DEPARTMENT OF HUMAN SERVICES
HEALTH SERVICES, OFFICE OF FAMILY HEALTH
IMMUNIZATION PROTOCOL

SMALLPOX
Live Virus Vaccine

I. ORDER

1. Screen for contraindications.
2. Provide a current Smallpox Pre-Vaccination Information Packet, answering any questions.
3. Obtain a consent signature on the most recent copy of the CDC (Section D) Patient Medical History and Consent Form.
4. Administer vaccinia (the smallpox vaccine - *Dryvax®)* with a bifurcated needle into the skin overlying the deltoid region of non-dominant arm. Rapidly puncture the skin **3 times for a primary vaccinee**[1] and **15 times for a revaccinee**[2] in an area 5 mm in diameter.
   a. Use strokes vigorous enough to allow a trace of blood to appear after 15 to 20 seconds. If no trace of blood is visible, an additional 3 punctures should be made using the same bifurcated needle without reinserting the needle into the vaccine vial (see Section VA for more administration details).
   b. Smallpox vaccine can be administered simultaneously with any inactivated vaccine.
   c. With the exception of varicella vaccine, smallpox vaccine can be administered simultaneously with other live-virus vaccines. (see Section X A).

NOTE**: VACCINE MUST BE GIVEN WITHIN 90 DAYS OF RECONSTITUTION AND STORED AT 2º TO 8ºC (36º TO 46ºF)**

[1] A person is determined to be a **primary vaccinee** based on medical history. If they don't know or did not receive the smallpox vaccine previously, then they are a primary vaccinee. If there is a verbal or written history of "no take" on their previous smallpox vaccination, they are not considered previously vaccinated and should be treated as a primary vaccinee.

[2] A person is determined to be a **revaccinee** if there is a written record of vaccination, or a visible vaccination scar, or born before 1972, or served in the military before 1984. (source: CDC *Smallpox Vaccination Status and Procedures-Guidelines for Grantees using Licensed Undiluted Wyeth Dryvax Vaccine*; 7/03)

Signature Health Officer or Medical Provider Date

II. DHS RECOMMENDATIONS FOR VACCINATION

A. Non- emergency situation

In the absence of disease or intentional release of variola virus, vaccination is recommended for:

- Laboratory workers who directly handle cultures or animals contaminated or infected with non-highly attenuated vaccinia viruses (e.g., the NYCBOH, Temple of Heaven, Copenhagen, or Lister vaccinia strains), and recombinant vaccinia viruses derived from non-highly attenuated vaccinia strains;
- Laboratory workers exposed to other orthopoxviruses that infect humans (e.g., monkeypox or cowpox);
- Health care workers who come into contact with materials such as dressings that may be contaminated with vaccinia or recombinant vaccinia (clinical trials or administering the vaccine); and
- Consenting medical and public health response personnel approved for pre-event vaccination by local and state bioterrorism preparedness programs.
- Persons administering smallpox vaccine.

B. Emergency situation

In the event of an intentional release of variola virus, vaccination would be recommended for persons exposed to cases, either suspected or confirmed, including:

- Persons exposed to the initial release of the virus;
- Close personal and household contacts, defined as face-to-face contact or within 6.5 feet for 4 hours or more;
- Medical providers involved in assessment or treatment of suspect cases;
- Public health investigators who may have contact with cases;
- Persons transporting confirmed or suspect cases;
- Laboratory personnel who collect or process clinical specimens from suspect cases;
- Persons with risk of contact with infectious materials from suspect cases (e.g., persons handling medical waste, linen, and room waste); and
- Others as identified by public health investigators.

III. SMALLPOX VACCINE SCHEDULE:

Primary Vaccination: One successful dose[1]		
Dose	**Minimum Age[2]**	**Recommended Age**
1	18 years	≥18 years
Revaccination: Every 10 years[3]		

[1] A successful dose results in a major reaction or "take" which is defined in Section VII. A person is considered protected with the development of a permanent scar at vaccination site. All other responses are referred to as equivocal and vaccination should be repeated at least one more time (Section VII).

[2] Under routine circumstances the vaccine should not be administered to persons < 18 years of age. In an emergency post-release situation, there would be no age limit for vaccination of persons exposed to a person with confirmed smallpox.

