**STANDING ORDERS FOR PRE- AND POST-EXPOSURE VACCINATION IN RESPONSE TO SMALLPOX OR MONKEYPOX: ACAM2000**

**Purpose:** To reduce the morbidity and mortality associated with smallpox (*variola virus*) or monkeypox by providing pre- and post-exposure vaccination with ACAM2000 (Smallpox Vaccinia Vaccine, Live).

**Policy:** These standing orders allow eligible healthcare providers to vaccinate persons who have or may become exposed to smallpox or monkeypox.

**Indications, Contraindications, Precautions, Special Populations, and Side Effects:**
The dose and safety precautions for this vaccine may change over time. Clinicians should seek the most current and comprehensive product information before using ACAM2000.

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<tr>
<th>ACAM2000</th>
<th>Pre-Exposure</th>
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<tr>
<td><strong>Indications</strong></td>
<td>1. Designated Michigan (MI) Laboratory Response Network (LRN) staff.</td>
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<td>2. Designated MI Biowatch federal officials.</td>
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<td>3. Vaccinators, vaccinator assistants, and “take” evaluators prior to serving in any of these positions are recommended for vaccination.</td>
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<td>4. Persons investigating suspected human and animal monkeypox cases and health care workers (HCW) who care for monkeypox patients, including veterinary and animal control personnel may receive vaccine on a voluntary basis; under an Investigational New Drug (IND) protocol.</td>
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<td><strong>Contraindications</strong></td>
<td>1. Persons &lt; 18 years of age and ≥ 65 years of age.</td>
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<td>2. Individuals diagnosed with a heart condition with or without symptoms, including coronary artery disease, heart failure, cardiomyopathy, stroke, transient ischemic attack, chest pain or shortness of breath with activity, or other heart conditions under medical care. Also, individuals with 3 or more of the following cardiovascular risk factors: high blood pressure, high blood cholesterol, diabetes, first degree relative that had a heart condition before age 50, or current cigarette user should not receive the smallpox vaccine.</td>
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<td>3. Individuals with a history of prior adverse reaction to smallpox vaccine or with severe, life-threatening reaction to latex (anaphylaxis).</td>
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<td>4. Individuals who are allergic to any component of the vaccine or diluent, and including the two antibiotics in ACAM2000™ vaccine: 1) phenol 2) glycerin 3) polymyxin B (polymyxin B sulfate) 4) neomycin (neomycin sulfate).</td>
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<td>5. Individuals with eczema, atopic dermatitis, pityriasis rubra pilaris, or</td>
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Darier's Disease or a past history of eczema/atopic dermatitis. *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.*

6. Individuals who have other acute, chronic, or exfoliative skin conditions (e.g., contact dermatitis, rosacea, wounds, burns, impetigo, Grover's disease, or varicella zoster). *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.* Persons with any of these conditions may be vaccinated when their condition or that of their household contact or sexual partner is completely resolved.

7. Individuals receiving therapy with systemic corticosteroids within the last month at immunocompromising doses (e.g. ≥ 2mg/kg body weight or ≥ 20 mg/day of prednisone for ≥ 2 weeks), with immunosuppressive drugs (e.g., alkylating agents, antimetabolites), or with radiation. *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.* Note: This does not apply to potential vaccine candidates or individuals with household contacts who are receiving only inhaled corticosteroids.

8. Individuals with congenital or acquired deficiencies of the immune system, including individuals with HIV/AIDS. *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.*

9. Individuals with immunosuppression (e.g., leukemia, lymphomas of any type, generalized malignancy, solid organ transplantation, hematopoietic stem cell transplantation, cellular or humoral immunity disorders, agammaglobulinemia, or other malignant neoplasms affecting the bone marrow or lymphatic systems). *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.*

10. Persons with severe autoimmune conditions such as systemic lupus erythematosus (SLE) that may significantly suppress the immune system.

11. Women that are pregnant, suspect they might be pregnant, are planning a pregnancy in the next month, or who are breastfeeding. *Individuals with household contacts or sexual partners with these conditions should not be vaccinated.*

12. Individuals receiving topical ocular steroid medications.

**Precautions**

1. Individuals with moderate to severe illness should defer vaccination until their illness improves or resolves.

2. Persons with the following diseases should consult with their physician prior to vaccination: fibromyalgia, hepatitis B & C, multiple sclerosis, rheumatoid arthritis, diabetes, bilateral pterygium, erythema multiforme,
Guillain-Barre Syndrome, seizures, vitiligo, agent orange exposure, and panhypopituitarism.

3. Vaccinia vaccine may be administered with any inactivated vaccine to encourage appropriate receipt of all indicated vaccines. Inactivated vaccines may be administered either simultaneously or before or after the vaccinia vaccine.

4. With the exception of varicella vaccine, vaccinia vaccine may be administered simultaneously with other live virus vaccines. To avoid confusion in ascertaining which vaccine may have caused post-vaccination skin lesions or other adverse events, and to facilitate managing such events, varicella vaccine and vaccinia vaccine should only be administered ≥28 days apart.

5. If other live virus vaccines are not given simultaneously with vaccinia vaccine, then the second parenteral, live virus vaccine should be administered at least 28 days after the first to avoid interference with the replication of the second vaccine virus.

6. Having Stevens-Johnson syndrome (SJS) in the past is not a contraindication from smallpox vaccine receipt, if there are no other contraindications presently to the antibiotics in the vaccine (polymyxin B sulfate, neomycin sulfate).

**Special Populations**

See contraindications.

**Side Effects**

A red, itchy lesion will appear at the injection site. The lesion will begin as a fluid filled blister that develops pus and will eventually scab. Rash, fever, sore arm, headaches, lymphadenitis, fatigue, and body aches may develop.

Vaccinia virus may be cultured from the site of primary vaccination beginning at the time a papule develops (2 to 5 days after vaccination) until the scab separates from the skin lesion (14 to 21 days after vaccination). During this entire time, care must be taken to prevent spread of the virus to another area of the body or to another person.

Additional side effects include myocarditis, pericarditis, brain or spinal cord swelling, and severe allergic reaction.

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<td><strong>Indications</strong></td>
<td>1. Persons who have been exposed to a person or animal or who have been designated by the Michigan Department of Community Health as at-risk for smallpox or monkeypox infection.</td>
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2. The CDC is advising that people investigating monkeypox outbreaks and involved in caring for infected people or animals should get a smallpox vaccine to protect against monkeypox. People who have had close or intimate contact with individuals or animals that have monkeypox also should get the vaccine. These people can get the vaccine up to 14 days after they have been exposed to monkeypox.

### Contraindications

People who have had severe, life-threatening allergies (anaphylaxis) to latex or to the smallpox vaccine or any of its components (e.g., polymyxin B, neomycin) should NOT get the smallpox vaccine.

**SMALLPOX POST-EXPOSURE:**

There are very few absolute contraindications to this vaccine for those who are at high risk for smallpox. The risk for experiencing serious vaccination complications must be weighed against the risks for experiencing a potentially fatal smallpox infection.

**MONKEYPOX POST-EXPOSURE:**

People with weakened immune systems due to treatments or certain health conditions (e.g., cancer treatment, organ transplant, HIV, and Primary Immune Deficiency disorders) should NOT get the smallpox vaccine, even if they have been exposed to monkeypox.

### Precautions

Individuals with immunosuppression who are exposed to smallpox or monkeypox will need evaluation to determine if the risks associated with disease are higher than risks associated with vaccine. Immune diseases include: leukemia, lymphoma, bone marrow or organ transplants, malignant cancer, HIV/AIDS, cellular or humoral immune deficiency, radiation recipients, or those who are being treated with steroids, prednisone, or cancer drugs.

### Special Populations

If there is a smallpox outbreak, anyone who is exposed to smallpox should be considered for vaccination regardless of health problems. In general, there is a greater risk for illness and death from smallpox than there is from the vaccine.

However, the safety and effectiveness of ACAM2000 have not been established in the age groups from birth to age 16. Clinical studies of ACAM2000 did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. ACAM2000 has not been studied in pregnant or lactating women.

### Side Effects

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Vaccinia virus may be cultured from the site of primary vaccination beginning at the time a papule develops (2 to 5 days after vaccination) until the scab separates from the skin lesion (14 to 21 days after vaccination). During this entire time, care must be taken to prevent spread of the virus to another area of the body or to another person.

Additional side effects include myocarditis, pericarditis, brain or spinal cord
Vaccinia Vaccination Criteria:

- Adverse events must be reported nationally through the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or www.vaers.hhs.gov. Contact the Michigan Department of Community Health at (517) 335-8159 for additional information.

- The CDC recommends that the vaccinia vaccine be given within 4 days from the date of exposure in order to prevent onset of the disease. If given between 4 to 14 days after the date of exposure, vaccination may reduce the symptoms of the disease, but may not prevent the disease.

- Reye's Syndrome has occurred in children and adolescents following natural varicella infection, the majority of whom had received salicylates. It is advised that varicella vaccine recipients not to use salicylates for six weeks after vaccination. Vaccinees should elect to take NSAIDs to treat the robust reactions whenever possible. However, chronic aspirin use for non-vascular indications such as arthritis, should not be deemed a contraindication.

- Individual who have an asthma attack after being vaccinated, can receive steroid treatments, with their primary health care provider's consultation.

- If the dose of steroids has been given long enough to cause significant immune suppression, vaccination providers should wait 1 month after discontinuation of therapy before administering a live-virus vaccine to patients who have received high systematically absorbed doses of corticosteroids for 2 weeks.

- Women should wait until the vaccine site has completely healed and the scab has fallen off before trying to become pregnant after vaccination. Generally, this means women who have received the smallpox vaccine should wait at least four weeks (28 days) before becoming pregnant.

- Women who are pregnant should not have close contact with anyone who has recently (within the last 28 days) received the smallpox vaccine. A close contact includes anyone living in the household and anyone with whom they have close, physical contact (such as a sex partner or someone they share a bed with).

- Individuals who are not successfully vaccinated (i.e., vaccination failures) after primary vaccination may be revaccinated again in an attempt to achieve a satisfactory take.

- In an individual vaccinated for the first time (primary vaccination), the expected response to vaccination is the development of a major cutaneous reaction (characterized by a pustule) at the site of inoculation. The lesion evolves gradually, with appearance of a papule at the site of vaccination after 2-5 days. The papule becomes vesicular, then pustular, and reaches its maximum size at 8-10 days after vaccination. The pustule dries and forms a scab, which usually separates within 14-21 days, leaving a pitted scar. (See Figure 1) Formation of a major cutaneous reaction by day 6-8 is evidence of a successful 'take' and acquisition of protective immunity. An equivocal reaction is any reaction that is not a major reaction, and indicates a non-take (vaccination failure) due to impotent vaccine or inadequate vaccination technique.
• Previously vaccinated individuals who do not have a cutaneous response on revaccination do not require revaccination to try to elicit a cutaneous response.

SMALLPOX SPECIFIC CONSIDERATIONS:
• Smallpox vaccination provides high level immunity for 3 to 5 years and decreasing immunity thereafter. The CDC is recommending that people have written documentation of vaccination dated within 3 years to be considered protected.

MONKEYPOX SPECIFIC CONSIDERATIONS:
• The vaccine is not licensed for pre-exposure prophylaxis to monkeypox. Use of the vaccinia vaccine for post-exposure prophylaxis to monkeypox must be conducted under an Investigational New Drug (IND) protocol. This includes a requirement that each vaccinee signs an informed consent form. The physician under whose signature these standing orders are implemented should assure that all requirements of the IND protocol are met.
• If exposure to the monkeypox virus has occurred and the exposed has not received the smallpox vaccine within the last 3 years, they should receive the smallpox vaccine unless contraindicated.

Figure 1: Progression of major cutaneous reaction after primary vaccination on days 5, 8, 10, and 14 respectively.

Medical Emergency or Anaphylaxis: Written emergency medical protocols, as well as equipment and medications, must be available at administration site. Anaphylaxis includes rash, difficulty breathing, swollen tongue or throat, itchiness of throat, and collapse.

Dosage and Administration Information:
A dose is considered to be 0.0025ml and the route is percutaneous (scarification) with bifurcated needle. ACAM2000 should not be injected by the intradermal, subcutaneous, intramuscular, or intravenous route.
Each vial of ACAM2000 has approximately 100 doses (2.5 – 12.5 \times 10^5 \text{ PFU}) of live vaccine once it is reconstituted. ACAM2000 is reconstituted by addition of 0.3 mL of diluent to the vial containing lyophilized vaccine. ACAM2000 should never be diluted to make additional doses than what is allotted in the vial.

