



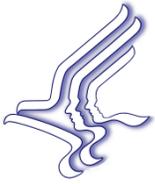
**United States Department of
Health & Human Services
Office of the Assistant Secretary for Preparedness and Response (ASPR)**



Smallpox Vaccine Countermeasures

Biomedical Advanced Research and Development Authority (BARDA)

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HHS/ASPR/BARDA**



Smallpox Disease

- **Smallpox is caused by orthopoxvirus variola**
- **Clinical manifestations and timelines for smallpox disease if infected by respiratory tract:**
 - 7-17 day incubation post infection
 - 2-3 day prodrome—fever, malaise, myalgia
 - Weeks—skin lesions progressing from eruption through papules, vesicles, pustules, crusts, and desquamation
- **Readily transmitted from person to person**
 - Respiratory droplets
 - Direct contact
- **The mortality rate is ~30% in unvaccinated**





Smallpox MCM response strategy



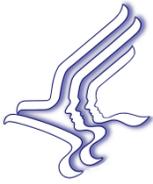
In the event of a smallpox release, the full complement of USG MCMs would be used to protect the population:

- **Vaccines:**

- A smallpox vaccination program in all high risk areas. Vaccination with replication competent vaccine will be the primary means for controlling the spread of the disease.
- Immune globulin or antivirals may be given for individuals who have an adverse reaction to the vaccine

- **Antivirals:**

- Antivirals are critical for those individuals who have progressed to smallpox disease symptoms or have been exposed to variola. An antiviral is critical to reducing the viral load in the body and allowing the immune system to appropriately clear the infection.



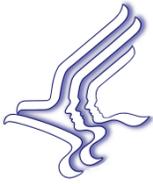
USG Smallpox Vaccine Countermeasure History (in brief)



- Routine vaccination of US civilians ended in the 1970s, and a large portion of the US population is susceptible to variola virus infection
- 1990s - USG began planning for the acquisition of new smallpox vaccine based on the NYCBOH strain of vaccinia (ACAM2000), the acquisition was increased in late 2001
- 2004 - DHS issued a Material Threat Determination for Smallpox
- 2007 - the PHEMCE Implementation Plan for CBRN Threats listed a next generation smallpox vaccine and smallpox antiviral drugs as high priorities

Current readiness for smallpox event:

- Enough vaccine for US population
- Vaccinia Immune Globulin for side effects of vaccination
- IMVAMUNE® doses stockpiled to address immunocompromised
- Contracts for the procurement of next generation vaccine and the development of smallpox antivirals



Smallpox Vaccine Requirements



- **HHS has a requirement for post-event vaccination as well as treatment**
- **Post-event pre-exposure vaccination:**
 - Maintain traditional replication competent vaccine program for US population (CDC)
 - Maintain Immune Globulin for adverse reactions to the vaccine
 - Development and procurement of smallpox vaccines for special populations (Immunocompromised, atopic dermatitis, etc.)
 - Address at-risk individuals per the Pandemic and All-Hazards Preparedness Act (PAHPA)

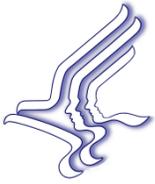


Addressing Requirements: BARDA's MVA Program



- **Contract awarded June 2007 to Bavarian Nordic A/S of Denmark to manufacture and deliver 20 million doses of a next generation modified vaccinia Ankara (MVA) smallpox vaccine, IMVAMUNE®**
- **This is the first use of advance and milestone payment under PBS as amended by PAHPA.**
 - Over 2 M doses of IMVAMUNE® delivered to SNS to date
 - CDC held pre-EUA
 - 36 month stability
 - End of phase 2
 - Options for warm base
 - Options for additional doses





Addressing Requirements: BARDA's MVA Program



- **Advanced Research and Development (ARD) contract awarded to Bavarian Nordic in 2009 for the development of a freeze-dried formulation of **IMVAMUNE®****



Intent is for product enhancement

- Storage at higher temperatures
- Longer retention of potency
- Advantages in CONOPs

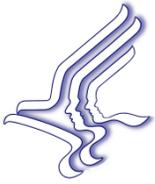




Addressing Requirements: BARDA's LC16m8 Program



- **Advanced Research and Development (ARD) contract awarded to Kaketsuken in 2010 for the development of an attenuated smallpox vaccine LC16m8**
- **Partially attenuated smallpox vaccine**
 - Passaged through primary rabbit kidney cells
 - Small plaque, cold selected
 - Effective in Animal Models
- **Intent is to address regulatory issues**
 - Dosing and immune correlate



Advanced Development—CBRN BAA



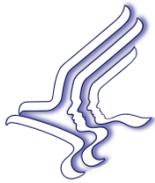
- **Opportunities to address smallpox needs within the CBRN BAA**

- **Area 1: Vaccines and vaccine enhancements**

- Improvements to current vaccines and other vaccine candidates at TRL-6 and above (pending availability of funds)
- Address regulatory hurdles-Animal Models for efficacy evaluation under the FDA Animal Rule, correlates of immunity

- **MCM portfolio reviews underway**

- New opportunities may arise



Engaging BARDA in Your Development Plan



- **TechWatch** – request a meeting with program and regulatory staff at www.medicalcountermeasures.gov
- **Broad Agency Announcements – Advanced Research and Development**
 - BAA open all-year round
 - Discuss with program and regulatory staff before submitting a proposal
 - Funding is typically for one year with multiple one-year options
 - Contracts are driven by well-designed development plans with go/no go milestones and decision points
- **Project BioShield**
 - Reserved for very late-stage products
 - Companies with licensed products with an interest in broadening label claims are highly encouraged to contact us



Interfacing with BARDA



- www.phe.gov
 - Program description, information, news, announcements
- www.medicalcountermeasures.gov
 - Portal to BARDA
 - Register, request a meeting
 - Tech Watch
- www.fedbizopps.gov
 - Official announcements and detailed information about all government contract solicitations

