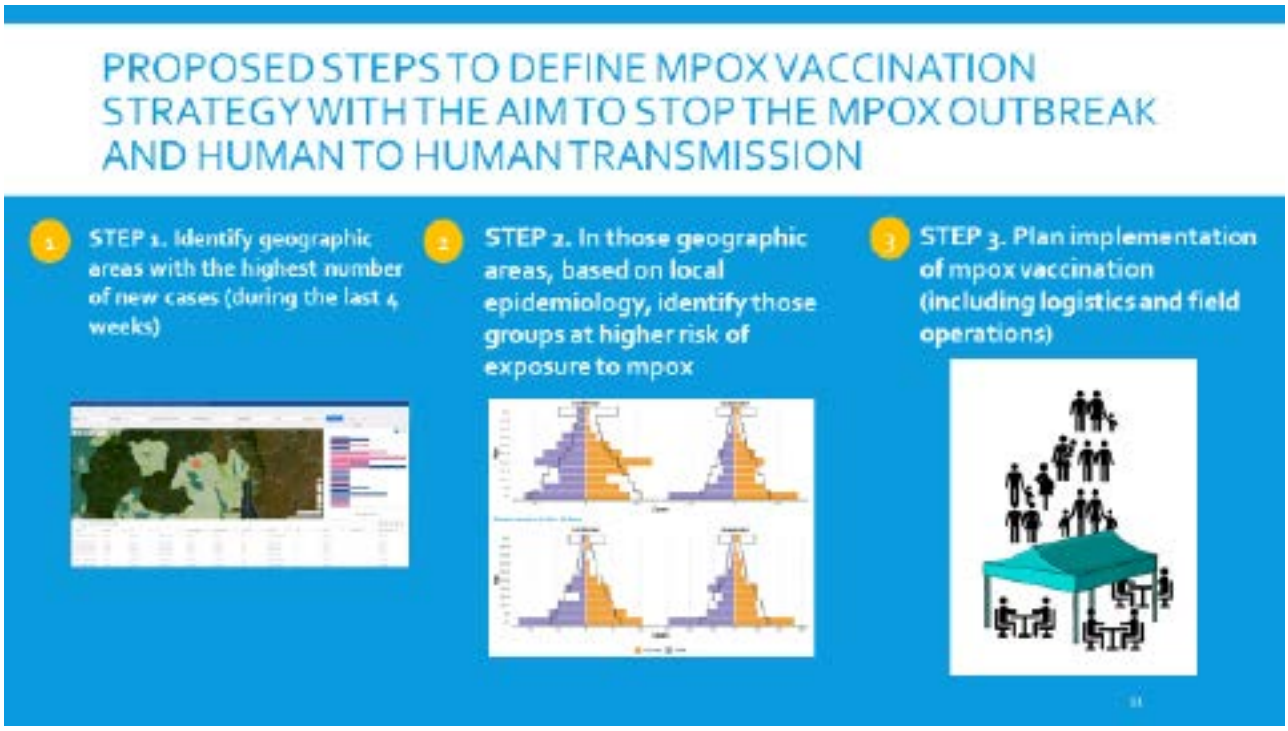


Figure 7. Proposed Steps to Define Monkeypox Vaccination Strategy (Technet Resource Package)



Resources/References

1. Country monkeypox surveillance information – MoH, Monkeypox Surveillance team, healthcare/ hospital databases
2. WHO monkeypox website; WHO emergency situation reports and data site; SAGE reports (2024, 2025 (or slides)
3. Africa CDC - updates, news, briefings
4. WHO AFRO - news, situation reports
5. WHO Clinical management and infection prevention and control for monkeypox: living guideline, May 2025
6. Technet Resource package – Monkeypox vaccination toolkit - TechNet-21
   a. Monkeypox Disease, Diagnosis and Self-Protection
   b. Monkeypox Vaccine, Vaccination Strategies for Outbreak Response
7. WHO - Monkeypox – Global Strategic and Response Plan – March 2025.
8. WHO – Strategic Framework for Enhancing Prevention and Control of Smallpox – 2024-2027 – (2024).
9. WHO Global Advisory Committee on Vaccine Safety – Oct 2024 Statement of the WHO Global Advisory Committee on Vaccine Safety (GACVS) on the safety of the monkeypox vaccines for use in high-risk groups

Scientific articles

- Ndembi, N., et al. Evolving Epidemiology of Monkeypox in Africa 2024. N Eng J Med 2025;392:666676. DOI: 10.1056/NEJMoa2411368
- Jadhav, V., et al. (2025). Global epidemiology, viral evolution, and public health responses: a systematic review on Monkeypox (1958–2024). Journal of Global Health, 15, Article 04061. doi.org/10.7189/jogh.15.04061
- Musuka, G., et al. (2024). A critical review of monkeypox outbreaks, risk factors, and prevention efforts in Africa: Lessons learned and evolving practices. IJID Regions, 100402 doi.org/10.1016/j.ijregi.2024.100402.
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- Cevik, M., et al. (2024). The 2023—2024 multi-source monkeypox outbreaks of Clade I MPXV in sub-Saharan Africa: Alarm bell for Africa and the World. International Journal of Infectious Diseases : IJID : Official Publication of the International Society for Infectious Diseases, 146, 107159. doi.org/10.1016/j.ijid.2024.107159
- Vakaniaki, E. H., et al. (2024). Sustained human outbreak of a new MPXV clade I lineage in eastern Democratic Republic of the Congo. Nature Medicine, 30(10), 27912795. doi.org/10.1038/s41591-024-03130-3

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- Katoto, P. D., et al. (2024). Shifting transmission patterns of human monkeypox in South Kivu, DR Congo. The Lancet. Infectious Diseases, 24(6), e354–e355. doi.org/10.1016/S1473-3099(24)00287-1
- Ugwu, C. L. J., et al. (2025). Risk factors associated with human Monkeypox infection: a systematic review and meta-analysis. BMJ Global Health, 10(2), e016937. doi.org/10.1136/bmjgh-2024-016937
- Mitjà, O., et al. Monkeypox in people with advanced HIV infection: a global case series. The Lancet, Volume 401, Issue 10380, 939 - 949.

DOMAIN 2: BENEFITS AND HARMS OF THE VACCINE

Definition

This domain focuses on gathering evidence about both the benefits and harms of the vaccine. It includes information on vaccine characteristics – such as dosage, administration, storage, and other logistical factors. It also examines vaccine outcomes in terms of safety, with particular attention to serious adverse events linked to immunization, as well as efficacy and effectiveness across the different populations targeted for vaccination.

Sources of Evidence

Primary sources of evidence for benefits and harms include the 2024 SAGE/WHO recommendations (section reference #1) on smallpox and monkeypox vaccines, updated SAGE presentations and guidance, as well as recommendations from other monkeypox advisory bodies such as the U.S. ACIP and the U.K. JCVI. Other important sources include vaccine manufacturers information, technical information developed by WHO and partners (e.g., Technet Monkeypox vaccination toolkit), and clinical trial reports and post-licensure evaluations of safety and effectiveness.

Vaccine Characteristics

Tables 4-7 below summarize each vaccine's key characteristics., including licensure, recommended dosing, presentation, administration, storage, and age and risk groups for which they are approved as of April 2025.

