

**OREGON HEALTH AUTHORITY
IMMUNIZATION PROGRAM**

SMALLPOX (ACAM2000[®]) PRE- and POST-EXPOSURE PROPHYLAXIS	
Last Reviewed	8 June 2021
Last Revised (Links updated and minor edits for clarity.)	8 June 2021
This protocol expires	30 June 2023

I. Protocol procedure:

1. Determine whether contact has had a significant exposure to an infectious case and is at high risk for smallpox infection.
2. Assess current smallpox vaccination status.
3. Screen for contraindications.³ Copy the following link into a web browser to download the Smallpox Vaccine Screening Form:
<https://www.health.mil/Reference-Center/Forms/2020/03/02/Smallpox-Vaccine-Screening-Form>
4. Provide a *Smallpox Vaccine Information Statement* and client education guide about after-care of the vaccination site.⁴
<https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142576.pdf>
5. Record all required data elements in the client's permanent health record.
6. Administer^{*} a droplet (~0.0025 mL) of ACAM2000[®] percutaneously (i.e., by "scarification")[◇] using 15 jabs with a bifurcated needle into the skin overlying the deltoid muscle, as follows:
 - a. Bring lyophilized powder to room temperature prior to reconstitution. Reconstitute ACAM2000[®] by addition of 0.3mL of diluent to the lyophilized vaccine vial; gently swirl to mix. NOTE: This is not the entire content of the diluent vial.
 - b. Swab each rubber stopper with alcohol swab(s) and let dry thoroughly. Alcohol contamination on the stoppers or skin will inactivate the live virus.
 - c. Gently swirl to mix without getting the solution on the rubber stopper of the container.
 - d. Inspect visually. The reconstituted vaccine should be a clear-to-slightly hazy, straw-colored liquid free from extraneous matter.
 - e. Do not clean the skin unless the site of vaccination is obviously dirty, in which case an alcohol swab(s) may be used to clean the

area. Allow the skin to dry thoroughly.

- f. Remove the vaccine vial cap. Submerge the bifurcated end of needle in the reconstituted vaccine solution. The fork of the bifurcation will pick up a droplet of vaccine (~0.0025 mL). Do not shake excess vaccine off the bifurcated end of the needle. Allow excess vaccine to drop from the needle into the vial. If no vaccine is seen between the prongs of the needle, and *the needle has not touched the skin of the vaccinee*, it may be dipped again.
- g. Pull the skin taut, and deposit the droplet of vaccine onto the clean, dry skin of the deltoid region, rapidly making 15 jabs of the needle perpendicular to the skin and within a diameter of about 5 mm. The jabs should be vigorous enough that a drop of blood appears at the vaccination site. If no blood appears, make an additional 3 jabs.
- h. Wipe any excess droplets of vaccine and blood off the skin.
- i. Recap the vaccine vial.
- j. Cover the vaccination site loosely with a dry gauze and adhesive tape. If the vaccinee is a healthcare worker, cover the gauze with a semipermeable (semi-occlusive) dressing to prevent contact spread.
- k. Do not use salves or ointments on the vaccination site.
- l. Dispose of all contaminated items in the appropriate biohazard containers. Wash hands with soap and warm water or a >60% alcohol-based hand-rub solution.

Signature	Health Officer or Medical Provider	Date
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* ACAM2000[®] must be administered only by vaccine providers with training to safely and effectively administer the vaccine by the percutaneous route.¹

◇ ACAM2000[®] should not be injected by the intradermal, subcutaneous, intramuscular, or intravenous route.¹

II. A. Table 1. RECOMMENDED POST-EXPOSURE PROPHYLAXIS FOR SMALLPOX⁵

Primary Vaccination: One successful dose[*]			
Age[◇]	Number of Doses	Route	Dosage
Any	1	Percutaneous (scarification)	0.0025 ml

Revaccination: Not recommended for general public.

