EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

MPOX- Overview of vaccines regulatory status

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Vaccine Regulatory status: smallpox indication (as of 28 Aug 2024)

Product	Date	Authorization status	Product info
MVA-BN (Bavarian Nordic) 3rd generation	July 2013	EMA (Imvanex) under exceptional circumstances	• 2-doses 4-weeks apart • Liquid-frozen • Use in adult population >18 yrs • Sub-cutaneous – 0.5ml
	Nov 2013	Health Canada (Imvamune) full MA	
	Sept 2019	US FDA (Jynneos) full MA	
	04 Aug 2023	Nigeria (Jynneos) Time limited EUA: till 15 July 2025	
	March 2024	Switzerland (Jynneos) full MA	
	24 June 2024	DRC (Jynneos) Time limited EUA: till 23 June 2025	
	Aug 2024	HSA Singapore (Jynneos) full MA	
LC16 (KM Biologics) 3rd generation	1975	MHLW/PMDA full MA	• Single dose • Use from infants to adults • Freeze-dried multidose vials • Bifurcated needle
ACAM2000 (Emergent BioSolutions) 2nd generation	Aug 2002	US FDA approved for those who have a chance of getting smallpox	• Single dose • Approved for use from 18 to 64 yrs • Freeze-dried multidose vials • Bifurcated needle
	May 2024	Health Canada full MA >16yrs at high risk	

EUA: Emergency use authorization MA: market authorization

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MVA-BN (Bavarian Nordic) 3rd generation	Sept 2019	US FDA (Jynneos) full MA	• 2-doses 4-weeks apart • Liquid-frozen • Use in adult population >18 yrs • Sub-cutaneous – 0.5ml
	Nov 2020	Health Canada (Imvamune) full MA	
	July 2022	EMA (Imvanex) under exceptional circumstances	
	Aug 2022	US FDA (Jynneos) • EUA for <18 yrs • EUA for intradermal admin 0.1ml	
	Sept 2022	UK (Imvanex) under exceptional circumstances	
	04 Aug 2023	Nigeria (Jynneos) Time limited EUA: till 15 July 2025	
	March 2024	Switzerland (Jynneos) full MA	
	24 June 2024	DRC (Jynneos) Time limited EUA: till 23 June 2025	
	Aug 2024	HSA Singapore (Jynneos) full MA	
LC16 (KM Biologics) 3rd generation	Aug 2022	MHLW/PMDA MA	• Single dose • Use from infants to adults • Freeze-dried multidose vials • Bifurcated needle
	June 2024	DRC EUA	
ACAM2000 (Emergent BioSolutions) 2nd generation	Aug 2022	US FDA During outbreak, allowed under the Expanded Access Investigation New Drug Application (EA-IND) protocol	• Single dose • Approved for use from 18 to 64 yrs • Freeze-dried multidose vials • Bifurcated needle
	Dec 2023	HSA (Singapore)	
	Dec 2023	TGA (Australia)	
	May 2024	Health Canada	

EUA: Emergency use authorization MA: market authorization

Evidence supporting regulatory clearance for third generation vaccines

Vaccines have demonstrated efficacy in stringent animal models of orthopoxvirus infection, including studies in NHPs challenged with lethal doses of Monkeypox Virus – of note, clade 1 strains were used in the animal models

Vaccines showed comparable immunogenicity in humans in terms of neutralizing and binding antibodies vs. orthopoxviruses, e.g. vaccinia, compared to earlier generation smallpox vaccines that showed efficacy in humans

Vaccines showed their ability to elicit monkeypox virus neutralizing antibodies and T cell responses

Regulators made prompt recommendations to support intradermal administration of MVA vaccine in an emergency setting with limited supply

FACT SHEET FOR RECIPIENTS AND CAREGIVERS ABOUT JYNNEOS (SMALLPOX AND MONKEYPOX VACCINE, LIVE, NON-REPLICATING) TO PREVENT MONKEYPOX DISEASE IN INDIVIDUALS DETERMINED TO BE AT HIGH RISK FOR MONKEYPOX INFECTION

You or your child is being offered JYNNEOS to prevent monkeypox disease. This Fact Sheet contains information to help you understand the risks and benefits of receiving JYNNEOS, which you or your child may receive because there is an outbreak of monkeypox.

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to:

- Allow use of JYNNEOS given between layers of the skin for prevention of monkeypox disease in individuals 18 years of age and older determined to be at high risk for monkeypox infection; and
- Allow use of JYNNEOS given beneath the skin for prevention of monkeypox disease to individuals younger than 18 years of age determined to be at high risk for monkeypox infection.

For more details about an EUA please see "**What is an Emergency Use Authorization?**" at the end of this document. JYNNEOS is not approved for use in individuals under 18 years of age in the United States. For individuals 18 years of age and older, JYNNEOS given between layers of skin (intradermally) is not approved in the United States. Read this Fact Sheet for information about JYNNEOS. Talk to your healthcare provider about your options or if you have any questions. Under the EUA, there is an option to accept or refuse JYNNEOS.

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19 August 2022
EMA/700120/2022
Emergency Task Force

Considerations on posology for the use of the vaccine Jynneos/ Imvanex (MVA-BN) against monkeypox

Conclusions

The results of the study in healthy adults demonstrated comparable humoral immunogenicity when MVA-BN was given as a standard SC dose or as 1/5th of a dose administered ID. The exact level of protection and duration of protection afforded by the vaccine regimens are unknown.

No new safety signal was raised for ID administration of MVA-BN but the higher local reactogenicity following the ID administration of MVA-BN may raise concerns during the vaccination campaigns. In the ongoing emergency situation with continuous spread among individuals at high risk of infection and with significant shortage of vaccine, the safety profile of the vaccine following ID route can be considered acceptable. However, these data are limited, and more data may be generated in additional studies.

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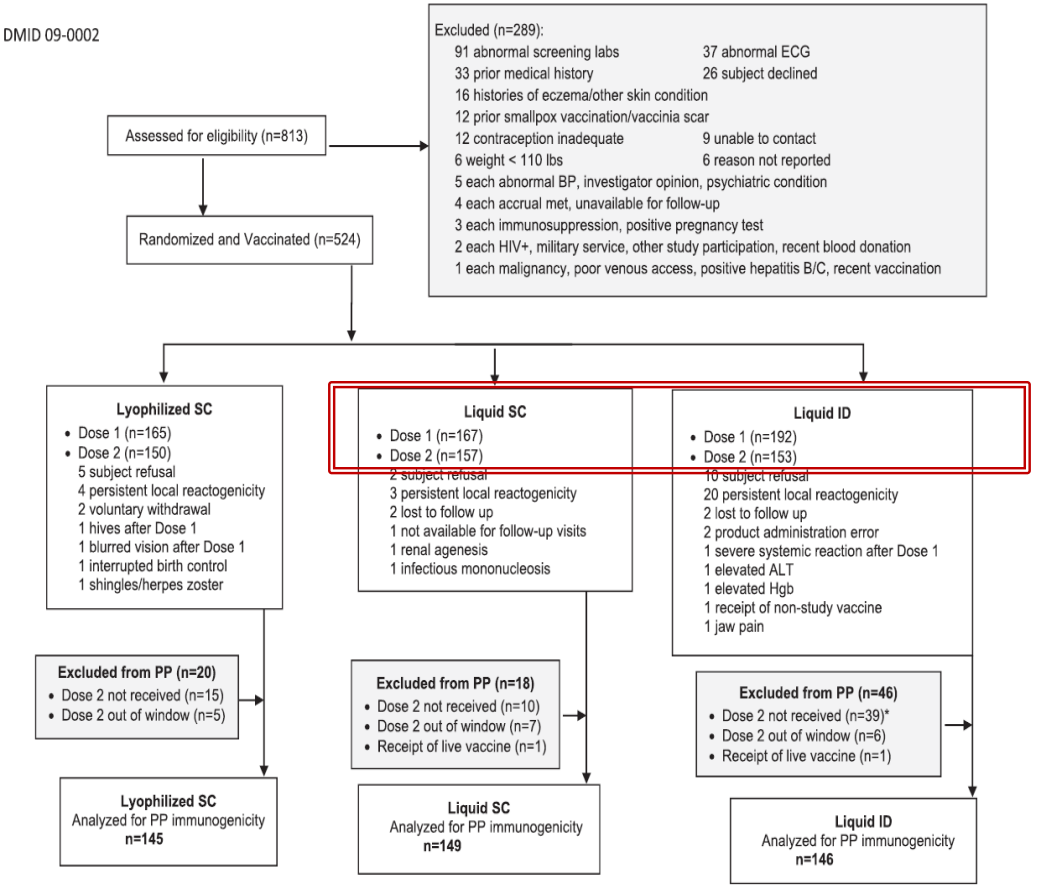
VACCINE – IMVANEX – CLINICAL EVIDENCE

POX-MVA-029. Intradermal Dosing Regimen

- Clinical trial conducted in accordance with GCP by NIAID indicates 1/5 of the dose (0.1 mL) given intradermally (ID) on the same schedule (day 1 and 28) produces similar efficacy to subcutaneous (SC).
- Frey SE et al, Vaccine 2015; 33: 5225-5234



MVA-BN vaccine – specific aspects

The safety profile of MVA-BN in adults has been well characterized in clinical trials. The most common side effects are local and expected systemic reactions which were mild to moderate.

The safety and efficacy in children below 18 years have not been established. However, Emergency Use Authorisation has been granted in some jurisdictions

BN has submitted data to EMA from a clinical study conducted in USA and Puerto Rico in adolescents 12-17 years of age and is under expedited assessment.

A study planned in children from 2-12 years of age in DRC and Uganda, partially funded by CEPI

Need and timing of booster doses is currently not defined

LC16m8 vaccine – specific aspects

Attenuated, minimally replicating vaccinia vaccine. LC16m8 virus has lower neurovirulence and replication competency than Lister or Dryvax.

Administered by scarification with bifurcated needle.

It was evaluated in over 50,000 children between 1974-1975.

The main safety concerns were skin reactions and auto-inoculation.

Not recommended for use in immunocompromised individuals and pregnant women

Regulators asked for vaccine effectiveness studies as part of post-approval commitments – Evidence generation does not stop at authorisation

MVA-BN vaccine – Vaccine effectiveness clade 2b

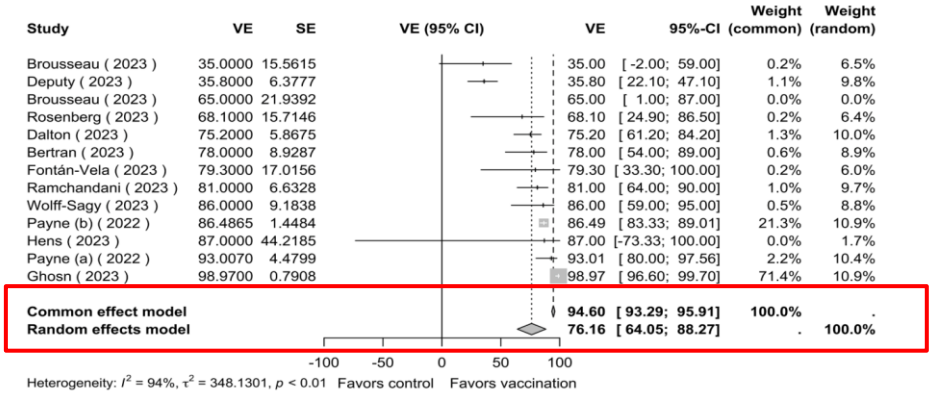


Fig. 2. Meta-Analysis of 1 dose of MVA-BN vaccine effectiveness for mpox.

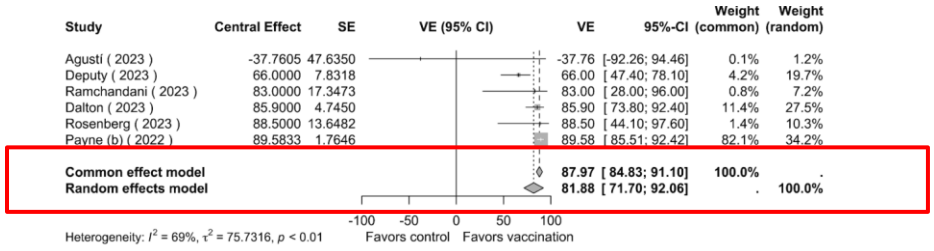


Fig. 3. Meta-analysis of 2 doses of MVA-BN vaccine effectiveness for mpox.