Highlights

- MVA-BN is non-replicating; LC16m8 minimally-replicating, and ACAM2000 is replicating
- Number of recommended doses – MVA-BN – 2 dose vs. LC-16m8, ACAM2000 – 1 dose
- Route administration – MVA-BN - subcutaneous (SQ) with standard syringe; LC16m8, ACAM2000 - bifurcated needle, percutaneous
- Option for use – MVA-BN may be given as single dose, and as reduced dose intradermal if constrained vaccine supply (off-label)
- Presentation – MVA-BN single dose vial; LC-16m8 and ACAM2000 multidose vials
- Storage requirements – long-term and during use (see below)

Table 4: Summary of Monkeypox Vaccines (WHO, 2024d)

Product	MVA-BN	LC16m8	ACAM2000
Description	Non-replicating vaccinia-based vaccine, 3rd generation	Minimally replicating vaccinia-based vaccine, 3rd generation	Replicating vaccinia-based vaccine, 2nd generation
Recommended Dosing Schedule	Two doses four weeks apart; May use as single dose if constrained vaccine supply (see below)	Single dose	Single dose
Administration	Standard needle syringe subcutaneous (SQ) route as a fractional dose May be given intradermally if constrained vaccine supply	Bifurcated needle percutaneous route	Bifurcated needle percutaneous route
Presentation	Liquid frozen Single dose vial 0.5 ml/dose[3] Intradermal dose is 0.1 mL	Freeze-dried multi-dose vials; Reconstitute with 0.5 ml diluent. Reconstituted contains >250 doses (.0017-.0029 ml each)	Freeze-dried multi-dose vial Reconstitute with 0.3 ml diluent. Reconstituted contains >100 doses (.0025 ml each)
Vaccine Storage	<-50 to -250C for 3 yrs (longer if lower temp) After thawed, 2-80C in dark for up to 8 weeks. Do not refreeze	-20 to -350C long term. 50C for 2 yrs. 370C for 4 wks. After reconstitution, 2-60C for 1 mo.; 23-270C for 24 hrs	-5 to -250C long term. After reconstitution, 2-60C for 30 days; room temperature for 6-8 hrs
Licensure[1]	WHO PQ – EUA ≥12 yrs USA, EU: ≥12 yrs UK: all ages DRC ≥1 yr	WHO – EUA >1 yr Japan: ≥1 yr DRC – EUA: ≥1 yr	USA, Australia, Singapore, Canada[2]

1. Licensure status may not reflect recommended use in country of licensure.
2. Although ACAM2000 is licensed in countries listed here, none have recommended it for monkeypox prevention.

Summary of Age and Risk Groups Considerations

Highlights

- MVA-BN – licensed for use in persons >12 yrs, can be used "off label" in infants <1 yr and children 1-11 yrs, pregnant women and immunocompromised
- LC16m8, ACAM2000 may be used in persons >1 yr, but as a live replicating vaccine, is contraindicated in pregnant women, immunocompromised persons, and persons with atopic dermatitis

Table 5: Monkeypox Vaccines Age and Risk Group Considerations (WHO, 2024d)

Product	MVA-BN 2	LC16m8 [3]	ACAM2000
Indicated Age Groups – Summary	≥12 yrs; Infants, children – may use Off-label[4]	All ages >1 yr	All ages >1 yr
Pregnant women	WHO – may use Off-label[5]	Contraindicated	Contraindicated
Infants <1yr	WHO - may use Off-label	Not Recommended	Contraindicated
Immunocompromised (including living with HIV with CD4<200)	WHO – may use Off-label	Contraindicated	Contraindicated
Other – Atopic Dermatitis	Can use	Contraindicated	Contraindicated

1. Based on WHO Sage recommendations – August 2024 and March 2025.
2. WHO Emergency Use Authorization >12 yrs; WHO pre-qualified.
3. EUA – WHO EUL >I yr age.
4. MVA-BN - Studies evaluating safety, immunogenicity in children >2–11 yrs in progress.
5. MVA-BN - Study in pregnant women and infants 4m-2 yrs to start Q2 2025.

Summary of Safety and Efficacy of Available Monkeypox Vaccines

Highlights

- All monkeypox vaccines are safe and effective in animal and human studies (Table 6)
- MVA-BN has been widely used since 2022 in response to monkeypox outbreaks, with extensive safety data and multiple studies across different populations demonstrating approximately 80% effectiveness in preventing monkeypox when administered before exposure. There is no established correlate of protection, and the duration of protection is unclear. Although antibody levels wane substantially within 1 year, a study conducted in DRC displayed an anamnestic response to a booster at 5 years after the primary series; ongoing studies are examining later time points. The need for booster doses remains uncertain, but doses are recommended by WHO once every 2 to 5 yrs for those remaining at risk of exposure.

- Live, replicating vaccines (LC16m8, ACAM2000)
  - All live, replicating vaccines have the potential for adverse events related to vaccinia infection, including progressive vaccinia, vaccinia encephalitis, autoinoculation, vaccinia keratitis, and myopericarditis. These vaccines also have several contraindications limiting their use within certain populations (e.g., pregnancy, immunocompromise).
    Experience is limited to the smallpox eradication era and only LC16m8 been used in recent monkeypox outbreaks.
  - LC16m8 has been used primarily in Japan to date, with estimated protective efficacy demonstrated in animal studies and immunogenicity observed in humans. Expanded data are expected with ongoing use and studies in DRC.
  - ACAM2000 safety and immunogenicity are based primarily on studies conducted in the U.S. for smallpox prevention. Its effectiveness is inferred from the use of live replicating vaccinia vaccines during the global smallpox eradication.

Table 6: Summary and Efficacy of Available Monkeypox Vaccines (WHO, 2024d)

Product	MVA-BN [1]	LC16m8	ACAM2000
Adverse reactions	Frequent minor local and systemic AEFI – headache, fever, chills, fatigue, redness, swelling at injection site	Frequent minor local and systemic AEFI – erythema, induration, lymphadenopathy	Frequent minor local and systemic AEFI
Serious Adverse Reactions	No serious reactions in 22 studies (17,420 participants) 4 cases myocarditis in 839,178 observational (4.77/million doses - not higher than background)	No myocarditis in 3,346 adults; 1 case autoinoculation	Myopericarditis – 187 cases in 900,253 (20.1 per 100,000 doses, vs. 2.2 /100,000 background) Generalized vaccinia, autoinoculation (<1 per 100,000 doses)
Groups at risk for severe adverse events		Immunocompromised, atopic dermatitis, <1 year of age	Immunocompromised, atopic dermatitis, <1 year of age
Contraindications	None; may use off-label in children, pregnant women	Pregnancy, immunocompromised, atopic dermatitis	Pregnancy, immunocompromised, atopic dermatitis, <1yr

Product	MVA-BN [1]	LC16m8	ACAM2000
Efficacy/ Effectiveness – Pre-Exposure[1]	1 dose – 75% (66%-85%) [15 studies] 2 dose – 82% (78%-88%) [9 studies]	No human data 100% Protective against lethal challenge – mice, rabbits, monkeys	No human data 100% Protective against lethal challenge in animals
	Immunocompromised 70 % (-38%-94%)(2 doses) [1 study] Persons living with HIV 35% (-73-+79%)(1 dose)[1 study]	No data	No data
Efficacy/ Effectiveness – Post-Exposure	16% (-23%-56%) [9 studies]1	No human data	No human data
Immunogenicity	98% seroconversion rate; antibodies return to baseline in ~ 2 years	90-100% take rate (3614 persons) 100% seroconversion (naïve) 60% previously vaccinated	~100% take rates (healthy 18-29 yrs) 97% seroconversion (naïve) 76% in previously vaccinated
Duration	No established correlate of protection. Antibody titers/ PRNT wane at ~ 1 yr; anamnestic response to booster after 5yrs. Booster 2-5 yrs (SAGE 2024)	Not studied	Not studied

1. Post-exposure effectiveness estimates controversial, as in many studies 95% CI overlapped zero, and many studies did not consider immortal time bias, which may inflate effectiveness estimates.