[3] Revaccination is recommended every 10 years for occupational exposure to non-highly attenuated vaccinia viruses, recombinant viruses, or other non-variola orthopoxviruses. Revaccination every 3 years is recommended for occupational exposure to more virulent orthopoxviruses (e.g. monkeypox) Reference: Atkinson, W ed. CDC, Atlanta: *Epidemiology and Preventon of Vaccine-Preventable Diseases*, 7th Edition, Jan 2002; pg 245)

IV. CONTRAINDICATIONS

Contraindications to smallpox vaccine (see details following table)

Non-emergency use	**During smallpox emergency**
A. History or presence of atopic dermatitis or eczema or close/household contacts with these conditions Other acute, chronic, or exfoliative skin conditions that are active at the time of proposed vaccination or close/household contacts with these conditions. B. Immunosuppression or close/household contact who is immunocompromised C. Pregnancy or pregnant household members D. Age <18 yrs E. Serious vaccine component allergy F. Breastfeeding G. Moderate or severe short term illness H. Use of steroid eye drops I. Diagnosed by a doctor as having a heart condition with or without symptoms (conditions listed in IV I)* J. Three or more heart related risk factors (risks listed in IV J)*	There are **NO** contraindications to smallpox vaccine if exposure to smallpox virus is suspected or confirmed. Anyone directly exposed to smallpox virus should be vaccinated, regardless of age, allergies, pregnancy or medical condition. Reminder: If no exposure is suspected – follow the contraindications for non-emergency use.

* These may be temporary exclusions and may change as more information is gathered. (source: CDC Smallpox Vaccine Information Statement (VIS) 3/31/03; Smallpox Vaccine and Heart Problems)

CONTRAINDICATIONS, continued

A. History or Presence of Eczema or Other Skin Conditions

Because of the increased risk for eczema vaccinatum in persons with a history of eczema or atopic dermatitis, smallpox vaccine should not be administered to persons with these conditions or a history of them, nor those whose household or close contacts have active eczema, or a history of eczema or atopic dermatitis.

Persons with other acute, chronic, or exfoliative skin conditions that cause breaks in the skin, such as burns, zoster, psoriasis, severe acne, impetigo, or herpes might also be at higher risk for eczema vaccinatum.

B. Immunosuppression

Replication of vaccinia virus can be increased among persons with conditions associated with decreased immunity, including HIV infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, cellular or humoral immunity disorders, or those receiving therapy with alkylating agents, antimetabolites or radiation.

Delay immunization of persons taking high-dose corticosteroid therapy (≥ 2 mg/kg body weight or 20 mg/day of prednisone for ≥ 2 weeks) for at least 3 months after the last dose. Also included in this risk group are hematopoietic stem-cell transplant recipients who are < 24 months post-transplant, and hematopoietic stem-cell transplant recipients who are ≥ 24 months post-transplant but who have graft-versus-host disease or disease relapse.

Persons with such conditions or whose household members or close contacts have such conditions should not be vaccinated.

C. Pregnancy

Smallpox vaccine is contraindicated for individuals who are pregnant or whose household contacts are pregnant. Pregnancy should be avoided for at least one month after vaccination.

D. Age <18 years

Before eradication, smallpox vaccine was administered routinely during childhood. However, smallpox vaccination is no longer indicated for infants or children <18 years of age in non-emergency situations.

cont.

CONTRAINDICATIONS, continued

E. Allergies to Vaccine Components

The currently available vaccinia vaccine (Dryvax®**)** contains trace amounts of polymyxin B sulfate, streptomycin sulfate, chlortetracycline hydrochloride, and neomycin sulfate. Persons who have experienced anaphylactic reactions (i.e., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) to any of these antibiotics or to a previous dose of smallpox vaccine should not be vaccinated. The vaccine does not contain penicillin.

F. Breastfeeding

Women who are breastfeeding should not get the vaccine. This applies to women who are breastfeeding as well as pumping and then bottle-feeding breast milk. Breastfeeding by a close contact is not a contraindication.