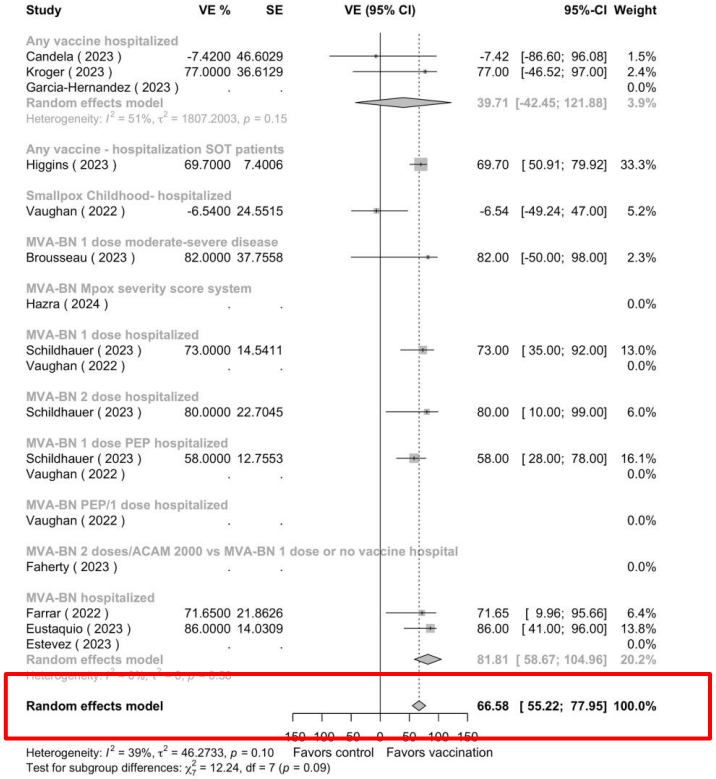


Fig. 5. Meta-analysis of any dose of MVA-BN vaccine or first-generation smallpox vaccine effectiveness for mpox hospitalization.

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Pischel L, et al. Vaccine In press

Regulators are engaging with developers of new MPOX vaccines

It needs to be discussed evidence to support approval in consideration of the vaccine construct and mechanism of protection

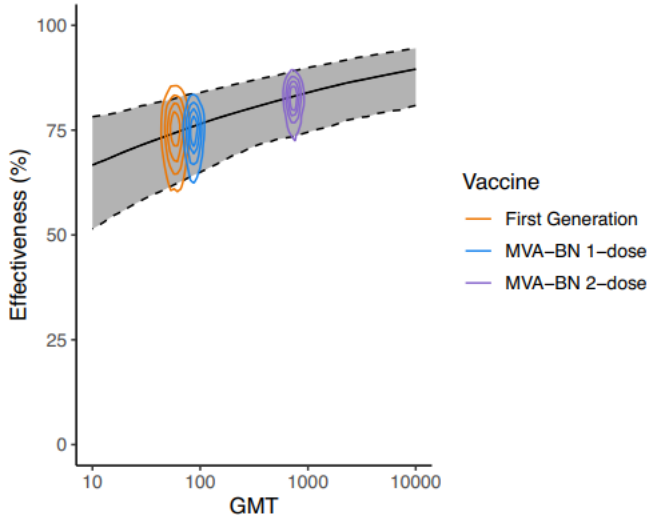

Fig. 3 | Relationship between vaccine effectiveness and the vaccinia-binding GMT. The contour lines, represent the 20%, 40%, 60% and 80% highest density regions of the joint-posterior distribution (i.e., smallest areas that contain x % of the posterior samples) for the different vaccines (indicated by colour). The association between antibody titers and effectiveness (solid black line) is fitted using all of the underlying data (accounting for the interstudy heterogeneity using a hierarchical model structure) (Table S5). The solid black line indicates the best estimate (median of posterior), and shaded region show the 95% credible intervals of the predicted effectiveness at different GMTs.

[Predicting vaccine effectiveness for mpox | Nature Communications]

Key Points

- Regulatory Agencies took rapid actions on vaccines approval or authorisation in the face of the MPOX emergency
- Data in stringent animal models and human immunogenicity have been considered sufficient for allowing regulatory decisions based on the current knowledge
- Data in specific populations such as immunosuppressed, paediatrics and during pregnancy need to be considered as appropriate
- Mechanisms of international collaboration among regulatory agencies have been utilised, such as discussion in specific fora and/or sharing of assessment reports
- Regulatory pathways for approval of next generation vaccines need to be established