Frequently Asked Questions (FAQ) on use of fractional dosing with intradermal administration of mpox MVA-BN vaccine in the context of vaccine supply-constrained outbreak response

19 June 2025

This document outlines key considerations for the use of fractional dosing with intradermal administration of the MVA-BN mpox vaccine in response to ongoing mpox outbreaks. In light of the limited availability of vaccine and current WHO recommendations, national authorities may, as a temporary outbreak response measure, consider administering MVA-BN vaccine via intradermal injection at a reduced dose to protect individuals at risk of exposure.

1. What are the **WHO recommendations** on mpox MVA-BN vaccine intradermal fractional dosing?

WHO has previously recommended the "off-label"[1] **use of a single full dose of MVA-BN vaccine (0.5mL/dose) administered subcutaneously or fractional dosing (0.1mL/dose) administered intradermally in supply-constrained outbreak situations**[2]. In this document, WHO further provides guidance on the **off-label use of a single or two-dose fractional regimen**. This approach is intended to maximize the number of individuals who can be vaccinated using the available vaccine supply.

At the same time, WHO emphasizes the need to collect further data on vaccine safety, effectiveness, and duration of protection in these circumstances.

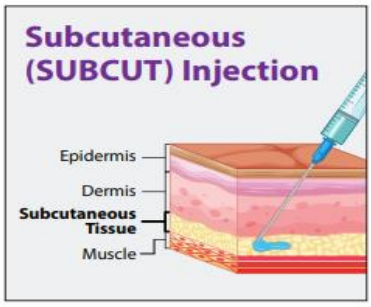
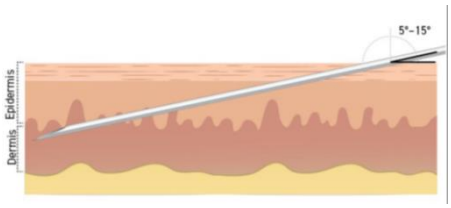
2. What is an **intradermal fractional dose** of mpox MVA-BN vaccine?

One full dose of MVA-BN vaccine is 0.5 mL suspension provided in a single-dose vial**. A fractional dose (0.1 mL) is a reduced dose of the same vaccine, equivalent to one-fifth of the usual dose (each single-dose vial provides 4-5 fractional doses).** As the volume of the given dose is smaller, a fractional dose will be administered intradermally (given just below the top layer of the skin) using a 0.1 mL auto disable (AD) syringe with a shorter needle (10-13 mm). A summary of MVA-BN vaccine characteristics is provided in Table 1.

[1] **"Off-label use":** WHO SAGE or National Immunization Technical Advisory Groups (NITAG)/equivalent body policy recommendations that differ from the manufacturer label use indications then leads to off-label public health use of a vaccine. https://www.who.int/publications/m/item/off-label-vaccine-use--explanatory-note-for-countries

[2] Smallpox and mpox (orthopoxviruses): WHO position paper, August 2024

Table 1. Summary of MVA-BN vaccine characteristics.

	FULL DOSE	FRACTIONAL DOSE
Volume per dose	0.5mL	0.1mL
Number of doses	One or two doses	One or two doses
Route of administration	Subcutaneous administration (administered at a 45-degree angle) 	Intradermal administration (administered at a 5–15-degree angle) 
Site of administration	The fatty tissue over the triceps area in the upper arm	Inner side of the forearm, deltoid area of the upper arm, or scapula

3. Is it **safe** to administer a fractional dose of mpox MVA-BN vaccine intradermally?

Yes, however, self-resolving non-severe side effects are more common following intradermal than subcutaneous administration.

A study conducted in the United States of America reported that although the intradermal vaccination site displayed erythema/induration (>30 mm), this mode of administration did not hamper the ability of the person vaccinated to perform routine activities.[3]

A study published in 2023 analyzing data from Australia's vaccine safety surveillance system examined adverse events following subcutaneous and intradermal administration of MVA-BN. Adverse events were highest after the first dose of intradermal vaccination (53%) and lowest after the second dose of subcutaneous vaccination (31%). The most common reported reactions included local redness, itching, and swelling for intradermal vaccination, and local pain, swelling, and redness for subcutaneous vaccination[4].

Another study published in 2024 reported the frequency of systemic and local side effects following intradermal and subcutaneous administration of MVA-BN vaccine in Italy. Systemic adverse events

[3] Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects - PubMed
[4] Short-term Adverse Events Following Immunization With Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) Vaccine for Mpox

were more frequently observed after intradermal vaccination compared to subcutaneous (59% versus 46%), as were local adverse events (94% versus 80%)[5].

