

Orthopoxvirus Work Group Background and Considerations

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Division of High Consequence Pathogens and Pathology

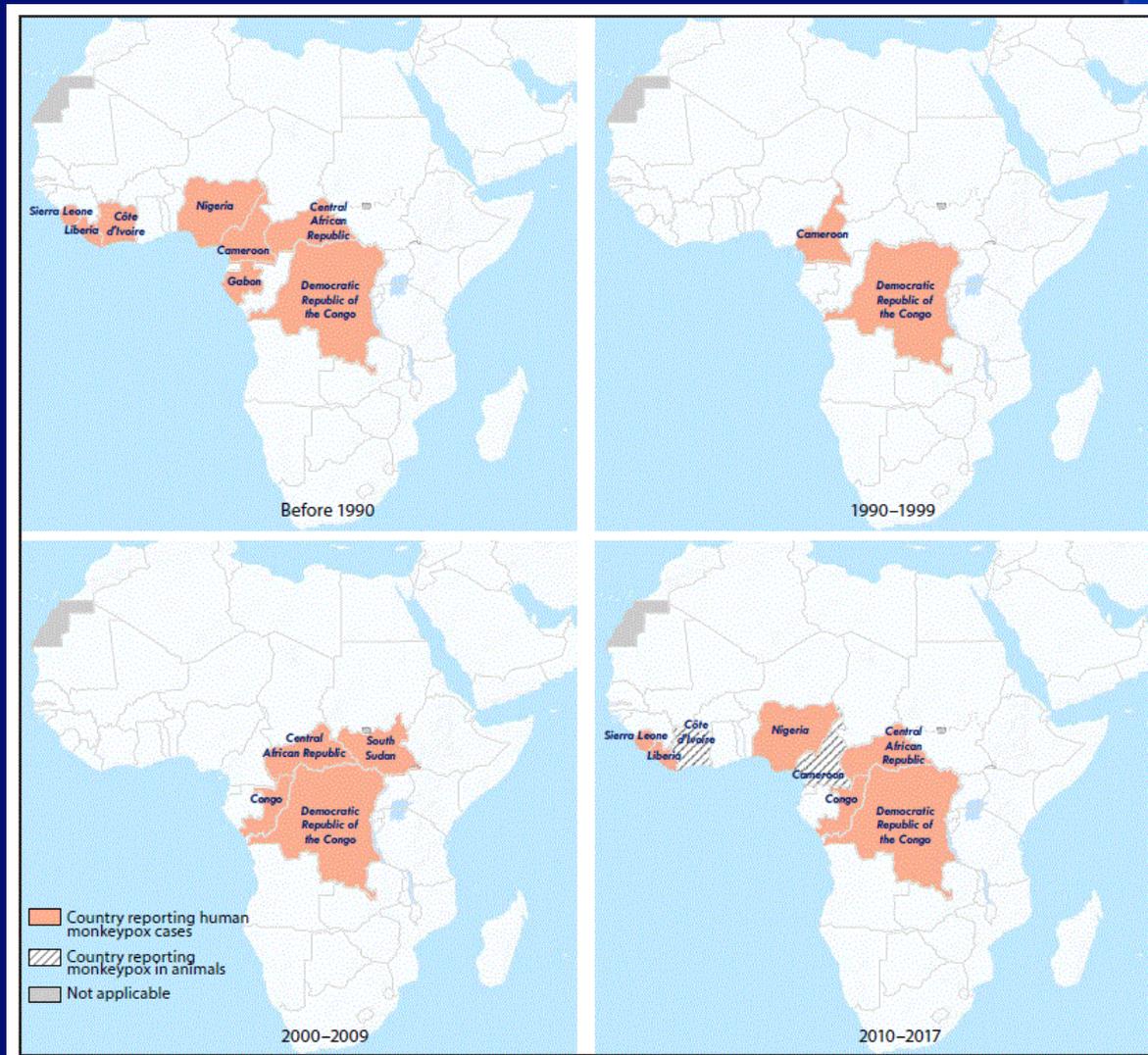


Background

- ❑ **Orthopoxviruses are a group of large double-stranded DNA viruses within the family *Poxviridae***
 - Species known to infect humans: Variola (Smallpox), Vaccinia (Smallpox Vaccine), Monkeypox, Cowpox, and newly discovered species (e.g., Akhmeta virus, Alaskapox virus)
- ❑ **Orthopoxvirus infection provides cross protection across species**
 - Development of vaccinia as a vaccine for smallpox
- ❑ **Orthopoxviruses remain an active subject of research**
 - Viral vector for expression of foreign genes (gene therapy or genetic engineering)
 - Recombinant vaccines
 - Oncolytic or immunotherapy for cancer