G. Moderate or Severe Short Term Illness

Anyone moderately or severely ill (including illness with fever) should defer vaccination until illness is resolved.

H. Steroid Drops

Anyone using steroid drops in his or her eyes for any reason should not get the smallpox vaccine until medication is finished.

I. Heart Problems including:

- Known coronary disease including
  - Previous myocardial infarction (heart attack)
  - Angina (chest pain caused by lack of blood flow to heart)
- Congestive heart disease
- Myocarditis (heart muscle becomes inflamed)
- Cardiomyopathy
- Stroke or transient ischemic attack (“mini-stroke” causing stroke-like symptoms but no lasting damage)
- Chest pain or shortness of breath with activity (e.g. walking upstairs)
- Other heart conditions under care of doctor.

cont.

CONTRAINDICATIONS, continued.

J. Heart related risk factors: (3 or more of these 5 contraindicate smallpox vaccine)

- You have been told by a doctor that you have high blood pressure.
- You have been told by a doctor that you have high blood cholesterol.
- You have been told by a doctor that you have diabetes or high blood sugar.
- You have a first degree relative (mother, father, brother, or sister) who had a heart condition before the age of 50.
- You smoke cigarettes now.

V. ADMINISTERING VACCINE

A. Vaccination

1. Reconstitute smallpox vaccine according to manufacturer package insert.
2. Secure vial of vaccine to eliminate possibility of a spill.
3. Cleanse the skin only, if grossly contaminated, with soap and water. Allow skin to dry thoroughly. **Do not use alcohol**; alcohol inactivates the vaccine.
4. Dip bifurcated needle into the reconstituted vaccine causing a droplet of vaccine to adhere between the prongs of the needle. Hold perpendicular to the vial to allow any excess vaccine to drop from the needle. Do not shake the needle. The droplet contains the recommended dose of vaccine, and its presence within the prongs of the bifurcated needle should be confirmed visually. 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.

5. Pull the skin over the deltoid muscle of the non-dominant arm, taut with one gloved hand. Hold bifurcated needle perpendicular to the skin with the other gloved hand while resting wrist on the patient's arm. Rapidly puncture the skin **3 times for a primary vaccinee** and **15 times for a revaccinee** in an area 5 mm in diameter. Use strokes vigorous enough to allow a trace of blood to appear after 15 to 20 seconds. If no trace of blood is visible, an additional 3 punctures should be made in the same spot using the same bifurcated needle without reinserting the needle into the vaccine vial. Even if there is no trace of blood after the additional insertions, proceed with an evaluation of the reaction on day 6,7,or 8 post-vaccination.
6. Absorb excess vaccine gently with sterile gauze and discard gauze in a biohazard waste receptacle.
7. Cover the vaccination site with a single layer of sterile gauze and secure with tape. If vaccinee is a health care worker, cover the gauze with a semipermeable dressing (e.g., Opsite).

B. Post Vaccination Site Care

Vaccinia virus can be cultured from vaccination site from time the initial papule forms (2-5 days post-vaccination) until the scab separates from the skin, as long as 21 days after the vaccination. During this time, attention is necessary to prevent spread of the virus to another area of the body or to another person.

DOs:

- **COVER vaccination site and change cover frequently to allow site to breathe.**
- **When working in a health care setting**, cover vaccination site loosely with gauze, using first aid adhesive tape to hold in place. Then **cover gauze with a semipermeable dressing** (e.g., OpSite®). **Change bandage at least every 3-5 days in order to prevent build-up of fluids and irritation of the site. Also wear a shirt to cover the bandaged site** as additional barrier to spreading virus to other areas of body or to other people.
- **When not working in a health care setting**, cover vaccination site loosely with **gauze and tape**. Change gauze bandage every 1-3 days and **wear a shirt** that covers the site. This is particularly important in situations of close physical contact.
- **Keep vaccination site dry**. Change bandage or gauze if it gets wet. Bathe as normal by covering vaccination site with a water-resistant bandage (e.g., saran wrap) during bath or shower. Do not scrub site while bathing. Do not touch site and then touch another area of body (such as genitals or eyes). Replace water-proof covering with regular dressing as soon as area has dried.
- **Handle contaminated materials safely**. Place used bandages and gauze in a plastic zipper bag before throwing away. Do the same with scab when it falls off. Dispose of bags in regular trash. Use normal laundering (warm or hot water with bleach or detergent) to wash clothing, towels, washcloths, or sheets that have touched the vaccination site.
- **WASH HANDS with soap and water after touching the vaccine site or other things that have touched the site like bandages or clothing**.