Options for Use of MVA-BN Vaccine – Single Dose and Fractional Dose – may be Considered at Times of Limited Vaccine Availability.

Highlights

- Either single dose or fractional dose intradermal (ID) may be considered in times of limited vaccine availability, expanding reach to include more persons receiving the vaccine (Table 7). If only one dose is given initially and longer duration protection is desired, a second dose may be given at a later time; impact on longer-term effectiveness has not been evaluated.
- When used pre-exposure, short term effectiveness of single dose appears to be similar to that of the full two-dose series.
- In the current context of limited MVA-BN vaccine supply due to funding constraints, and in alignment with previous recommendations, WHO released an FAQ on use of intradermal fractional

dosing of monkeypox MVA-BN vaccine. The use of dose-sparing options, particularly intradermal fractional dosing was endorsed by the AFRO Regional Immunization Technical Advisory Group (RI-TAG) on 26 June 2025 (WHO. Monkeypox: Multi-Country External Situation Report no.55, July 11, 2025).

Table 7: Alternative Regimens for MVA-BN Monkeypox Vaccines

Alternative MVA-BN Regimen	2 doses	1 dose	Fractional Dose[1]
Administration	0.5 ml SQ	0.5 ml SQ	0.1 ml Intradermal
No. Doses	2 doses, 4 weeks apart	1	1 dose, or 2 doses, 4 weeks apart
Licensure (EUA)	WHO EUA, pre-qualified	WHO EUA, pre-qualified	EUA United States 2022
Efficacy/ Effectiveness Pre-exposure1	82% (78%-88%) [9 studies]	75% (66%-85%) [15 studies]	80% (23%-95%) – 2 doses 81% (56%-91%) 1 dose [1 study]
Safety	No serious reactions	No serious reactions	No serious reactions, slightly more reactogenicity
Duration of protection	Antibody wanes at about 1 yr; No correlate of protection	Not defined	Not defined
Suggested Use	Routine or emergency vaccination	Emergency vaccination in time of constrained supply	Emergency vaccination in time of constrained supply
Advantages	Fully licensed and recommended schedule; Efficacy, duration protection defined	Doubles the number of at-risk persons who can be reached in time of constrained vaccine supply. Short term effectiveness comparable to 2 doses Can offer second dose when vaccine supply improves	Increases (up to 400%) the number of at-risk persons who can be reached in constrained supply Short-term effectiveness appears to be same as SQ full dose
Disadvantages	When vaccine supply limited, fewer at-risk persons can be vaccinated than with other options	Long term protection is unknown	Off-label, no EUA from WHO Limited experience in Africa Possible increased reactogenicity

1. May be given initially as single dose or as a 2 dose series.

Monkeypox vaccine use to prevent monkeypox to present

1. Since 2022, there has been wide use of MVA-BN in multiple countries – US >1.2 million doses.
2. During 2024-2025 epidemic in Africa through November 2025, over 4.9 million vaccine doses have been delivered to 13 countries, including 1.49 million doses of MVA-BN vaccine and 3.05 million doses of LC16m8 vaccine from Japan to the DRC. app.powerbi.com/view?r=eyJrIjoiMDQzZWRjMzAtYjg5OC00N2EzLWJmOTgtZTFmMjFlMzBlZTZkIiwidCI6ImY2MTBjMGI3LWJkMjQtNGIzOS04MTBiLTNkYzI4MGFmYjU5MCIsImMiOjh9
3. Monkeypox vaccination activities have been initiated in thirteen countries with MVA-BN vaccine (Angola, CAR, Cote D'Ivoire, DRC, Ghana, Kenya, Liberia, Malawi, Nigeria, Rwanda, Sierra Leone, South Africa and Uganda), most of which are implementing a single-dose strategy targeting population groups at high risk of exposure. More than 1.2 million MVA-BN vaccine doses have been administered, of which roughly 50% were in DRC. Other countries that recently reported monkeypox cases are developing their national monkeypox vaccination plans, however funding is needed to facilitate access to additional MVA-BN vaccine doses. (WHO. Monkeypox: Multi-Country External Situation Report no.60 December 2025)

Vaccine Availability and Regulatory Authority

1. Current availability – overall, from donors; source of info – AFRO, GAVI, WHO, UNICEF, donors- See Domain 4 – Resources
2. Current regulatory – WHO EUA, Prequalification; Country EUA: - focus on Africa – Tables from SAGE March 2025

Vaccine Benefits and Harms Resources and Tools

1. WHO Smallpox and Monkeypox Position Paper – Smallpox and Monkeypox (Orthopoxviruses)(August 2024) Immunization, Vaccines and Biologicals (who.int)
2. WHO SAGE – Slides from Monkeypox presentation to SAGE March 2025
3. WHO prequalification MVA-BN extranet.who.int/prequal/vaccines/p/imvanexr
4. Vaccine Package inserts
5. Technet Resources Monkeypox vaccination toolkit - TechNet-21
   WHO_MVA-BN vaccine recommendations_March2025; Final_LC16m8_mpox_WHO_interim guidance_22April2025 (also provides guidance on administration by bifurcated needle)
6. Frequently Asked Questions (FAQ) on use of fractional dosing with intradermal administration of monkeypox MVA-BN vaccine in the context of vaccine supply-constrained outbreak response
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Scientific articles

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DOMAIN 3: VALUES AND PREFERENCES

Definition

Values and Preferences refer to the interest in, and acceptability of, the monkeypox vaccine among the populations intended to receive it. These are summarized in **Annex A: Criteria Evidence Tables,** and encompass three key elements:

1. **Perceived benefits and harms** This includes how target populations perceive both the disease and the vaccine, as well as factors influencing their views, such as the availability and clarity of information, and levels of vaccine confidence or hesitancy.
2. **Differences across population segments** Variations in values and preferences among different subgroups within the target populations, which must be considered individually.
3. **Vaccine Demand** The level of demand for the monkeypox vaccine among the intended recipients.

Sources of Evidence

Primary sources of information should come from within the country and may include data from the Ministry of Health (MOH), Knowledge, Attitudes, and Practices (KAP) surveys, social listening, focus groups, and other relevant studies (Table 8).