^{*} A successful dose results in the development of a major cutaneous reaction or “take.” A person is considered protected with the development of a permanent scar at vaccination site.⁵

[◇] In a post-exposure situation, there would be no age limit for vaccination of persons exposed or high-risk contacts.⁵

II. B. Table 2. RECOMMENDED PRE-EXPOSURE PROPHYLAXIS FOR SMALLPOX²

Primary Vaccination: One successful dose[*]			
Age	Number of Doses	Route	Dosage
≥18 years	1	Percutaneous (scarification)	0.0025 ml
Revaccination for those who work with:			
Replication-competent vaccinia viruses and recombinant viruses developed from replication-competent vaccinia viruses			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 (e.g., MVA, NYVAC, TROVAC, and ALVAC) [◇]			Not recommended

^{*} Laboratories that use both replication-competent and replication-deficient vaccinia virus strains but where working areas for these viruses cannot be clearly segregated should follow increased biosafety precautions because laboratory infections due to contamination have previously been documented.²

[◇] Modified vaccinia Ankara, New York vaccinia virus from the Copenhagen vaccinia strain, canary pox and fowl pox viruses, and Avipoxviruses.²

III. Table 3. LICENSED LIVE SMALLPOX VACCINE¹

Product Name	Vaccine components	Acceptable Age Range	Diluent
ACAM2000 [®]	Plaque purification cloning from Dryvax [®] Trace amounts of the antibiotics neomycin and polymyxin B	≥18 years of age ^{*, ◇}	50% glycerin 0.25% phenol, USP, in water

* In a post-exposure situation, there would be no age limit for vaccination of persons exposed to the intentional release or high-risk cases.⁵

◇ ACAM2000[®] has not been studied in pregnant or lactating women. Limited research has been done in all pediatric age groups and in people ≥65 years of age or older. Before the eradication of smallpox, live vaccinia vaccine was administered routinely in all pediatric age groups and was effective in preventing smallpox.¹

IV. A. INDICATIONS FOR USE:

Recommended post-exposure prophylaxis (PEP) for smallpox⁵

In the event of an intentional release of variola virus, vaccination would be recommended for persons exposed, including:

- Persons exposed to the initial release of the virus;
- Persons who had face-to-face, household, or close-proximity contact (≤2 meters) with a confirmed or suspected smallpox patient after the patient developed fever.
- Medical providers involved in assessment or treatment of cases;
- Public health investigators who may have contact with cases;
- Persons transporting or handling cases;
- Laboratory personnel who collect or process clinical specimens from cases;
- Persons with risk of contact with infectious materials from cases (e.g., persons handling medical waste, linen and room waste);
- Others whose jobs put them at increased risk of exposure to smallpox;
- Persons present at the hospital during the time that a case presented and was not yet placed in isolation; and,
- Others as identified by public health investigation.

Vaccination within 3 days of exposure will significantly modify risk of disease. Vaccination 4–7 days after exposure will likely offer some protection from disease or modify the severity of the disease.⁵

IV. B. INDICATIONS FOR USE:

Occupational primary or pre-exposure vaccination:²

Laboratory Personnel who directly handle cultures or animals contaminated or infected with replication-competent vaccinia viruses, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., monkeypox, cowpox, and variola). **n.b. CDC Advisory Committee on Immunization Practices (ACIP) Category A Recommendation – applies to all laboratory personnel meeting these criteria.**

The following groups could be offered vaccination under an ACIP Category B Recommendation – recommendation for individual clinical decision-making.

Healthcare personnel (e.g., physicians and nurses) who currently treat or anticipate treating patients with vaccinia virus infections, who could reasonably be expected to come in contact with replication-competent vaccinia viruses from lesions or contaminated materials (e.g., dressings), and who have no contraindication to vaccination.

Animal care personnel whose contact with replication-competent vaccinia virus is limited to contaminated materials (e.g., dressings or cages) may be offered vaccination as long as there are no contraindications.

Persons administering ACAM2000[®] smallpox vaccine who adhere to appropriate infection prevention measures may be offered vaccination with ACAM2000[®] as determined on a case-by-case basis, if there are no contraindications.

Vaccination **is not recommended** for persons who work only with replication-deficient poxvirus strains (e.g., MVA, NYVAC, TROVAC, and ALVAC).

V. A. CONTRAINDICATIONS FOR POST-EXPOSURE USE:

There are no absolute contraindications to vaccination of a person with a high-risk exposure to smallpox. If a relative contraindication exists, the risk of serious vaccination complications must be weighed against the risk of potentially fatal smallpox infection. See VI Precautions.⁶

V. B. CONTRAINDICATIONS FOR NONEMERGENCY USE:

1. History or presence of skin problems, or a close or household contact with such conditions^{*2}
2. Immunosuppression, or a close or household contact who is immunocompromised^{◇2}
3. Pregnancy (proven, possible, or intended) or pregnant household members²
4. Currently breastfeeding²
5. Serious vaccine component allergy⁶
6. Age <1 year old²
7. Use of steroid eye drops or ointments²
8. A heart condition or blood vessel problems^{§2}
9. Three or more heart-related risk factors^{‡2}