DON'Ts:

- **Don't use a bandage that blocks all air from vaccination site**. This may cause skin to soften and wear away.
- **Don't put salves or ointments on the site.**
- **Don't scratch site.**
- **Don't forget to wash hands.**
- Don't let persons who haven't been vaccinated touch the vaccination site or things that have touched the vaccination site, like bandages or clothes.

VI. NORMAL PRIMARY VACCINATION REACTIONS

A. Normal Reaction Time

Day	Description
0	Vaccination
3-4	Papule
5-6	Vesicle with surrounding erythema Vesicle with depressed center
8-9	Well-formed pustule
12+	Pustule crusts over → scab
17-19	Scab detaches, revealing scar
Source: www.bt.cdc.gov/training/smallpoxvaccine/reactions/normal.html	

A. Normal Variants

These are not considered adverse events and usually require no specific treatment.

1. Local satellite lesions – secondary blisters adjacent to the vaccination site; in contrast to lesions from accidental implantation. Frequency ranges from 2.4-6.6%.
2. Lymphangitis from the site to regional nodes.
3. Considerable local edema.

B. Typical Symptoms

Symptoms usually begin about one week after vaccination. Possibly 1/3 of persons getting the vaccine may feel sick enough to miss work, school, recreational activities, or may have temporary trouble sleeping.

Symptom	**Occurrence**
Soreness at vaccination site	
Intense erythema (viral cellulitis) around site	
Malaise	
Lymphadenopathy (local)	25.0 – 50.0%*
Myalgia, headache, chills, nausea, fatigue	0.3 – 37.0%*
Fever > 100ºF	2.0 – 16.0%*
Pruritus	Common

***** Occurrence of these reactions varies from study to study. These percentages indicate the range of occurrences. (www.bt.cdc.gov/training/smallpoxvaccine/reactions/normal.html)

VII. EVALUATING A "TAKE" AFTER VACCINATION

Vaccination sites should be examined for the expected vesicle or pustule on day 6, 7, or 8 post-vaccination to determine whether the vaccination was successful. The medical provider who evaluates the "take" will document the results (take and no take) on the vaccinee's Current Vaccination Information and Take Evaluation Form (Section C of the Patient Medical History and Consent Form in the CDC Smallpox Pre-Vaccination Information Packet) and on an adult immunization card for the vaccinee to keep.

Take Evaluation

Reaction	Description	Immune Status
Major (Take)	Area of definite induration or redness surrounding a central lesion that may be a clear-cut pustule, scab or ulcer 6-8 days after vaccination. The evolution of the lesion is more rapid with revaccination than following a primary reaction.	**Status: Immune** Virus replication has taken place and vaccination was successful.
Equivocal (No Take)	Any other reaction or response; e.g., an "allergic" reaction, or no reaction.	**Status: Not Immune** Repeat vaccination as soon as possible to achieve a primary take. At least 1 additional vaccination attempt should be made for the revaccinee, and 2 additional attempts for the primary vaccinee , switching skin sites and vaccine vial after 1st unsuccessful attempt.[1]

[1] If the reaction following either primary vaccination or revaccination is equivocal, repeat vaccination with 15 vigorous insertions using potent vaccine and proper technique. If no trace of blood is seen with this repeat revaccination, give 3 additional insertions. Even if no trace of blood is seen after the additional insertions, response to vaccination should be evaluated on day 6,7,or 8 after vaccination. Repeat vaccination can be done on the same day as the "no take" reading and on the same arm, 1-2 cm from the previous vaccination site.

NOTE: If a **second equivocal reaction occurs in a revaccinee, the vaccinee can be considered immune**. If a second equivocal reaction occurs in a primary vaccinee, a third vaccination should be given.