Persons at continued high risk of exposure to smallpox (e.g., research laboratory workers handling variola virus) should receive repeat ACAM2000 vaccination every three years.

Alcohol, soap and water, or other chemical agents are not needed for preparation of the skin for vaccination unless the area is grossly contaminated. If needed, soap and water are the preferred cleaning agents. If any cleaning agent is used, the skin must be thoroughly dry in order to prevent inactivation of the vaccine.

Use 15 (fifteen) insertions (within an area of 5 millimeters in diameters) of the bifurcated needle. (Note, this is different from the 3 (three) insertions previously for the Dryvax primary vaccination). With ACAM2000 there is no longer the need to differentiate between “primary” and “secondary” vaccinees. However, it is useful to know should an adverse event occur.

With the same needle, and using multiple-puncture technique, vaccinate through drop of vaccine to penetrate the superficial layers of the skin. Never reintroduce a used needle into the vaccine bottle.

There is no need for additional insertions if no trace of blood is visible after vaccination.

**Distribution:**
ACAM2000 (Sanofi Pasteur Biologics) is licensed in the United States by the US Food and Drug Administration for active immunization against smallpox. ACAM2000 will be released via the Centers for Disease Control and Prevention Strategic Nation Stockpile Program.

**Storage and Handling:**
ACAM2000 contains live vaccinia virus that is transmissible and should be handled as an infectious agent once the vial is opened.

ACAM2000 should be stored in a freezer with an average temperature of -15 \text{ °C} to -25 \text{ °C} (+5 \text{ °F} to -13 \text{ °F}).

Prior to reconstitution, ACAM2000 vaccine retains a potency of 1.0x10^8 \text{ PFU} or higher per dose for at least 18 months when stored at refrigerated temperatures of 2 – 8 \text{ °C} (36 – 46 \text{ °F}). During shipment, ACAM2000 should be maintained at a temperature of -10 \text{ °C} or colder.

When not in actual use, store reconstituted vaccine at 2° to 8°C (36° to 46°F). The vaccine may be stored (under proper conditions) for no more than 30 days after reconstitution. (Note, this is different from the 90 days previously for Dryvax). Do not freeze.

To break up any clumps and to help facilitate a more uniform suspension, the vaccine product may be gently agitated with a bifurcated needle if the needle is sterile and discarded appropriately after use.
Inspect visually for particulate matter and discoloration prior to administration. If the product appears discolored or has visible particulate matter, discard the vial.

**Care of the Vaccination Site and Potentially Contaminated Materials:**

Patients must be given the following instructions:

- The vaccination site must be completely covered with a semipermeable bandage. Keep site covered until the scab falls off on its own.
- The vaccination site must be kept dry. Normal bathing may continue, but cover the vaccination site with waterproof bandage when bathing. The site should not be scrubbed. Cover the vaccination site with loose gauze bandage after bathing.
- Don't scratch the vaccination site. Don't scratch or pick at the scab.
- Do not touch the lesion or soiled bandage and subsequently touch other parts of the body particularly the eyes, anal and genital areas that are susceptible to accidental (auto-) inoculation.
- After changing the bandage or touching the site, wash hands thoroughly with soap and water or >60% alcohol-based hand-rub solutions.
- To prevent transmission to contacts, physical contact of objects that have come into contact with the lesion (e.g. soiled bandages, clothing, and fingers) must be avoided.
- Wash separately clothing, towels, bedding or other items that may have come in direct contact with the vaccination site or drainage from the site, using hot water with detergent and/or bleach. Wash hands afterwards.
- Soiled and contaminated bandages must be placed in plastic bags for disposal.
- The vaccinee must wear a shirt with sleeves that covers the vaccination site as an extra precaution to prevent spread of the vaccinia virus. This is particularly important in situations of close physical contact.
- The vaccinee must change the bandage every 1 to 3 days. This will keep skin at the vaccination site intact and minimize softening.
- Don't put salves or ointments on the vaccination site.
- When the scab fall off, throw it away in a sealed plastic bag and wash hands afterwards.

This protocol shall remain in effect for all persons needing pre- and post- exposure vaccination for smallpox and monkeypox until rescinded.

Approved by:

[Signature]

Chief Medical Executive
Michigan Department of Community Health

October 11, 2011