* Persons with acute, chronic or exfoliative skin conditions that cause breaks in the skin, such as burns, zoster, psoriasis, eczema, atopic dermatitis, severe acne, impetigo, keratosis follicularis, or herpes might be at a higher risk for eczema vaccinatum.²

◇ Replication of vaccinia virus can be increased among persons with conditions associated with decreased immunity.⁶

§ Heart problems include:²

- Coronary disease, including previous myocardial infarction and angina
- Congestive heart disease
- Myocarditis
- Cardiomyopathy

‡ Three or more of the following heart-related risk factors:²

- High blood pressure.
- High serum cholesterol.
- Diabetes or high blood sugar.
- First-degree relative with history of a heart condition before the age of 50
- Current tobacco smoker.²

VI. PRECAUTIONS⁶

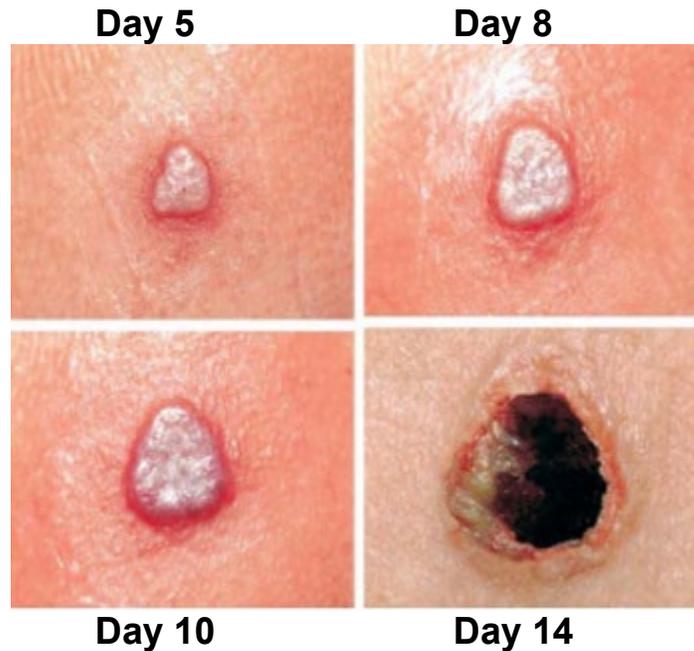
In the event of an emergency, the risk for experiencing serious vaccination complications must be weighed against the risk of developing a potentially fatal smallpox infection. High-risk contacts should be vaccinated unless they have certain problems with their immune system. Immune system problems include:

- Leukemia
- Lymphoma
- Bone marrow or organ transplant
- Cancer that has spread
- HIV, AIDS
- Cellular or humoral immune deficiency
- Current radiation therapy
- Current treatment with steroids, prednisone, or cancer drugs

VII. A. OTHER CONSIDERATIONS

- a. **Vaccine “Take”:** It is important to monitor the vaccine site for evidence of “take.” For individuals receiving their first vaccine, 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 8–10 days after vaccination. The pustule dries and forms a scab, which usually separates within 14–21 days, leaving a pitted scar. Formation of a major cutaneous reaction by day 8 is evidence of a successful “take” and acquisition of protective immunity (Figure 1).¹

Figure 1: Progression of major cutaneous reaction after primary vaccination



Successful vaccination in a previously vaccinated individual is confirmed when a major cutaneous reaction is observed 6–8 days after vaccination. However, any prior vaccination may reduce the cutaneous response upon revaccination, such that the absence of a cutaneous response does *not* necessarily indicate vaccination failure. (Figure 2)¹

Figure 2: Progression of major cutaneous reaction after revaccination¹



b. Equivocal (No “Take”):¹ An equivocal reaction is any reaction that is not a major reaction and indicates a lack of “take.” Individuals who are not successfully vaccinated may be revaccinated. The vaccination procedures should be checked, and vaccination repeated with vaccine from a different vial or vaccine lot. If a repeat vaccination is conducted using vaccine from another vial or vaccine lot fails to produce a major reaction, contact the state immunization program, which will report it to CDC.