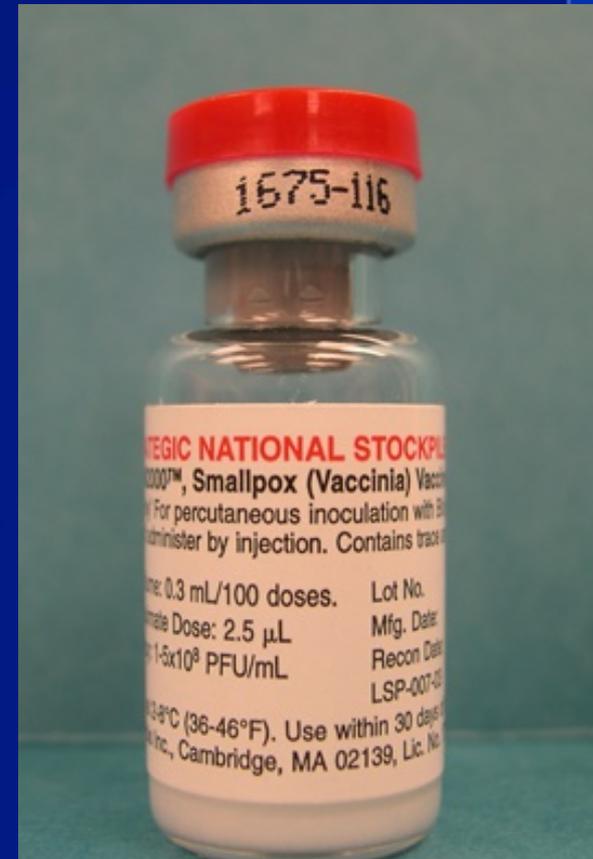
Monkeypox

- Increase in monkeypox case reports in Africa
- Exportations:
 - United States, 2003
 - United Kingdom X 2, 2018
 - Israel, 2018
 - Singapore, 2019
 - United Kingdom, 2019



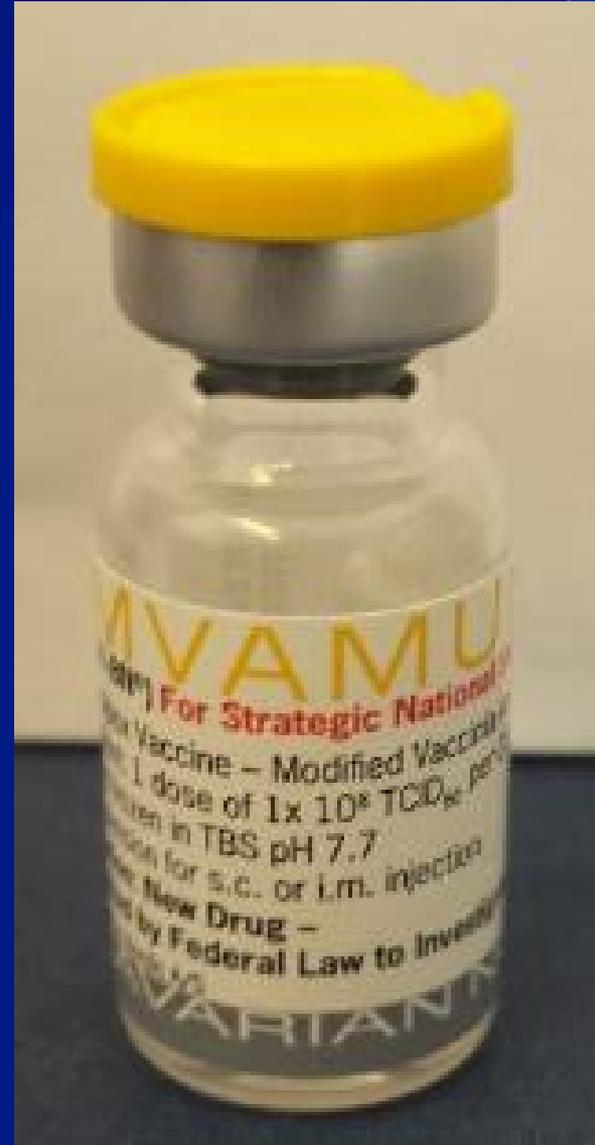
ACAM2000

- ❑ ACAM2000 is a live vaccinia virus vaccine
- ❑ Licensed by FDA in August 2007
- ❑ Replaced Dryvax - license withdrawn by manufacturer and remaining vaccine destroyed
- ❑ Indication
 - ACAM2000 is indicated for active immunization against smallpox disease for persons determined to be at high risk for smallpox infection



JYNNEOS

- ❑ **JYNNEOS is a live vaccine produced from the strain Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN), an attenuated, non-replicating orthopoxvirus**
 - Also known as IMVAMUNE, IMVANEX, MVA
- ❑ **Licensed by FDA in September 2019**
- ❑ **Indication**
 - JYNNEOS is indicated for prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection



JYNNEOS and ACAM2000

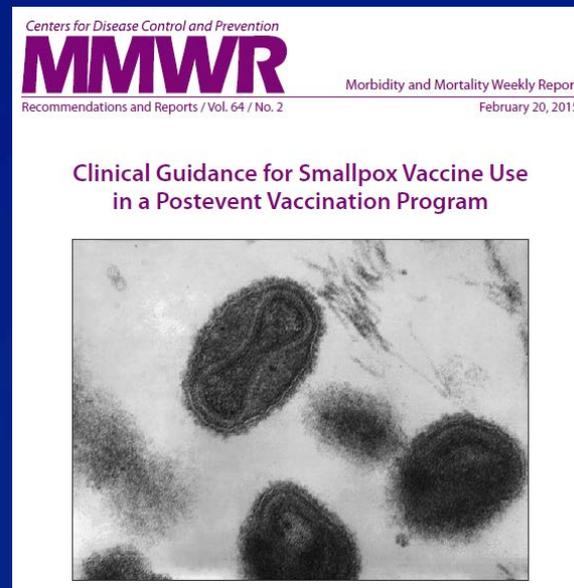
	ACAM2000	JYNNEOS
Vaccine virus	Replication-competent vaccinia virus	Replication-deficient MVA
Administration	Administered via multiple puncture technique in a single dose	Administered subcutaneously in 2 doses 28 days apart
Take	Successful vaccination produces a major cutaneous reaction or “take”	No cutaneous reaction or “take” is produced
Inadvertent inoculation and autoinoculation	Vaccine site lesion presents a risk of inadvertent inoculation and autoinoculation	No risk of inadvertent inoculation and autoinoculation
Serious adverse events	Risk for serious adverse events secondary to uncontrolled viral replication (e.g., progressive vaccinia and eczema vaccinatum)	No risk for uncontrolled viral replication
Cardiac adverse events	Suspect cases of myopericarditis observed in up to 5.7 per 1,000 primary vaccinees	No serious cardiac adverse events considered causally related reported to date
Effectiveness	Effectiveness was assessed by comparing the immunologic response and “take” rates to Dryvax	Effectiveness was assessed by comparing the immunologic response to ACAM2000

Consolidating Orthopoxvirus Vaccine Recommendations and Guidance

- ❑ **Multiple recommendations and guidance documents currently exist**
 - Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. MMWR, March 17, 2016, Vol 65, #10.
 - Recommendations for Using Smallpox Vaccine in a Pre-Event Vaccination Program. MMWR, April 4, 2003, Vol 52, #RR-07.
 - Vaccinia (Smallpox) Vaccine. MMWR, June 22, 2001, Vol 50, #RR-10.
- ❑ **The working group intends to update and revise the existing recommendations and guidance and present them in a consolidated document with the new recommendations and guidance**

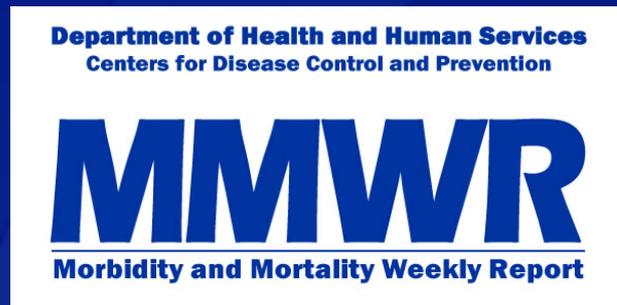
Defining the Scope of Recommendations

- ❑ ACIP provides vaccine recommendations pre-event (i.e., before a smallpox or other orthopoxvirus emergency)
- ❑ Smallpox vaccine use in a postevent vaccination program is addressed in separate clinical guidance



Defining the Scope of Recommendations

- ❑ **Current ACIP recommendations address persons who are at occupational risk for orthopoxvirus exposures:**
 - Laboratory and healthcare personnel (2015, 2003)
 - Smallpox response and health-care teams (2003)



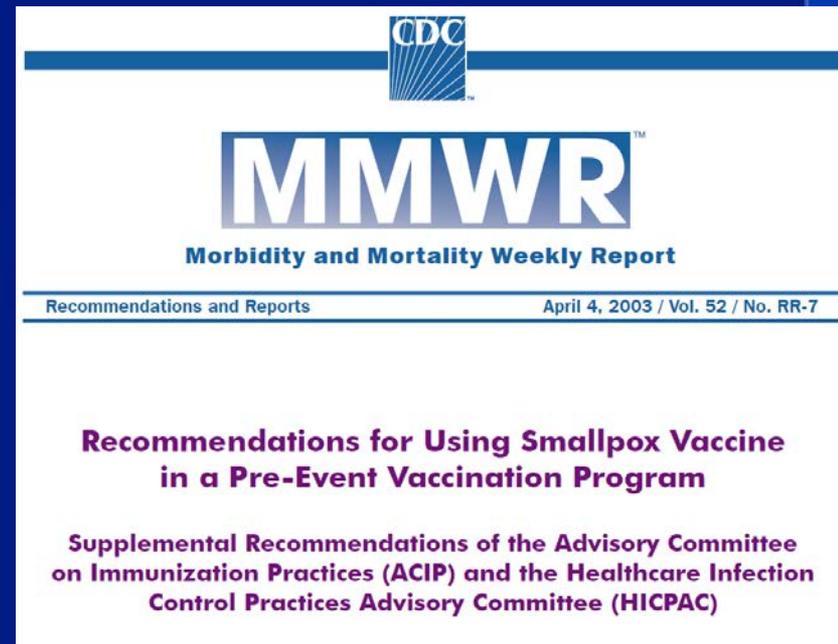
Morbidity and Mortality Weekly Report

Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015

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MMWR / March 18, 2016 / Vol. 65 / No. 10

257



Recommendations and Reports

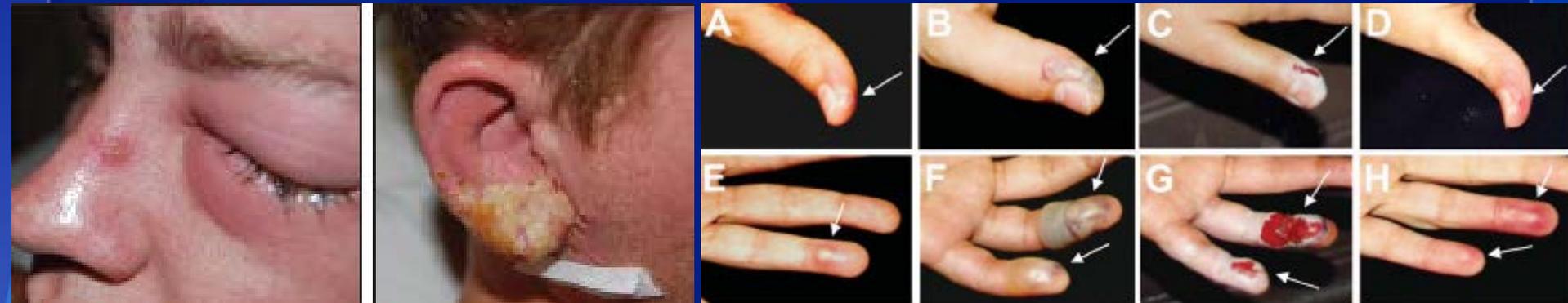
April 4, 2003 / Vol. 52 / No. RR-7

**Recommendations for Using Smallpox Vaccine
in a Pre-Event Vaccination Program**

**Supplemental Recommendations of the Advisory Committee
on Immunization Practices (ACIP) and the Healthcare Infection
Control Practices Advisory Committee (HICPAC)**

Research Laboratory Personnel

- ❑ Serious infections have occurred among research laboratory personnel
- ❑ Vaccination with an orthopoxvirus vaccine can protect against these infections
- ❑ ACIP currently recommends vaccination with ACAM2000 for research laboratory personnel



Laboratory-acquired vaccinia virus infection of the left eye and right ear

Needlestick inoculation of researcher using vaccinia virus as a vector

Revaccination of Laboratory and Healthcare Personnel with ACAM2000

2015 ACIP Recommendations

Orthopoxvirus	Revaccination Schedule
Replication-competent vaccinia viruses and recombinant viruses developed from replication-competent vaccinia viruses	At least every 10 years
More virulent orthopoxviruses (e.g., variola, monkeypox)	Every 3 years
Replication-deficient vaccinia viruses and recombinant viruses developed from replication-deficient vaccinia viruses*	Not recommended

Persistence of Immunity Following Smallpox Vaccination

- ❑ Epidemiologic studies demonstrated that an increased level of protection against smallpox persists for <5 years after primary vaccination and substantial but waning immunity can persist for >10 years
- ❑ Data on the persistence of neutralizing antibody following vaccination
 - Neutralizing antibody titers of greater than or equal to 1:10 are found among 75% of persons for 10 years after receiving second doses

<https://www.cdc.gov/mmwr/preview/mmwrhtml/00042032.htm>, <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm>

World Health Organization Expert Committee on Smallpox Eradication: second report. WHO Tech Rep Ser 1972;493:5--64.

Public Health Service. Recommendations of the Public Health Service Advisory Committee on Immunization Practices: smallpox vaccine. Washington, DC: Public Health Service, 1972.

Lublin-Tennenbaum T, Katzenelson E, El-Ad B, Katz E. Correlation between cutaneous reaction in vaccinees immunized against smallpox and antibody titer determined by plaque neutralization test and ELISA. *Viral Immunol* 1990;3:19-25.

El-Ad B, Roth Y, Winder A, et al. The persistence of neutralizing antibodies after revaccination against smallpox. *J Infect Dis* 1990;161; 446-8.

Considerations for Revaccination of Laboratory and Healthcare Personnel with JYNNEOS

- ❑ **Greater importance for protection of persons working with more virulent orthopoxviruses (e.g., variola and monkeypox)**
 - Individual level - severe systemic disease
 - Societal level - contagious pathogens with epidemic potential
- ❑ **Difficult to precisely define the duration of protection for vaccines**
- ❑ **JYNNEOS duration of protection is not known**
 - Neutralizing antibodies generally do not persist beyond 6 months following primary vaccination with JYNNEOS
 - A single booster dose of JYNNEOS given 2 years following primary vaccination with JYNNEOS produces a robust increase in neutralizing antibodies
 - Data suggests that a robust anamnestic immune response is present 2 years following primary vaccination

Smallpox Response and Health-Care Teams 2003 ACIP Recommendations

□ Smallpox Response Teams

- Smallpox vaccination is recommended for persons designated by appropriate terrorism and public health authorities to conduct investigations and follow-up of initial smallpox cases that might necessitate direct patient contact
- ACIP recommends that each state and territory establish and maintain ≥ 1 smallpox response team

□ Smallpox Health-Care Teams

- ACIP and HICPAC recommend that in the first stage of the pre-event smallpox vaccination program, each acute-care hospital identify groups of health-care workers to be vaccinated and trained to provide direct medical care for the first smallpox patients requiring hospital admission and to evaluate and manage patients who are examined at emergency departments with suspected smallpox

Considerations for Orthopoxvirus Response and Healthcare Teams

- ❑ **Working group recognizes the benefit of having cadres of vaccinated public health and healthcare personnel available to respond and care for orthopoxvirus infected individuals**
 - The recent increase in monkeypox cases in Africa and importation into other countries (UK, Israel, and Singapore) suggests the risk of monkeypox exportation is increasing
- ❑ **Desire to avoid being overly prescriptive in defining who and how many such persons be vaccinated as assessments of the threat level of these pathogens changes over time**
- ❑ **Empower appropriate local, state, and federal public health and antiterrorism authorities to make decisions**

Questions?

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