Resources to support vaccine uptake and guide risk communication and community engagement (RCCE) strategies are available through the Technet Resource Package, including:

- Monkeypox Vaccine Uptake Brief and AEFI Response
- Africa CDC/WHO RCCE Module: Vaccine Demand

Additional information specific to various risk groups in the African region and globally can be found in the reference list. This includes a study on vaccine hesitancy in the region (Du, et al., 2025).

Table 8: Sources of Information for Values and Preferences

Element	Categories of Evidence	Sources of Evidence
3.1 Perceived benefits and harms	• Relative importance that the target population attributes to the benefits and harms of the intervention • Management of misinformation, anti-vaccine information	Country information /data – MOH information, KAP surveys, social listening, focus groups, other studies; information on uptake of other vaccines by target populations. Technet Resource Package References from literature – Regional, Global for different risk groups (see below)
3.2 Differences by segments of target population	• Differences in values and preferences (ethical, religious, financial) for different target populations	
3.3 Demand	• Demand for vaccine of target population	

Summary of Key Evidence

Monkeypox vaccine acceptance, intention, and uptake in the WHO African Region (AFR) are among the lowest globally across all population groups. In a comprehensive meta-analysis conducted by Sulaiman et al. (2024) which included 61 studies and 263,857 participants worldwide including sub-groups such as healthcare workers, the general public, and high-risk groups like people living with HIV (PLHIV) and LGBTQI+ communities. The intervention examined was monkeypox vaccination, with outcomes measured in terms of vaccine acceptance, intention to vaccinate, and actual vaccine uptake. Comparisons were made between the African Region and other WHO regions.

The study revealed that the overall acceptance rate in AFR was 41.9%, significantly below the global average of 59.7%, and lagging behind regions like WHO South-East Asia Region (SEAR) (72.2%) and WHO Western Pacific Region (WPR) (67.3%). Among the general public in Africa, both acceptance and intention to vaccinate were 41.9%, in contrast to much higher rates in regions such as WPR (70.3%) and WHO Europe Region (EUR) (56.5%). Vaccine uptake in AFR remains critically low, with just 5.0% of the general public having received the monkeypox vaccine, compared to 33.5% in WPR and 36.9% in EUR. Among healthcare workers in AFR, intention to vaccinate was only 39.0%, again much lower than in WPR (81.9%) or SEAR (77.3%). (Tables 9-12)

Subgroup data (e.g., PLHIV and LGBTQI+) for Africa were not specifically available, but global comparisons show that acceptance and intention among these high-risk groups are substantially higher than in the general population, indicating a need for targeted outreach in AFR. Overall, the findings reflect low public confidence, limited access, and possibly structural barriers within the region's health systems.

Table 9: Monkeypox Vaccine Acceptance, Intention, and Uptake in the WHO African Region Compared to Global Averages Based on a Meta-Analysis of 61 Studies (n = 263,857) (Sulaiman, et al., 2024)

Outcome Measure	Region	Prevalence (%)	95% CI	No. of Studies	Participants (n)
Acceptance	Global	59.7	51.1–68.1	59	142,487
	AFR	41.9	38.5–45.3		
Intent to Vaccinate	Global	60.9	52.1–69.3	51	127,359
	AFR	41.9	36.6–47.4		
Uptake	Global	30.9	21.0–41.7	17	26,186
	AFR	5.0	3.7–6.7		

Table 10: Monkeypox Vaccine Acceptance by WHO Region on 59 Studies (n = 142,487) (Sulaiman, et al., 2024)

WHO Region	Acceptance (%)	95% CI
Global	59.7	51.1–68.1
AFR	41.9	38.5–45.3
AMR	48.9	24.9–73.2
EMR	52.0	44.2–59.8
EUR	63.8	54.6–72.6
SEAR	72.2	60.7–82.4
WPR	67.3	5.7–100

Table 11: Intention to Vaccinate Against Monkeypox by WHO Region based on 51 Studies (n = 127,359) (Sulaiman, et al., 2024)

WHO Region	Intention to Vaccinate (%)	95% CI
Global	60.9	52.1–69.3
AFR	41.9	36.6–47.4
AMR	59.5	37.9–79.4
EMR	52.0	44.2–59.8
EUR	59.3	49.3–69.0
SEAR	67.3	5.7–100
WPR	73.5	63.0–82.9

Table 12: Monkeypox Vaccine Uptake by WHO Region based on 17 Studies (n = 26,186) (Sulaiman, et al., 2024)

WHO Region	Uptake (%)	95% CI
Global	30.9	21.0–41.7
AFR	5.0	3.7–6.7
AMR	28.3	15.9–42.7
EMR	—	—
EUR	36.9	15.4–61.6
SEAR	—	—
WPR	33.5	21.9–46.3

Resources/ References

- Technet Resource Package – Mpox vaccination toolkit - TechNet-21

How to achieve and sustain high uptake of mpox vaccination in outbreak settings

Strengthening Risk Communication and Community Engagement (RCCE) to Drive Greater Demand and Acceptance of the Mpox Vaccine

Scientific Articles

African Countries

- Petrichko, S., et al. (2024). Acceptance of an Mpox Vaccine in the Democratic Republic of the Congo. Emerging Infectious Diseases cdc.gov/eid • Vol. 30, No.12, December 2024
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- Sulaiman, S. K., et al. (2024). Global prevalence and correlates of mpox vaccine acceptance and uptake: A systematic review and meta-analysis. Communications Medicine, 4(1), 136. nature.com/articles/s43856-02400564-1.pdf
- Du, M. et al. Mpox vaccination hesitancy, previous immunisation coverage, and vaccination readiness in the African region: a multinational survey. Lancet eClinicalMedicine 2025;80: 103047 Published Online doi.org/10.1016/j.eclinm.2024.103047

DOMAIN 4: RESOURCE USE

Definition

Resource use for monkeypox vaccine response requires consideration of factors including availability of vaccine, international technical and financial support for vaccine procurement and licensure for use in country, resources for vaccination planning and operations, as well as the time horizon for need for support during outbreak vs. longer term support post-epidemic.

Information for planning and executing monkeypox vaccine campaigns or planning for ongoing monkeypox vaccination includes 5 elements, summarized in the Monkeypox Criteria Evidence Tables (Annex A):

1. **Resource use and cost related to the vaccine**
    a. Monkeypox vaccine – Consider whether the vaccine will be purchased or received as donation, and the vaccine doses required, including whether the recommended vaccine series (e.g., MVA-BN, 2 doses) or vaccine sparing strategies (e.g., MVA-BN single or fractional dose) will be used.
    b. The Access Allocation Mechanism (AAM) provides a mechanism and application for countries to request vaccine donations during the current epidemic in Africa. The GAVI First Response Fund accepts vaccine donations by partners, which are then allocated by AAM. gavi.org/global-health-security/principles-mpox-dose-donation
2. **Costs of vaccine administration –** Costs may vary by target group and geographic area. One example of country data is available (see ImmunizationEconomics.org "What is the cost of delivering mpox vaccines?"). Templates to help estimate doses needed and operational costs are available at the Technet website (Monkeypox vaccination toolkit - TechNet-21). Funding support for vaccine administration may be available for GAVI eligible countries (GAVI website).
3. **Vaccine availability –** Information about monkeypox vaccine availability is available from AAM partners (WHO/UNICEF, GAVI), directly from manufacturers, and from donors (country, private).
    a. For the 2024-2025 epidemic in Africa, vaccine availability is coordinated through the Access Allocation Mechanism (AAM) – countries are required to apply for vaccines using a standardized template (link below). For regulatory considerations, coordinated by AVAREF (AFRO), guidance is available from Technet: "Use of Mpox vaccines in African countries - Regulatory Policy Considerations."
4. **Vaccine affordability –** Vaccine affordability depends on a country's available funding, vaccine pricing, and overall economic status, as well as the availability of donor support for both vaccines and operational costs.
    In the context of the current monkeypox outbreak in Africa:
    - Most low- and middle- income countries (LMICs) are eligible to receive donated vaccines through the Access Allocation Mechanism for immediate epidemic response.