Immunity after a Successful Take

Vaccination Status	Immunity
Primary vaccination	Fades after 5 years; after 20 years probably negligible.
Successful revaccination one or more times	Found to persist 30+ years. May protect against a fatal outcome, but may not against developing a milder form of smallpox.
Vaccination after exposure to smallpox	Within 2-3 days, can protect against smallpox. Within 4-5 days, may protect against a fatal outcome.

www.bt.cdc.gov/training/smallpoxvaccine/reactions/about_vac_immunity.html

VIII. ADVERSE REACTIONS FOLLOWING VACCINATION

Serious and Life–threatening Reactions

Adverse Events per Million Vaccinees*

	National Survey		Ten-State Survey	
	All primary vaccinees	Vaccinees > 1yr old	All primary vaccinees	Vaccinees >1 yr old
SERIOUS REACTIONS				
Accidental implantation	25.4	27.1	529.2	532.0
Generalized Vaccinia	23.4	17.7	241.5	222.8
Erythema Multiforme	Not Available	Not Available	164.6	131.3
Total	**48.8**	44.8	**935.3**	886.1
LIFE-THREATENING REACTIONS				
Post-vaccinial Encephalitis	2.9	2.4	12.3	8.6
Progressive Vaccinia (Vaccinia Necrosum)	0.9	1.0	1.5	1.7
Eczema Vaccinatum	10.4	10.6	38.5	41.5
Total	**14.2**	14.0	**52.3**	51.8
DEATHS	**1.1**	0.6	None reported	None reported

Source: CDC Smallpox Vaccination Program Guidelines, Annex 10, November 2002. This table data is based on 2 studies done in 1968 using different methodologies. References: 1). New Engl J Med 1969;281:1201-1208; 2). J Infect Dis 1970;122:303-309.

* Adverse events in the U.S. today might be more likely because there may be more persons with eczema, atopic dermatitis and immunosuppression. Adverse events may be less likely for persons previously vaccinated. (www.bt.cdc.gov/agent/smallpox/vaccine-safety/adverse-events-chart.asp)

B. Serious Reactions That Need Evaluation for Medical Attention

- **Accidental implantation** - a vaccinia rash or outbreak of sores limited to one area distant from the vaccination site. It usually occurs on the genitals or face, and can include the eyes, where it can damage sight or lead to blindness. **Note: If the eyes are affected, seek immediate medical attention**.
- **Generalized Vaccinia** - a widespread vaccinia rash. The virus spreads from the vaccination site, probably through the blood.
- **Erythema multiforme -** an allergic rash in response to the vaccine. This can take various forms such as red spots, bumps, or hives.
- Red streaks coming out from the vaccination site are most likely a normal reaction, but could be an infection and should be checked.

A. Life-Threatening Reactions That Need Immediate Attention

- **Eczema vaccinatum** - Widespread infection of the skin in people with skin conditions such as eczema or atopic dermatitis; it can lead to scarring, severe systemic illness, or death.
- **Progressive vaccinia or vaccinia necrosum** – an ongoing infection of skin at the vaccination site with tissue destruction. It can cause scarring, spread to other organs, or lead to death.
- **Post-vaccinial encephalitis** - Inflammation of the brain. This can lead to disability or death.

IX. POST-VACCINATION TREATMENT OF ADVERSE REACTIONS

A. Vaccinia Immune Globulin

Vaccinia Immune Globulin (VIG) is made from blood of persons who have gotten the smallpox vaccine more than once. The antibodies that give protection from vaccinia infection are taken out, purified, and bottled. VIG is not licensed by the Food and Drug Administration (FDA). Vials are stored and distributed by the National Pharmaceutical Stockpile and are available for treatment of adverse events under Investigational New Drug (IND) protocols.

VIG can be made available to a medical provider through a DHS epidemiologist at 503-731-4024 (business hours) or 503-731-4030 (after hours).

