Smallpox Vaccines Overview

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The BARDA Model

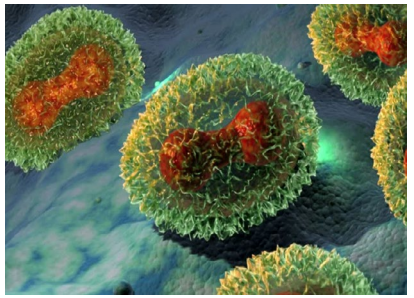
BARDA develops and makes available medical countermeasures (MCMs) by forming unique public-private partnerships to drive innovation off the bench to the patient to save lives.

- Flexible, nimble authorities
- Multi-year funding
- Cutting edge expertise
- Facilitate partnerships
- Promote innovation

ASPR's mission:
Assist the country in **preparing for**, **responding to**, and **recovering from** public health emergencies and disasters.

ASPR/BARDA Smallpox Vaccine Program

- In 2004 the Department of Homeland Security (DHS) issued a Material Threat Determination for *Variola major* (smallpox) in 2004, establishing it as a threat to national security.
- BARDA began working with NIAID to transition mid-stage products (beyond phase I clinical testing) into its pipeline of MCMs.
- In 2007 BARDA awarded a contract to Bavarian Nordic A/S to continue the development of their modified vaccine virus Ankara vaccine. The program spanned 10 years and supported nonclinical and clinical (phase 2/3) studies, manufacturing, scale-up, licensure, and procurement of the liquid frozen formulation (JYNNEOS®).
- The JYNNEOS® vaccine was approved in 2019 by FDA/CBER for the prevention of smallpox and mpox in adults 18yo+ who are at high risk for infection. The vaccine is administered in two-doses given 28 days apart. (Note: JYNNEOS® is the only vaccine with a label indication for mpox)
- During the 2022/2023 mpox outbreak, ASPR shipped over 1 million vials of JYNNEOS® to federal and jurisdictional partners.
- The current USG owned supply of JYNNEOS® is a mix between frozen bulk drug substance (BDS) and filled vials allowing the flexibility to fill as liquid for lyophilized (future).
- BARDA is also supporting the development of a lyophilized formulation of JYNNEOS® that will offer longer shelf-life at lower temps.



BAVARIAN NORDIC

USG Smallpox Vaccines

- There are two licensed vaccine countermeasures available to the USG: ACAM2000™ and JYNNEOS®

- ACAM2000™ is licensed by the U.S. Food and Drug Administration for immunization against smallpox for people determined to be at high risk for smallpox infection.
  - It is a live replicating vaccinia virus-based vaccine derived from Dryvax.
  - ACAM2000™ carries many contraindications when administered pre-event and has a documented set of adverse events, including death, in those with compromised immune systems.
  - There are no absolute contraindications to vaccination with ACAM2000™ in a smallpox post-event scenario.
  - The vaccine is stored as a kit, with lyophilized vaccine in a multi-dose vial packaged with diluent and a bifurcated needle for vaccine administration.
  - The vaccine provides the first line of defense against the spread of smallpox. It can be produced economically in large amounts. Although ACAM2000™ is the primary vaccine in a smallpox response, it is not recommended for preventing mpox or other orthopoxvirus infections due to the potential adverse events.

Second and Third Generation Vaccines

	ACAM2000	JYNNEOS®
	2nd generation vaccine	3rd generation vaccine
Regulatory	Licensed by FDA	Licensed by FDA; Lyophilized formulation under development (Phase 3)
Shelf life	84 months in freeze-dried formulation-stability monitoring program in place	3 yrs(-20C); 5yrs (-50C); 9yrs (-80C)
Technology	Live vaccinia virus derived from Dryvax aseptically propagated in cell culture	Dead virus derived from chorioallantois vaccinia Ankara (CVA); replication incompetent in human cells
Use in special populations (pre-event)	Not for patients with skin disorders & immunodeficiencies	Safer alternative for patients with skin disorders & immunodeficiencies
Dosage	Single dose using the traditional scarification method	Two doses (prime/boost injections), four weeks apart

Baseline capability

Fulfills special population needs

Path Forward

- The Strategic National Stockpile currently has sufficient live, replicating vaccine for the general population and a smaller amount of non-replicating vaccine for use in populations with contraindications

- The combination of a replication competent, single dose, vaccine in large amounts for the majority of the population and a safe, host range limited, vaccine for special populations provides the best mix for halting the spread of disease while reducing adverse events.

- The JYNNEOS® vaccine provides an option for protecting immune-compromised individuals and is also licensed for prevention of mpox.

- These licensed vaccines are appropriate and sufficient to protect the US population against an accidental or intentional release of smallpox. The near-term goals/focus of the ASPR program includes:
  - Procurement of JYNNEOS® to continue to grow the size of the available stockpile. Continue to store doses at ultra-cold temps to extend the shelf-life. Test product as it nears expiry.
  - Support the licensure of the lyophilized formulation of JYNNEOS® and transition to that product once licensed. Late-stage CMC activities are ongoing and stability data to date indicates formulation will be very stable at -20C easing the burden/cost of -80C storage.
  - Maintain the ACAM2000 stockpile and continue stability monitoring and extension program to ensure adequate supply to address any smallpox emergency.

medicalcountermeasures.gov
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