- Middle-income countries (MICs) may need to allocate domestic resources or explore alternative funding sources.
- For all countries, affordability planning will be important if long-term or sustained vaccination becomes necessary due to monkeypox becoming endemic.

5. **Socioeconomic considerations –** Costs to country via work loss, and indirect costs to patients and families due to monkeypox disease should be considered. These may have limited relevance for countries (LMIC, LIC) for which vaccine is donated, but may have more relevance for MIC countries and in the context of longer-term vaccine use.
6. **Economic impact of intervention on immunization program and health sector –** This element focuses on assessing the impact of vaccine program on healthcare costs (reduced care vs cost of vaccine program), and cost effectiveness (CE) of vaccination.
   a. Costs of monkeypox disease and of vaccination program during the epidemic response.
   b. Cost effectiveness analyses are important to justify vaccination programs, particularly outbreak response and ongoing vaccination post-epidemic. At present, there are no cost-effectiveness data relevant to the current monkeypox outbreak response in Africa. Cost effectiveness studies have been published related to sustaining monkeypox vaccination in HIC post-2022 global epidemic (Xu-Sheng, Z., et al. 2024).

Sources of Evidence

Primary sources of information for this domain include global and partner resources related to vaccine planning, availability, and access, such as the WHO monkeypox website, technical situation reports, the WHO/UNICEF Monkeypox Technet resource package, and the GAVI website (Table 13). Country-level health information on socioeconomic factors (e.g., healthcare and program costs, affordability) is also critical (see Table 13 and references below). Additionally, regional sources including Africa CDC, WHO AFRO, and data from neighboring countries along with scientific literature, can provide valuable context and guidance based on regional and global experiences with monkeypox vaccination.

Table 13: Suggested Key Sources of Information for Resource Use

Element	Categories of Evidence	Sources of Evidence
4.1 Resource use and cost related to the vaccine	• Costs of vaccine, syringes - Vaccine requirements - Dosing strategy • Direct and indirect costs to administer the vaccine	LMIC/LIC / Epidemic – AAM - WHO/GAVI/UNICEF Monkeypox strategic planning documents – Technet – Accessing mpox vaccines through the Access and Allocation Mechanism (AAM); "Estimate monkeypox vaccine doses"; "Mpox Vaccine deployment plan – budget template" (templates only) MIC/other – WHO, Vaccine manufacturer, Partners Country data Immunization economics (What is the cost of delivering mpox vaccines? - Immunization Economics)

Element	Categories of Evidence	Sources of Evidence
4.2 Vaccine availability	• Availability of vaccine and long-term supply • Available suppliers and competition dynamic in the market	Access Allocation Mechanism (AAM), AVAREF, WHO AFRO for Africa – requests and procurement of monkeypox vaccine in Africa outbreak response GAVI First Response Fund accepts donations to be allocated by AAM. gavi.org/global-health-security/principles-mpox-dose-donation Technet – "Use of Mpox vaccines in African countries - Regulatory Policy Considerations"
4.3 Vaccine affordability	• Availability of fiscal space to implement and sustain the programme • Prevailing prices for the vaccine in the market	Country – MOF, MOH GAVI Liability issues (AEFI) – Technet "Use of Mpox vaccines in African countries - Regulatory Policy Considerations"
4.4 Socio-economic	• School/work absenteeism • Indirect cost to patients and families • Productivity losses	Country data – Ministry of Health
4.5 Economic impact of intervention on immunization program and health sector	• Reduction in healthcare costs • Cost-effectiveness ratio of vaccination program	Country data No cost effectiveness data in Africa region Global data could be used as a proxy in the interim (Zeng X-S, et al. 2025) Modelling could be used to adapt the models to country-specific settings

Resources/References

The African Vaccine Manufacturing Accelerator has been established by the World Health Organization (WHO) in collaboration with key partners: the Africa Centers for Disease Control and Prevention (Africa CDC), the Coalition for Epidemic Preparedness Innovations (CEPI), Gavi, the Vaccine Alliance, and the United Nations Children's Fund (UNICEF), in coordination with WHO Member States.

- Technet Resource package – Monkeypox vaccination toolkit - TechNet-21
  - Accessing monkeypox vaccines through the Access and Allocation Mechanism (AAM)
  - "Estimate monkeypox vaccine doses"
  - "Monkeypox Vaccine deployment plan – budget template"
  - "Use of monkeypox vaccines in African countries - Regulatory Policy Considerations"
  - "Monkeypox Disease, Diagnosis and Self-Protection"

- "Monkeypox Vaccine, Vaccination Strategies for Outbreak Response"
- Frequently Asked Questions (FAQ) on use of fractional dosing with intradermal administration of monkeypox MVA-BN vaccine in the context of vaccine supply-constrained outbreak response
- GAVI First Response Fund. gavi.org/global-health-security/principles-mpox-dose-donation
- ImmunizationEconomics.org "What is the cost of delivering mpox vaccines?"
- Zhang X-S et al (2025). Cost effectiveness of vaccination strategies to control future mpox outbreaks in England: a modelling study. Lancet Regional Health - Europe 2025 55: 101364. https://doi.org/10.1016/j.lanepe.2025.10136

DOMAIN 5: EQUITY

Definition

Equity addresses key issues related to ensuring equitable access to vaccination among all targeted populations. It includes strategies for reaching diverse groups fairly, prioritizing populations in the context of limited vaccine supply, and ensuring those at highest risk of severe disease are appropriately considered. It also involves identifying and addressing potential stigma or barriers faced by specific groups (e.g., sex workers or other marginalized populations).

Elements

1. Equitable access
2. Ethics, legality
3. Stigma

Sources of Evidence

Primary sources of information should come from within the country and may include data from the Ministry of Health (e.g., the Expanded Programme on Immunization [EPI], HIV/AIDS units), national surveys, and qualitative research such as focus groups (Table 14).

In addition, relevant scientific literature and case studies from other countries can provide valuable insights into how equity considerations have been addressed in similar contexts.

In situations of limited vaccine supply, countries may need to prioritize high-risk groups and explore dose-sparing strategies to maximize impact and ensure equitable access.