Counseling:¹ Vaccinees must be informed of the adverse events associated with vaccination. They must also be informed that they should avoid contact with individuals who have vaccine contraindications. Household members of smallpox contacts who have contraindications to vaccination should consider housing themselves separately from vaccinated contacts, to avoid potential exposure to smallpox or inadvertent inoculation with vaccine virus, until their vaccination sites have healed. It is important for people to know that virus is shed from the cutaneous lesion at the site of inoculation from approximately day 3 until scabbing occurs. Accidental infection of skin at sites other than the site of intentional vaccination may occur by trauma or scratching.

c. Care of the Vaccination Site and Contaminated Materials:¹

Vaccinees must be given the following information:

- The vaccination site must be completely covered with a semipermeable bandage 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 a waterproof bandage when bathing. The site should not be scrubbed. Cover the vaccination site with a 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, which 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 any 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 or bleach. Wash hands afterwards.
- Place soiled and contaminated bandages in plastic bags for disposal.
- The vaccinee must wear a shirt with sleeves that cover the vaccination site as an extra precaution to prevent spread of the vaccinia virus. This is particularly important in situations of close physical interpersonal contact.
- The vaccinee must change the bandage every 1–3 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 falls off, throw it away in a sealed plastic bag, and wash hands afterwards.

d. Simultaneous Administration with Other Vaccines:^{6, 7}

- ACAM2000[®] can be administered simultaneously with any inactivated vaccine (e.g., influenza vaccine) to encourage appropriate receipt of all indicated vaccines. **With the exception of varicella vaccine**, ACAM2000[®] vaccine can be administered simultaneously with other live-virus vaccines.

- To avoid confusion in ascertaining which vaccine might have caused post-vaccination skin lesions or other adverse events, and facilitate managing such events, varicella vaccine and ACAM2000[®] should only be administered ≥ 4 weeks apart.
- e. Interference with laboratory tests:**¹ ACAM2000[®] may induce false-positive tests for syphilis
- Persons should not receive a tuberculin skin test for 1 month after smallpox vaccination, to prevent a possible false-negative reaction.⁷

f. Vaccination and Blood Donation:⁸

Smallpox vaccination and did not develop complications:

Wait 8 weeks (56 days) from the date of having a smallpox vaccination as long as you have had no complications. Complications may include skin reactions beyond the vaccination site or general illness related to the vaccination.

Smallpox vaccination and developed complications:

Wait 14 days after all vaccine complications have resolved or 8 weeks (56 days) from the date of having had the smallpox vaccination whichever is the longer period of time. You should discuss your particular situation with the health historian at the time of donation. Complications may include skin reactions beyond the vaccination site or general illness related to the vaccination.

Smallpox vaccination – close contact with someone who has had the smallpox vaccine in the last eight weeks and you did not develop any skin lesions or other symptoms.

Eligible to donate.

Smallpox vaccination – close contact with someone who has had the vaccine in the last eight weeks and you have since developed skin lesions or symptoms.

Wait 14 days after all evidence of vaccinia infection has resolved or 8 weeks (56 days) from the date of the first skin lesion or sore, whichever is longer. You should discuss your particular situation with the health historian at the time of donation. Complications may include skin reactions or general illness related to the exposure.

- g. Pregnancy:**¹ Rarely, smallpox vaccine administered during pregnancy may lead to infection of the unborn baby. This infection usually results in stillbirth or death. Pregnancy should be avoided for at least 4 weeks or until the vaccination site has healed.
- h. Vaccinia Immune Globulin¹ is indicated for certain complications of vaccination with ACAM2000[®]. If VIG is needed or additional information is required, physicians should contact the CDC at (404) 639–3670, M–F 8 AM to 430 PM Eastern Standard Time; at other times call (404) 639–2888.**

VIII. A. SIDE EFFECTS AND ADVERSE EVENTS

1. Serious, but not life-threatening reactions

- **Myocarditis**⁹
- **Pericarditis**⁹
- **Inadvertent inoculation:** Occurs when vaccinia virus is transferred from a vaccination site to a second location on the vaccinee or to a close contact. The most common sites involved are the face, eyelid, nose, mouth, lips, genitalia, and anus. Ocular vaccinia infections account for the majority of recognized inadvertent inoculations.²
- **Generalized vaccinia:** Is characterized by a disseminated maculopapular or vesicular rash, frequently on an erythematous base, that usually occurs 6–9 days after primary vaccination. The rash spans the spectrum of vaccinia lesions, from macules to papules to vesicles. The skin lesions are caused by virus spread via the hematogenous route.⁶
- **Erythema Multiforme:** Is an allergic response that might appear as different types of lesions, including macules, papules, hives, and typical “bull’s-eye” lesions. Patients can suffer residual cerebral impairment and hemiplegia.⁵