VIG Administration

VIG Use	Adverse Event
Indicated	• Accidental implantation (extensive lesions) • Eczema vaccinatum • Generalized vaccinia (if severe or recurrent) • Progressive vaccinia
NOT Recommended	• Accidental implantation (mild instances) • Generalized vaccinia (mild or limited – most instances) • Erythema multiforme • Post-vaccinial encephalitis
Contraindicated (might be used if other life-threatening complications also existed)	• Vaccinia keratitis
Source: www.bt.cdc.gov/training/smallpoxvaccine/reactions/vig	

B. Investigational Vistide® (Cidofovir)

Cidofovir is not licensed to treat the problems caused by smallpox vaccine so it is only available through an IND protocol. Its use should be evaluated and monitored by experts at the National Institutes of Health and CDC. Cidofovir might be used to treat severe cases of generalized vaccinia, eczema vaccinatum, or progressive vaccinia.

Cidofovir can be made available to a medical provider by a DHS epidemiologist at 503-731-4024 (business hours) or 503-731-4030 (after hours).

X. OTHER CONSIDERATIONS

A. Simultaneous Administration With Other Vaccines

1. To avoid confusion in ascertaining which vaccine might have caused post vaccination skin lesions or other adverse events, varicella vaccine and smallpox vaccine should only be administered ≥ 4 weeks apart.
2. To minimize potential risk for interference, live vaccines (e.g. smallpox, mmr) not administered on the same day should be administered ≥ 4 weeks apart. If live vaccines are separated by < 4 weeks, the vaccine administered 2nd should not be counted as a valid dose and should be repeated. The repeat dose should be administered ≥ 4 weeks after the last, invalid dose.
3. Persons scheduled to receive an annual PPD (tuberculin) skin test should not receive the skin test for 1 month after the smallpox vaccination to prevent a possible false-negative reaction.

B. Vaccination and Blood Donation

The Food and Drug Administration (FDA) has recommended that smallpox vaccinees be deferred from donating blood for 21 days or until the scab has separated. Contacts of vaccinees who have inadvertently contracted vaccinia also should be deferred from donating blood for 14 days after complete resolution of their complications.

C. Vaccine and Heart Problems

If you have received the smallpox vaccine, you should see a health care provider right away if you develop chest pain, shortness of breath, or other symptoms of cardiac disease.

XI. ADVERSE EVENT REPORTING

The State of Oregon DHS Immunization Program will track reports of adverse reactions to the smallpox vaccine. Serious and life-threatening reactions to the smallpox vaccination are uncommon.

All adverse events following smallpox immunization should be **reported by all providers to the DHS Immunization Program**, using a Vaccine Adverse Events Reporting System (VAERS) form by fax. Life-threatening events must be reported within 24 hours and all other events within 7 days. Completed forms should be **FAXED (preferable, due to timeliness) to 503-731-3095.** If faxing is not possible, please mail completed forms to the DHS Immunization Program, PO Box 14450, Portland, OR 97214-9929. If there are questions about the VAERS program or reporting, please call the Immunization Program at **503-731-4020.** All VAERS reports received by the state will be forwarded to the VAERS program in Rockville, MD.

If clinical consultation is needed, or VIG or Cidofovir is indicated, contact the DHS epidemiologist on call at **503-731-4024 (business hours) or 503-731-4030 (after hours).**

XII. REFERENCES

1. CDC Smallpox Pre-Vaccination Information Packet, 1/16/03.
2. CDC Smallpox Vaccination Status and Procedures-Guidelines for Grantees using Licensed Undiluted Wyeth Dryvax Vaccine, 7/03.
3. CDC websites: www.bt.cdc.gov or www.cdc.gov/smallpox for current fact sheets on smallpox vaccinations.
4. Dryvax® (smallpox vaccine) package insert
5. Smallpox. In: *Epidemiology and Prevention of Vaccine-Preventable Disease* ("Pink Book"). Atkinson W, Hamborsky J, Wolfe S, eds. 8th ed. Washington, DC: Public Health Foundation, 2004: 257-80.
6. Smallpox Vaccine Administration Video Transcript, 12/2002.
7. Vaccinia (Smallpox) Vaccine Recommendations of ACIP, MMWR, Vol. 50, RR-10, 06/22/01.

For more information or to clarify any part of the above order, consult with your health officer, bioterrorism coordinator, or contact DHS Immunization Program at 503-731-4020.

Visit our website at http://www.healthoregon.org/imm
To request this material in an alternate format (e.g., Braille), please call 503-731-4020.