Table 14: Summary of Sources of Information for Equity

Element	Categories of Evidence	Sources of Evidence
5.1 Equal access	• Access for each of the target groups • Strategies to reach the most vulnerable and hard-to-reach populations • Ensuring equity amidst potential limited vaccine supplies	Country information – e.g., Ministry of Health/HIV unit, EPI programme; surveys, focus groups Lessons from African countries implementing the vaccination program Consider the 4 principles: maximizing benefits and minimizing harm, promoting justice, mitigating health inequalities, and promoting transparency. Am J Transplant. 2022 Dec 30;21(1):420–425. doi: 10.1111/ajt.16437).
5.2 Ethics, legality	• Ethical and legal considerations for prioritizing specific target groups • Ethical and legal considerations for vaccine requirements for groups with occupational exposure	
5.3 Stigma	• Stigma around disease and vaccination for each of target groups	

Resources/References

- Roundtable Report: Discussion on monkeypox in DRC and social science considerations for operational response - socialscienceinaction.org/resources/roundtable-report-discussion-on-mpox-in-drc-and-social-science-considerations-for-operational-response/ (2024)
- Am J Transplant. 2022 Dec 30;21(1):420–425. doi.org/10.1111/ajt.16437).

DOMAIN 6: ACCEPTABILITY

Definition

Acceptability refers to the acceptance of a specific intervention by the general public, medical community, and key stakeholders. It includes defining key stakeholders for the monkeypox vaccination program; exploring perceptions regarding each target group; and examining issues such as vaccine hesitancy for each. The three critical elements of acceptability are:

1. Factors related to the disease and the vaccine itself
2. Factors related to other interventions, such as other vaccines or healthcare measures used within the target populations
3. Factors related to ethical, programmatic, and financial considerations that may influence stakeholder acceptability

As part of this assessment, key stakeholders for the monkeypox vaccination program should be identified. Perceptions of each target group including issues like vaccine hesitancy should also be examined (see Annex A: Criteria Evidence Tables).

Sources of Evidence

Each of these factors affecting acceptability including perceptions of the disease and vaccine, attitudes toward other health interventions, and ethical, programmatic, or financial concerns are best understood through country-specific data. This can be gathered from Ministry of Health reports, KAP (Knowledge, Attitudes, and Practices) surveys, social listening, focus groups, and other relevant studies (Table 15).

Resources to support strategies for improving vaccine uptake, risk communication, and community engagement are available through TechNet, including:

- Monkeypox Vaccine Uptake Brief and AEFI Response
- Africa CDC/WHO RCCE Module: Vaccine Demand

Examples of insights and lessons learned from other countries implementing monkeypox vaccination programs are provided in the references below and in the Values and Preferences Resources.

Table 15: Summary of Sources of Information for Acceptability

Element	Categories of Evidence	Sources of Evidence
6.1 Related to disease and vaccine	• Perception of the public, stakeholders, and medical community about disease and vaccine (balances of benefits and harms) for each target group • Management of misinformation, rumors, anti-vaccine information	Country information – MOH information, KAP surveys, focus groups, other studies Lessons learnt from African countries implementing the vaccination program Technet Resource Package WHO's How to achieve and sustain high uptake of mpox vaccination in outbreak settings cdn.who.int/media/docs/default-source/crs-crr/how-to-achieve-and-sustain-high-uptake-of-mpox-vaccination-in-outbreak-settings.pdf?sfvrsn=66bba0ac_1
6.2 Related to other interventions	• Impacts of program on efficacy and safety of other vaccines and health care interventions e.g. malaria, polio, measles control programs	
6.3 Related to ethics, program, finances	• Ethical, programmatic, or financial issues that may affect acceptability of intervention by stakeholders	

Resources/References

- Technet Resource Package – Monkeypox vaccination toolkit - TechNet-21
  How to achieve and sustain high uptake of monkeypox vaccination in outbreak settings
  Strengthening Risk Communication and Community Engagement (RCCE) to Drive Greater Demand and Acceptance of the Monkeypox Vaccine

Scientific articles

- Schmidt-Sane, M., et al. (2024). Infrastructures of epidemic response: Mpox and everyday repair work in southwestern Nigeria. Social science & medicine (1982), 58, 117246. doi.org/10.1016/j.socscimed.2024.117246

DOMAIN 7: FEASIBILITY

Definition

Considerations for **Feasibility** include the ability to deliver the vaccine to the proposed target populations, manage vaccine receipt, storage, and distribution, ensure licensure, and monitor vaccine administration, safety, and impact on disease. **Feasibility** includes five elements summarized in the Monkeypox Criteria Evidence Tables (Appendix A):

1. **Accessibility –** The ability to identify and reach the intended monkeypox risk groups may vary by target population (e.g., health care workers/responders; case contacts; sex workers/contacts, etc). For each target group, the accessibility and resources required for access should be considered.
2. **Resources for vaccine storage, distribution and administration –** Should consider resources (cold chain requirements and availability at each distribution level) needed to store, transport, distribute and administer the vaccine. Vaccine storage requirements for each monkeypox vaccine are summarized in the Benefits and Harms section (Table 4).
3. **Licensure of the vaccine –** Responsibility of the country vaccine regulatory agency. For the Africa epidemic, countries may be assisted/coordinated by African Vaccine Regulatory Forum (AVAREF), and may be guided by WHO pre-qualification of monkeypox vaccines for specific age groups. (see also Resources sect 2)
4. **Information management –** The ability to track implementation of the program, including vaccine distribution, doses administered, vaccine wastage, etc. WHO/Africa CDC documents are available to guide monitoring of monkeypox vaccination program. (Technet - Monitoring monkeypox vaccination; monkeypox vaccine uptake brief and AEFI response)
5. **Disease and AEFI surveillance –** Monitoring and investigation of adverse events following monkeypox vaccination (Technet - monkeypox vaccine uptake brief and AEFI response). Ongoing disease surveillance is needed to assess vaccine impact, vaccine effectiveness, and to guide ongoing program focus (changes in geographic, persons at risk). Research into monkeypox vaccine safety and efficacy in countries with vaccination programs is ongoing.

Sources of Evidence

Primary sources of information for this domain include country Ministry of Health (MoH) data related to monkeypox vaccination planning, immunization programs, and vaccine regulatory authorities. Additionally, global and regional technical resources—such as those from Africa CDC, WHO AFRO, and partner organizations provide critical information on vaccine planning, availability, and access. Key references include the WHO/UNICEF Monkeypox Technet resource package and the WHO Monkeypox website (see Table 16 and references below).

Table 16: Sources of Information for Feasibility

Element	Categories of Evidence	Sources of Evidence
7.1 Accessibility	• Accessibility of target population(s)	Country information/monkeypox response plan, EPI program Any documented lessons learned in deploying COVID-19 vaccines to similar target geographical locations (literature search)
7.2 Resources for vaccine storage, distribution, and administration	• Availability of resources for vaccine storage, distribution, and administration —physical (cold chain storage), human, technical, and financial	Country information/monkeypox response plan EPI program Vaccine storage requirements (see Benefits and Harms section)
7.3 Licensing of vaccine	• National Regulatory Authority (NRA) requirements to register available vaccines for use in target population	Country regulatory authority WHO prequalification of monkeypox vaccines Technet - Use of monkeypox vaccines in African countries - Regulatory policy considerations AVAREF, WHO AFRO
7.4 Information management	• Availability of information systems to manage the vaccine supply, cold chain, measure related performance metrics, i.e., coverage and vaccine utilization	Country information/monkeypox response plan EPI program Technet guidance
7.5 Disease and AEFI surveillance	• Existence and reliability of surveillance systems to monitor disease and AEFI	Country information/monkeypox response plan; EPI Country disease and AEFI surveillance programs Technet guidance