2. Life-threatening Reactions

- **Stevens–Johnson Syndrome**⁹
- **Post-vaccinia encephalitis:** Typically affects children <2 years of age and reflects cerebral damage as a result of vascular changes. Acute onset of symptoms occurs 6–10 days after vaccination and can include seizures, hemiplegia, aphasia, and transient amnesia.²

- **Progressive vaccinia:** A rare, severe, and often lethal complication that occurs among persons with immunodeficiency. It is characterized by painless, progressive necrosis at the vaccination site with or without metastases to distant sites. This diagnosis should be suspected if the vaccination lesion continues to progress without apparent healing ≥ 15 days after smallpox vaccination. During the weeks that follow, patients might experience bacterial infections and signs of inflammation.²
- **Eczema vaccinatum:** A localized or generalized papular, vesicular, or pustular rash that can occur anywhere on the body, with a predilection for areas of previous atopic dermatitis. Onset of the characteristic lesions can be noted either concurrently with or shortly after the development of the local vaccinia lesions.²

VIII. B. Table 4. SIDE EFFECTS AND ADVERSE EVENTS¹

Number followed for Safety	ACAM 2000 [®] Study 1 N =873 Adverse Reaction %	ACAM 2000 [®] Study 2 N=1371 Adverse Reaction %
	18–30 years Primary Vaccine	31–84 years Re-vaccination after >10 years previously
At least 1 adverse event	99	97
Local Reaction, Injection site		
Pain	67	37
Redness	74	61
Swelling	48	28
Rash	11	6
Systemic Complaints		
Lymph node pain	57	19
Feeling Hot	32	20
Nausea	19	10
Malaise	37	28
Fatigue	48	34
Headache	50	32
Muscle pain	46	27
Package insert page 7, table 3, 2015 ¹		

IX. Table 5. STORAGE AND HANDLING ¹

All clinics and pharmacies enrolled with the Vaccines for Children (VFC) Program must immediately report any storage and handling deviations to the Oregon Immunization Program at 971-673-4VFC (4823).

Vaccine	Temp	Storage Issues	Notes
ACAM2000 [®]	Store at 2°–8°C (36 to 46°F)	Do not freeze Protect from light	Administer as soon as possible after being removed from refrigeration

X. ADVERSE EVENTS REPORTING

Public providers are to complete the Vaccine Adverse Events Reporting System (VAERS) report online at <https://vaers.hhs.gov/reportevent.html>

Private providers are to report events directly to VAERS and can read about options on how to do so at <http://vaers.hhs.gov/index>.

VAERS Smallpox Pregnancy Supplemental Form, June 29, 2017. Available at: <https://health.mil/Military-Health-Topics/Health-Readiness/Immunization-Healthcare/Vaccine-Preventable-Diseases/Smallpox/Smallpox-Resource-Center> Accessed 31 July 2018.

Table 6. VAERS Reporting Table ^{*}
[https://vaers.hhs.gov/docs/VAERS Table of Reportable Events Following Vaccination.pdf](https://vaers.hhs.gov/docs/VAERS%20Table%20of%20Reportable%20Events%20Following%20Vaccination.pdf) Copy and paste into browser.

Event and interval from vaccination in which it would be reportable
A. Anaphylaxis or anaphylactic shock (7 days)
B. Shoulder injury related to vaccine administration (7 days)
C. Vasovagal syncope (7 days)
D. Guillain-Barré Syndrome (42 days)

- E. Any acute complication or sequelae (including death) of above events (interval - not applicable)
- F. Events described in manufacturer's package insert as contraindications to additional doses of vaccine (interval - see package insert)

Effective date: March 21, 2017. The Reportable Events Table (RET) reflects what is reportable by law (42 USC 300aa-25) to the Vaccine Adverse Event Reporting System (VAERS) including conditions found in the manufacturer package insert. In addition, healthcare professionals are encouraged to report any clinically significant or unexpected events (even if not certain the vaccine caused the event) for any vaccine, whether or not it is listed on the RET.

An electronic copy of this protocol is available [here](#).

For more information or to clarify any part of the above protocol, consult with your health officer or call the OHA/ Public Health Division Immunization Program at 971-673-0300 (or 711 for TTY); or with the Acute and Communicable Disease Prevention Section at 971-673-1111.

**To request this material in an alternate format (e.g., braille),
please call 971-673-0300**

REFERENCES

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