Finally, an analysis of the Bavarian Nordic global safety database published in 2024, reported that fainting episodes were more common with intradermal administration[6].

4. Is intradermal fractional dose as **immunogenic and effective** as a subcutaneous full dose?

Yes.

Regarding immunogenicity, a clinical trial published in 2015 involving approximately 500 adults compared intradermal fractional dosing with subcutaneous administration of the MVA-BN vaccine as two-dose schedules with a 28-day interval between doses. The study concluded that individuals receiving the vaccine intradermally produced similar levels of antibodies as those who received the full subcutaneous dose[7]. Similarly, other studies found no significant difference in neutralizing antibody titers between subcutaneous and intradermal administration[8,9]. One study even reported that intradermal administration resulted in higher neutralizing antibody levels one month after MVA-BN vaccination compared with subcutaneous administration[10].

With respect to vaccine effectiveness (VE), a case-control study conducted in the United States reported that VE did not significantly differ between subcutaneous and intradermal routes of administration. These VE estimates pertain to the global outbreak associated with the Clade IIb MPXV genetic lineage. Notably, the published VE data are based on studies conducted among gay, bisexual, and other men who have sex with men (MSM), aged 18–49 years, in North America and Europe, with a relatively short follow-up period after vaccination[11].

These results support the use of intradermal fractional dosing.

[5] Reactogenicity and Immunogenicity Against MPXV of the Intradermal Administration of Modified Vaccinia Ankara Compared to the Standard Subcutaneous Route
[6] Real-world safety data for MVA-BN: Increased frequency of syncope following intradermal administration for immunization against mpox disease
[7] Comparison of lyophilized versus liquid modified vaccinia Ankara (MVA) formulations and subcutaneous versus intradermal routes of administration in healthy vaccinia-naïve subjects
[8] Comparison of Waning Antibody Responses After Natural Monkeypox Virus Infection and Mpox Vaccination Beyond 6 Months in South Korea
[9] The two-dose MVA-BN mpox vaccine induces a nondurable and low avidity MPXV-specific antibody response
[10] Reactogenicity and Immunogenicity Against MPXV of the Intradermal Administration of Modified Vaccinia Ankara Compared to the Standard Subcutaneous Route
[11] US CDC unpublished data.

Table 2. Summary of MVA-BN vaccine effectiveness available data[12].

Route of administration	**Subcutaneous**		**Intradermal**	
Number of doses	Two full doses	One full dose	Two fractional doses	One fractional dose
Vaccine effectiveness	• **82%** (95% CI 78-88) based on a systematic review of 9 studies • **87%** (95% CI 68-95) based on US CDC unpublished data	• **75%** (95% CI 66-85) based systematic review of 15 studies • **71%** (95% CI 53-83) based on US CDC unpublished data	**91%** (95% CI 78-97) based on US CDC unpublished data	**75%** (95% CI 55-86) based on US CDC unpublished data

5. **How many** intradermal **fractional doses** are recommended?

Available data on intradermal administration of the MVA-BN vaccine are based on one or two fractional doses. A case-control study conducted in the United States showed that a single dose or two doses, whether administered subcutaneously or intradermally, provided similar vaccine effectiveness[13]. Countries may consider the off-label use of one or two intradermal fractional doses, spaced at least 28 days apart. A second dose is expected to provide more durable immunity. However, in the context of outbreaks with vaccine supply-constraints of MVA-BN, **prioritizing the administration of a single fractional dose may be considered to maximize the number of people vaccinated.**

6. For which **ages** could intradermal fractional dosing be considered?

While MVA-BN is currently not prequalified for persons under 12 years of age, this vaccine may be used off-label in infants and children as per WHO SAGE and national recommendations as relevant[14]. As part of the ongoing mpox outbreak response, the Democratic Republic of Congo (DRC) has issued an Emergency Use Authorization (EUA) for use of the MVA-BN vaccine from 1 year of age. As of June 2025, more than 130,000 doses have been administered to children from 1 year to 11 years of age[15], with no serious adverse events reported in DRC. To date, studies on use of MVA-BN intradermal fractional dosing have been only conducted in adults. However, **in the context of supply-constrained outbreak situations, the use of intradermal fractional dosing below 18**

[12] This data includes the updates presented at SAGE meeting on 12 March 2025 of an interim living systematic review on mpox vaccine effectiveness, data, and immunogenicity conducted by Yale School of Medicine and unpublished US CDC data.
[13] US CDC unpublished data.
[14] MVA-BN (Modified Vaccinia Ankara – Bavarian Nordic) smallpox and mpox vaccine: WHO interim guidance, 27 November 2024; Smallpox and mpox (orthopoxviruses): WHO position paper, August 2024
[15] WHO Regional dashboard on mpox vaccination

years of age may be considered based on country epidemiological context, national recommendations, and programmatic considerations.