Resources/References

1. WHO HQ – Vaccine prequalification extranet.who.int/prequal/vaccines
2. Africa CDC – africacdc.org/mpox
3. Technet Resource package – Monkeypox vaccination toolkit - TechNet-21
   a. Accessing monkeypox vaccines through the Access and Allocation Mechanism (AAM)
   b. Monkeypox Disease, Diagnosis and Self protection
   c. Monkeypox vaccine, Vaccination strategies for outbreak response

d. Sample Monkeypox Training Objectives and Agenda
e. Use of monkeypox vaccines in African countries - Regulatory Policy Considerations
f. Monitoring monkeypox vaccination
g. Monkeypox vaccine uptake brief and AEFI response

4. Hrynick, T., et al. (2024). Roundtable report: Discussion of mpox in DRC and social science considerations for operational response. opendocs.ids.ac.uk/articles/report/Roundtable_Report_Discussion_on_mpox_in_DRC_and_Social_Science_Considerations_for_Operational_Response/26434924?file=48184294

06

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GENERAL MONKEYPOX

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ANNEX A: MONKEYPOX PICO-SPECIFIC CRITERIA TABLES: DECEMBER 2024

Policy Question: Should country X recommend monkeypox vaccines for populations in the community at high risk* of monkeypox during the current outbreak?

PICO Question: In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that monkeypox vaccine is safe and can reduce the incidence of infection, hospitalization, and death?

Domain 1: Problem

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
1.1 Burden of disease	• Incidence of morbidity & mortality • Age-specific morbidity and mortality • Risk groups	Incidence, hospitalizations and deaths due to monkeypox before and during outbreak Age specific incidence, hospitalizations, mortality **Risk groups (severe disease)** – immunocompromised, pregnant and breast-feeding women, young children **Persons at risk during outbreaks –** Laboratory staff and clinical persons treating disease Outbreak response team and frontline workers Contacts of cases Key populations (commercial sex workers MSM, persons with multiple casual sex partners, transgender), congregate settings (prisons, people living in camps, internal displaced populations), etc **Geographic Hotspots**	Critical	Surveillance (country), AFR CDC, WHO AFRO Rapid review (NISH/UCT) Persons at risk during outbreaks to be defined by country MOH/govt

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
	• Serotype distribution • Disease occurrence over time • Changes in epidemiology over time	Monkeypox virus clade, genomic sequences Incidence prior to outbreak and time course during outbreak		AFRO CDC, Country Country information
1.2 Clinical characteristics of the disease	• Signs and symptoms of disease • Severe forms • Long-term complications of disease • Medical management of disease	Skin rash (systemic, genital), fever, lymphadenopathy, headaches, etc???Severe systemic rash, secondary skin lesions, encephalitis, hepatitis, pneumonitis, hospitalization, death Scarring, corneal and facial scarring impaired vision/blindness, sexual impairment Prevention secondary infection, other; antivirals	Critical	WHO SAGE, Website; AFR CDC Country information
1.3 Use and Costs of Health Care	• Primary/secondary/tertiary care implications • Short- and long-term use of healthcare (e.g., treatments, hospitalization)	Clinic care, hospital care,? ICU Treatment of complication (secondary infection, sepsis, pneumonia, encephalitis) Clinic care use for immunocompromised persons 'HIV+, patients under-immunosuppressive treatment)	Critical Important	Country information from MoH, health system Clinical management and infection prevention and control for monkeypox: interim rapid response guidance, 10 June 2022 https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
1.4 Alternative preventive and control measures	• Alternative preventive and control measures (e.g., health education, hygiene) and their effectiveness, costs, practicality	Infection prevention/control – isolation, handwashing, gloving/gowning, clinical care Surveillance, contact tracing, self-monitoring; Health education, hygiene, ? other	Critical	Country information WHO Strategic Framework for Enhancing Prevention and Control of Monkeypox Clinical management and infection prevention and control for monkeypox: interim rapid response guidance, 10 June 2022 https://www.who.int/publications/i/item/WHO-MPX-Clinical-and-IPC-2022.1
1.5 Regional and international considerations	• Existence of regional and global recom-mendations • Disease potential for international spread and pandemic risk	WHO SAGE, RITAG recommendations, emergency committee, EPR/TAG statements Substantial risk of cross border transmission – neighboring countries, distant travel (IHR, Africa CDC)	Critical	WHO SAGE, AFR CDC, WHO AFR

Domain 2: Benefits and Harms of the Options

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
2.1 Vaccine characteristics	• Vaccine presentation, formulation, dosage, and route of administration • Administration schedule and possibility of co-administration with other vaccines and drugs • Flexibility of vaccination schedule • Cold chain and logistic requirements	MVA-BN (non-replicating) (2 dose –SQ or ID , 4 weeks apart); LC-16 (minimally replicating)(1 dose, percutaneous with bifurcated needle) ACAM-2000 (replicating, 1 dose, bifurcated needle) # doses/vial No data re. Co-administration with other vaccines MVA-BN – 18+ yrs; <18 EUA; LC-16 – all ages; unsuitable for immunocompromised, pregnant, proliferative skin diseases ACAM2000 – immunocompetent adults: unsuitable for immunocompromised, pregnant, proliferative skin diseases, infants <1yr Liquid frozen (MVA-BN) or freeze dried (MVA-BN, LC-16)	Important	WHO SAGE August 2024 Vaccine Product package inserts

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
2.2 Safety	• Type, consequences and frequency of short and long-term adverse events following vaccination • Risk groups or risk factors for adverse events • Contraindications or precautions	Identified type, consequences and frequency of short and long-term adverse events following vaccination during clinical trials - Local or muscle pain, redness, swelling, headache, fatigue No serious AEFI identified for MVA-BN, LC-16; ACAM2000- Myopericarditis – 20.1/100000 doses LC-16, ACAM2000 - immunocompromised, pregnant persons, proliferative skin diseases ACAM2000 – infants <1 yr	Critical	WHO SAGE Metanalyses 2022, 2024 Vaccine package inserts Country information
2.3 Efficacy and effectiveness	• Vaccine efficacy/effectiveness and types of specific • Critical determinants of the immune response associated with protection • Duration of protection and waning of immunity in general and risk groups • Interference regarding protection or immunity with other vaccines	MVM-BN , ACAM2000 , LC16 efficacy, effectiveness for primary preventive vaccination for high-risk population of exposure (by age, previous vaccination with Small pox vaccine) Determinants of vaccine efficacy and effectiveness in populations with underlying conditions such as immunocompromised, malnutrition, pregnant women Effectiveness when co-administrated with other vaccines (YF, MR, DPT booster) Duration of protection and waning of protection in high risk population Efficacy only shown for 12 + months; neutralizing antibodies persist many years Booster doses q. 2-5 yrs depending on exposure.	Critical	WHO SAGE recommendations Metanalyses for SAGE MVA-BN – pre-exposure – 76 % (1 dose), 82% (2 doses); post-exposure – 20% Immunocompromise – 51-70% efficacy LC-16, ACAM2000 – protective in non-human primates; neutralizing antibody in 95% (naïve, 80-95% previously vaccinated

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
2.4 Vaccine indirect effects	• Herd immunity/protection • Potential negative population impact of emergence of non-vaccine serotypes	TBD		

PICO Question: In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that monkeypox vaccine is safe and can reduce the incidence of monkeypox infection, hospitalization, and death?