7. Are there **other vaccines** administered **intradermally**?

Yes. BCG vaccine is routinely administered intradermally in children. Inactivated polio vaccine (IPV) and rabies vaccine have been used off-label intradermally in multiple countries, also in the African region, as a dose-sparing measure.

8. Can MVA-BN be administered as intradermal fractional dosing in **immunocompromised individuals**?

Yes. MVA-BN can be safely used in immunocompromised individuals —either as a full subcutaneous (SC) dose or a fractional intradermal (ID) dose—in accordance with WHO recommendations. While no studies to date have specifically assessed the immunogenicity or vaccine effectiveness of intradermal fractional dosing in immunocompromised individuals, data from immunocompetent populations indicate that intradermal fractional dosing provides immunogenicity and effectiveness equivalent to or greater than a single full subcutaneous dose, with even higher responses observed when two intradermal fractional or two subcutaneous full doses are administered (Table 2).

Countries may therefore consider administering one or two fractional doses (where feasible and aiming for higher effectiveness to enhance protection[16]) to immunocompromised individuals taking into account national recommendations and programmatic considerations.

9. Have **other countries** administered mpox MVA-BN vaccine through intradermal fractional dosing?

Yes. Several countries have implemented fractional dosing strategies for the MVA-BN vaccine, primarily to extend limited vaccine supply during outbreaks. In 2022, the United States FDA issued an Emergency Use Authorization (EUA) permitting the intradermal administration of MVA-BN for the prevention of mpox among adults aged 18 years and older at high risk of infection[17]. The same year, the European Medicines Agency (EMA) Emergency Task Force also released a statement concluding that intradermal fractional use of MVA-BN vaccine was acceptable in view of the outbreak situation and significant vaccine shortage[18]. Fractional dosing was critical to expand supply during the outbreak response in 2022.

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[16] One study found that vaccine effectiveness was lower in people living with HIV (PLHIV) who received only one subcutaneous dose of MVA-BN, compared to those who received two doses. However, this study assessed subcutaneous, and not intradermal fractional dosing administration. Safety and effectiveness of MVA-BN vaccination against mpox in at-risk individuals in Germany (SEMVAc and TEMVAc): a combined prospective and retrospective cohort study

[17] https://www.fda.gov/media/160774/download#:~:text=The%20FDA%20has%20granted%20an,high%20risk%20for%20monkeypox%20infection

[18] EMA's Emergency Task Force advises on intradermal use of Imvanex / Jynneos against monkeypox | European Medicines Agency (EMA)

10. What **planning considerations** should be taken into account for intradermal fractional dosing?

When planning for intradermal fractional dosing, there are several important considerations:

- First, the **injection ancillaries required** include AD syringes with needles in the range of 26G-27G and a 10-13 mm length, along with AD syringe safety boxes to ensure safe disposal. AD syringes are dose volume specific, and the 0.1 ml size usually requires placing a specific order and a distribution planning. A number of 0.1 ml AD syringes are listed in the WHO catalogue and can be procured either through UNICEF or via self-procurement. While standard 0.5 ml AD syringes are typically stocked at health centres, 0.1 ml AD syringe require tailored logistics to ensure sufficient stock at each location at the time of the planned vaccination activity. Therefore, air freight is likely needed for timely delivery, which may increase programme costs. The indicative lead time for the production and air shipment of 0.1 ml AD syringes is approximately two months from the date of order placement.

The implementation of fractional dosing requires additional health worker training to ensure proper administration of the smaller dose and to address any potential risks associated with the intradermal technique.

- **Health workers and local community leaders** should be equipped with the **content and capacity to address questions on intradermal fractional dosing** and reassure caregivers and other community members.
- To **achieve high vaccine uptake**[19]:
    - Deliver vaccines at times and places that offer ease of access, with tailored and culturally sensitive delivery strategies for priority populations.
    - Engage with community representatives as partners in designing local plans to implement intradermal fractional dosing.
    - Communicate early, using trusted voices and local language(s) about intradermal fractional dosing administration.
    - Be ready with strategies and messaging to respond to any potential vaccine-related events.

[19] Adapted from: How to achieve and sustain high uptake on mpox vaccination in outbreak settings. WHO, IFRC, UNICEF; 2025

11. What are **key operational steps** to administer a fractional dose intradermally (training module for health workers is available[20])?

Some of the key operational steps for administering a fractional dose intradermally are outlined below. Additional details can be found in the WHO interim guidance on the MVA-BN vaccine[21]:

1. Adapt data collection materials as needed and ensure that vaccine wastage continues to be monitored and document.
2. Take the number of vials required for the session.
3. Place the unopened vaccine vials in a vaccine carrier with conditioned frozen water packs (ice packs that have been partially thawed to prevent freeze damage from direct contact) and a foam pad. Keep vaccine carrier lid closed when not in use.
3. Thawed vaccine is ready to use.
4. Swirl the vaccine vial gently for at least 30 seconds. Do not shake.
5. Visually inspect the vial.
    - Vaccine should appear as milky, light yellow to pale white colored suspension, free of particulate matter.
    - If discoloured or containing any particulate matter, do not administer and safely discard the vial. Record the number of discarded doses for wastage monitoring.
6. Open vaccine vial one at a time.
7. Draw up 0.1 mL of vaccine in an AD syringe just before administration.
    - One vial can be used for 4 to 5 vaccinees.
    - Do not prefill syringes with vaccine.
    - Use the vaccine immediately after loading the AD syringe.
8. Administer the dose intradermally on the inner side of the forearm, deltoid area of the upper arm, or scapula[22].
9. Discard the used AD syringe immediately in the safety box.
10. Record administered fractional dose on vaccination card and tally sheet/electronic registry.
11. Observe the vaccinee for up to 15 minutes for any reaction.
12. Discard unused doses 6 hours after opening the vial or at the end of the immunization session, whichever comes first.

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[20] Training module: MVA-BN vaccine overview, March 2025. Available at: https://www.technet-21.org/en/resources/training/module-3-mva-bn-vaccine-overview

[21] MVA-BN (Modified Vaccinia Ankara – Bavarian Nordic) smallpox and mpox vaccine: WHO interim guidance, 27 November 2024;

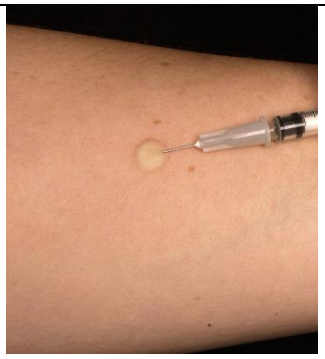
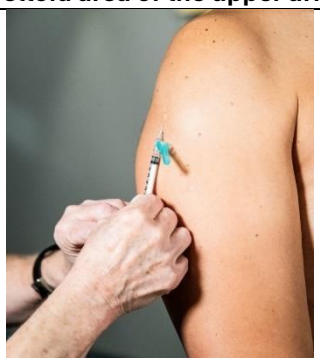
[22] Personal protective equipment (PPE) —including gloves, medical masks, gowns, and eye protection— is not required for vaccine administration if the skin of either the health worker or the vaccine recipient is intact. If skin is non-intact, consider wearing single-use, non-sterile gloves. If used, gloves must be changed between each individual. WHO. Infection prevention and control and water, sanitation, and hygiene measures during mpox vaccination activities, February 2025 and WHO best practices for injections and related procedures toolkit. WHO, 2010

12. What is the **technique** to administer a fractional dose intradermally?

Only health workers that have experience and/or have received appropriate training to give injections intradermally should administer the MVA-BN vaccine with this technique[23]:

- Hold the syringe (bevel side up) at an angle close to flat on the skin: 5-15 degrees angle as shown in the images below.
- Administer the vaccine slowly until the formation of a "**bleb**" is observed (5-10 mm in diameter). A bleb is a wheal that forms as skin is stretched by injected fluid.
- Withdraw gently, do not press or massage the site.
- Do not repeat the vaccination, even if no bleb is formed after the injection.

Table 3. Options for intradermal administration of MVA-BN vaccine.

Side of the forearm	Deltoid area of the upper arm	Scapula
		

[23] Further guidance and illustrative images on administering a fractional dose of MVA-BN vaccine intradermally can be found at: https://www.cdc.gov/mpox/hcp/vaccine-considerations/intradermal-administration.html