Domain 3: Values & Preferences

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
3.1 Benefits and harms	• Relative importance the target population attributes to the benefits and harms of the intervention as well as the comparison	Relative importance to each of the target groups Management of misinformation, rumors, anti-vaccine information	Critical	Country information /data – MOH information, KAP surveys, social listening, focus groups, other studies
3.2 Differences by segments of target population	• Differences in values and preferences (ethical, religious, financial) for different segments of the target population (disadvantaged, religious)	Differences in values for each of the target groups/population subgroups	Critical	
3.3 Demand	• Demand for vaccine of target population	Demand for vaccine for each of the target groups	Critical	

Domain 4: Resource Use

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
4.1 Resource use and cost related to the vaccine	• Direct and indirect costs to administer the vaccine as they compare to other prevention or control measures • Cost using different strategies	Costs of vaccine Costs of vaccine administration to each of the target groups Costs for planning, training/support of HCWs, community mobilization Costs of different vaccine administration strategies (intradermal vs. subcutaneous – MVA-BN)	Critical	WHO/GAVI/UNICEF Country data Monkeypox strategic planning documents Immunization economics (What is the cost of delivering monkeypox vaccines? - Immunization Economics)
4.2 Vaccine availability	• Availability of vaccine and long-term supply • Available suppliers and competition dynamic in the market	Information from WHO, GAVI, partners Doses allocated/ shipped/planned to the country through the partners Access and Allocation mechanism for monkeypox treatment, vaccines and test	Important	WHO/GAVI/UNICEF/AfrCDC
4.3 Vaccine affordability	• Availability of fiscal space to effectively implement and sustain the recommendation in the programme • Prevailing prices for the vaccine in the market and price estimations for the local community	Resources to implement emergency/ outbreak vaccination program Budget of monkeypox vaccine deployment plan	Critical	Country – MOF, MOH ? GAVI

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
4.4 Socio-economic	• School and work absenteeism • Indirect cost to patients and families • Productivity losses	Considerations of impact/cost of outbreak on each of these factors Opportunity costs of not implementing the emergency/ outbreak vaccination program	Important	Country data
4.5 Economic impact of intervention on immunization program and health sector	• Reduction in healthcare costs	Reduction in acute healthcare costs due to vaccine outbreak response Costs incurred by the health system (e.g. to manage sequelae) in the absence of a quality vaccination program	Important	Country data
	• Cost-effectiveness ratio of vaccination program	Cost-effectiveness at various outbreak intervention scenarios – high and low disease incidence Positive impact on immunization program (e.g opportunity to provide other vaccines in addition to monkeypox) Negative impacts on immunization program (e.g human resource shortages dedicated to immunization program that results to reduced vaccination rates)		No cost effectiveness data in Africa region Global data could be used as a proxy in the interim (https://www.medrxiv.org/content/10.1101/2024.08.20.24312301v1.full ; https://www.valueinhealthjournal.com/article/S1098-3015(23)04141-4/fulltext) Modelling could be used to adapt the models to country -specific settings

PICO Question: In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that monkeypox vaccine is safe and can reduce the incidence of monkeypox infection, hospitalization, and death?

Domain 5: Equity

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
5.1 Equal access	• Universality, accessibility, and affordability of services for all the inhabitants in the country, including vulnerable, hard to reach and immigrant populations	Focus for each of the target groups Strategies to reach the most vulnerable and hard to reach populations Ensuring equity in face of potential limited vaccine supplies	Critical	Country information – e.g. Ministry of Health/HIV unit, EPI programme; surveys, focus groups Consider the 4 principles: maximizing benefits and minimizing harm, promoting justice, mitigating health inequalities, and promoting transparency. Am J Transplant. 2022 Dec 30;21(1):420–425. doi: 10.1111/ajt.16437).
5.2 Ethics, legality	• Non-health related effects of vaccination • Ethical considerations • Legal implications	Ethical and legal considerations for prioritizing specific target groups Ethical and legal considerations for vaccine requirements for groups with occupational exposure	Critical	
5.3 Stigma	• Stigma around the disease or around vaccination	Stigma around disease and vaccination for each of target groups	Critical	

Domain 6: Acceptability

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
6.1 Related to disease and vaccine	• Perception of the public, stakeholders, and medical community about disease and vaccine (balances of benefits and harms)	Identification of stakeholders, and perceptions of stakeholders re. each of the target vaccination groups Management of misinformation, rumors, anti-vaccine information	Important	Country information – MOH information, KAP surveys, focus groups, other studies Any lessons learnt from African countries implementing the vaccination program
6.2 Related to other interventions	• Impacts of program on efficacy and safety of other vaccines and health care interventions	Impact on childhood vaccination programs, other important health interventions (eg. malaria, polio, measles control programs)	Important	
6.3 Related to ethics, program, finances	• Ethical, programmatic, or financial issues that may affect acceptability of in-tervention by stakeholders	Ethical, programmatic issue for stakeholders for each target group; financial access for vaccine procurement	Important	

PICO Question: In persons at high risk of monkeypox in the community during an monkeypox outbreak, what is the evidence that monkeypox vaccine is safe and can reduce the incidence of monkeypox infection, hospitalization, and death?

Domain 7: Feasibility

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
7.1 Accessibility	• Accessibility of target population	Accessibility of each of the target populations, especially rural or disadvantaged	Critical	Country information/ monkeypox response plan, EPI program Any documented lessons learnt in deploying COVID-19 vaccines to similar target geographical locations
7.2 Resources for vaccine storage, distribution, and administration	• Availability of resources for vaccine storage, distribution, and administration — physical (cold chain storage), human, technical, and financial	Vaccine storage, cold-chain Vial size, doses and cold chain storage and transport for each of the vaccines Availability of skilled health care and public health workers	Critical	Country information/ monkeypox response plan , EPI program
7.3 Licensing of vaccine	• National Regulatory Authority (NRA) requirements to register available vaccines for use in target population and/or use in a different schedule as originally recommended	Monkeypox vaccine registration by regulatory agency or use of WHO-EUL/ prequalified monkeypox vaccines Off label authorization	Critical	Country regulatory authority

Element	Categories of Evidence	PICO-Specific Evidence to Collect	Priority	Sources of Evidence
7.4 Information management	• Availability of information systems to manage the vaccine supply, cold chain, measure related performance metrics, i.e., coverage and vaccine utilization	Information systems to manage vaccine supply, cold chain, vaccine utilization and coverage of target groups Information systems to record and store vaccination (clinic and/or homebased records)	Critical	Country information/ monkeypox response plan , EPI program
7.5 Disease and AEFI surveillance	• Existence and reliability of surveillance systems to monitor disease and AEFI	Monkeypox surveillance systems, lab capacity; AEFI reporting systems	Critical	Country information/ monkeypox response plan; EPI Country disease and AEFI surveillance programs


PIVI
The TASK FORCE for GLOBAL HEALTH
Partnership for International Vaccine Initiatives


CDC
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION