

# Wyeth® Smallpox Vaccine Dried Calf Lymph Type Dryvax® dried smallpox vaccine

A.H.F.S. Category 80:12

3. For persons of any age receiving therapy with Xray, ACTH, corticosteroids, or immunosuppressive drugs.
4. For individuals with congenital or acquired deficiencies of the immune system, including individuals infected with the human immunodeficiency virus (HIV).
5. For individuals with leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone-marrow or lymphatic systems.
6. During pregnancy.
7. For prevention or treatment of recurrent herpes simplex infections, warts, or any other diseases.

## Precautions

### GENERAL

After completion of the multiple-pressure or multiple-puncture vaccination, blot off any vaccine remaining on skin at vaccination site with clean, dry gauze or cotton.

The vaccine vial, its stopper, the diluent cartridge, the needle used for administration, and any gauze or cotton that came in contact with the vaccine should be burned, boiled, or autoclaved before disposal.

Individuals susceptible to adverse effects of vaccinia virus, e.g., those with eczema, immunodeficiency states, including HIV infection, should be identified and measures taken to avoid contact with persons with active vaccination lesions. Contact-spread of vaccinia from recently vaccinated military personnel has been reported.<sup>2,3</sup>

In the past, it has been generally recommended that there be an interval of no less than one month between administrations of live-virus vaccines, whenever possible. However, simultaneous administration of various live-virus vaccines offers some obvious advantages, particularly when there is a threat of concomitant exposure, when the individual to be immunized may be inaccessible for further immunization, or when a one-month interval would disrupt immunization programs. Such situations are valid reasons for simultaneous administration of poliovirus, measles, smallpox, and yellow fever vaccines, provided no contraindication is present to use of any of the individual vaccines. If the theoretically desirable one-month interval is not feasible, the vaccines should be given on the same day—at different sites for parenteral products. An interval of two days to one month between live-virus-vaccine administrations should always be avoided.

### PREGNANCY CATEGORY C

Animal reproduction studies have not been conducted with smallpox vaccine. Smallpox vaccine should not be given to a pregnant woman.

### PEDIATRIC USE

Smallpox vaccine should not be given to children under 12 months of age unless they are at risk of contracting smallpox.<sup>4,5,6,7</sup>

See also "Contraindications," 1 to 5.

### Adverse Reactions

Complications that may follow either primary or revaccination include: encephalitis, encephalomyelitis, encephalopathy, transverse myelitis, acute infectious polyneuritis; vaccinia necrosum; eczema vaccinatum; generalized vaccinia; accidental infection (autoinoculation); generalized rashes (erythematous, urticarial, nonspecific); and secondary pyogenic infections at the site of vaccine applications. Such complications may result in severe disability, permanent neurological sequelae, and/or death. Accidental infection (autoinoculation) of the eye may result in blindness. Lane and Millar<sup>4</sup> have analyzed the available data and estimated the risks of occurrence of complications after primary vaccination as follows:

COMPLICATION RATES PER MILLION PRIMARY SMALLPOX VACCINATIONS IN THE UNITED STATES BY AGE AND DIAGNOSIS:

	Age at vaccination (in years)			
	1	1-4	5-19	20+
Death (from all complications)	5	0.5	0.5	unknown
Postvaccinial encephalitis	6	2	2.5	4
Vaccinia necrosum	1	0.5	1	7
Eczema vaccinatum	14	44	35	30
Generalized vaccinia	394	233	140	212
Accidental infection	507	577	371	606
Erythematous urticarial reactions	unknown	9,600	unknown	unknown

The risk associated with revaccination is low but, as stated above, such complications have occurred, especially in patients with underlying diseases or receiving therapy which impairs immunologic competence or in subjects who have not been vaccinated for many years. Subjects who have not been vaccinated for many years may respond as primary vaccinees as regards both the local and systemic reaction to vaccine administration and risk of occurrence of the above-mentioned serious complications.

### Dosage and Administration

#### DIRECTIONS FOR RECONSTITUTION

Reconstitution of DRYVAX utilizes the principle of transfer of diluent from its container to the vaccine vial by means of the vacuum present in the vaccine vial. Careful attention to the following directions will preserve the vacuum until needed for diluent transfer and will assure proper reconstitution of the lyophilized vaccine.

## Description

DRYVAX, SMALLPOX VACCINE, DRIED, is prepared from calf lymph. The calf lymph is purified, concentrated, and dried by lyophilization. During processing, not more than 100 units of polymyxin B sulfate, 200 micrograms of dihydrostreptomycin sulfate, 200 micrograms of chlortetracycline hydrochloride, and 100 micrograms of neomycin sulfate per mL are added, and trace amounts of these antibiotics may be present in the final product. The reconstituted vaccine has been shown by appropriate test methods to contain not more than 200 viable bacterial organisms per mL.

The Diluent for DRYVAX, SMALLPOX VACCINE, DRIED, contains 50% glycerin, 0.25% phenol in Sterile Water for Injection, USP, with 0.005% brilliant green.

The reconstituted vaccine which contains approximately 100-million living vaccinia viruses per mL is intended only for multiple-pressure or multiple-puncture use.

## Clinical Pharmacology

Introduction of potent smallpox vaccine containing living vaccinia viruses into the superficial layers of the skin results in viral multiplication, immunity, and cellular hypersensitivity. With the primary vaccination, a papule appears at the site of vaccination on about the third day. This becomes a vesicle on the fifth or sixth day, which becomes pustular, umbilicated, and surrounded by erythema and induration. The maximal area of erythema is attained between the eighth and twelfth day following vaccination (usually the tenth). The erythema and swelling then subside, and a crust forms which comes off about the twenty-first day. At the height of the primary reaction known as the Jennerian response, there is usually regional lymphadenopathy and there may be systemic manifestations of fever and malaise.

The primary vaccination elicits immunity, which wanes after several years, and an allergic sensitization to viral protein which persists. This allergy is manifested by the appearance of a papule and a small area of redness appearing within the first 24 hours after revaccination; this may be the maximum reaction but not infrequently vesicles appear in 24 to 48 hours with ultimate scabbing. The peak of this type of reaction is passed within three days and may follow the application of heat-inactivated or fully potent vaccine; with inactivated vaccine there is no increase in antibodies, but with potent vaccine antibody rise occurs in roughly half of those who exhibit such a reaction. As immunity wanes, revaccination with potent vaccine elicits this allergic response followed by the changes produced by propagating virus. The lesion may then go through the same course as the primary vaccination or may exhibit an accelerated development of the lesion and its attendant erythema. Viral propagation can be reliably assumed to have occurred (and an immune response evoked) when the greatest area of skin involvement (erythema) occurs after the third day following revaccination.

## Indication and Usage

Smallpox vaccine is indicated for immunization against smallpox.

The judicious use of smallpox vaccine has been reported to have eradicated smallpox. At the World Health Assembly in May 1980, the World Health Organization (WHO) declared the world free of smallpox. Smallpox vaccination of civilians is now indicated only for laboratory workers directly involved with smallpox or closely related orthopox viruses (e.g., monkeypox, vaccinia, and others).<sup>1</sup> For those in the above special-risk category, revaccination is recommended at appropriate intervals (every three to five years).

The Armed Forces continue to recommend use of smallpox vaccine for certain categories of personnel. See the most recent issue of Immunization Requirements and Procedures, Department of the Army, the Navy, the Air Force, and Transportation (AR40-562, BUMEDINST 6230.1, AFR 161-13, CG COMDTINST 6230.4) for current recommendations concerning use.

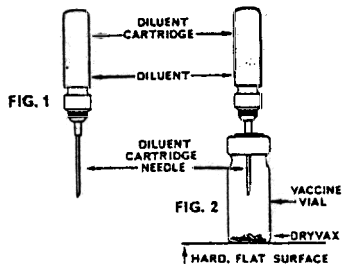
There is no evidence that smallpox vaccination has therapeutic value in the treatment or prevention of recurrent herpes simplex infection, warts, or any other disease. Smallpox vaccine should never be used therapeutically.

## Contraindications

Primary AND revaccination with smallpox vaccine are contraindicated:

1. For infants manifesting failure to thrive.
2. For individuals of any age with eczema, other skin conditions, wounds, or burns and for siblings or other household contacts of such individuals.

1. Lift up tab of aluminum seal on vaccine vial. DO NOT BREAK OFF OR TEAR DOWN TAB.
  2. Wipe off vial stopper with an alcohol sponge and allow to dry.
  3. Place vaccine vial upright on a hard, flat surface.
  4. To reduce viscosity of cold diluent, warm by holding diluent-cartridge in palm of hand for a minute or so. Remove rubber needle cover from needle of diluent-cartridge with needle pointing UP to prevent accidental loss of diluent.
  5. Turn diluent-cartridge so that needle is pointing down. If diluent has not moved to needle-end of diluent-cartridge, AS ILLUSTRATED IN FIG. 1, snap diluent-cartridge with finger. DILUENT MUST BE IN THE NEEDLE-END OF DILUENT-CARTRIDGE BEFORE CARRYING OUT STEP 6.
  6. With a rapid, forceful motion, THRUST diluent-cartridge needle PERPENDICULARLY through stopper of vaccine vial (Fig. 2). The THRUST should be forceful enough to insert the needle to its full length—up to the hub. The vacuum present in vaccine vial will pull diluent from the cartridge into the vial.
- NOTE: Should diluent fail to enter vaccine vial, withdraw diluent-cartridge from vaccine vial and repeat Steps 5 and 6. If correct reconstitution technic has been followed, and if repetition of Steps 5 and 6 fails to cause diluent to be pulled into vaccine vial, the vaccine vial has probably lost vacuum and should be decontaminated and discarded. (See "Precautions"—"General.") However, loss of vacuum is an extremely rare occurrence. Each vial is tested for presence of vacuum before shipment from the manufacturing unit. Therefore, prior to assuming loss of vacuum has occurred, make sure Reconstitution Steps 1 through 6 have been performed correctly.



7. Withdraw diluent-cartridge and discard.
8. Allow vaccine vial to stand undisturbed for 3 to 5 minutes. Then if necessary, swirl vial gently to effect complete reconstitution.
9. Record date of reconstitution in space provided on vaccine vial label.
10. Store reconstituted vaccine below 4° C (39° F), preferably below 0° C (32° F), when not in actual use.

#### DIRECTIONS FOR USE OF RECONSTITUTED VACCINE

1. Remove aluminum seal from vaccine vial by pulling down "tear off" tab.
2. Remove rubber stopper from vaccine vial and discard.
3. Remove white beaded foam platform from carton and break platform at its thinnest point. Discard larger portion of platform.
4. Place opened vial of vaccine upright in hole of remaining portion of platform. When so placed, the vaccine vial is at the proper angle for efficient dipping with the bifurcated needle.
5. Prepare site chosen for vaccination with suitable cleansing agent and allow to dry.
6. Remove plastic cap from needle-case.
7. Gently shake out (by wrist-rotating action rather than by vigorous vertical shaking) the butt-end of a sterile needle. Catch butt-end of needle and gently pull bifurcated point end free.
8. Dip bifurcated point of needle into vaccine. The needle will pick up a drop of vaccine in space between the two points.
9. Deposit the drop of vaccine onto clean, DRY site already prepared for vaccination. Do not redip needle into vaccine if needle has touched skin.
10. With the same needle, and using multiple-pressure or multiple-puncture technic, vaccinate through drop of vaccine. Only 2 or 3 needle pressures or punctures are recommended for primary vaccination; 15 for revaccination.

11. Discard needle.
12. Repeat steps 7 through 11 for each individual to be vaccinated.
13. If vaccine is to be stored for subsequent use, push vial, neck-end first, into proximal, open end of needle-case cap. In so doing, the vial will engage a protective stopper-cap. Remove capped vial from needle-case cap and replace needle-case cap on needle-case. WITHOUT REMOVING FROM PLATFORM, store capped vial below 4° C (39° F), preferably below 0° C (32° F).
14. When next needed, remove vial from refrigerator or freezer and carefully take off stopper-cap.
15. Repeat Steps 5 through 11.
16. If vaccine is to be restored for subsequent use, replace stopper-cap and store below 4° C (39° F), preferably below 0° C (32° F).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

#### INTERPRETATION OF RESPONSES

The vaccination site should be inspected 6 to 8 days after vaccination. The response should be interpreted as follows:

##### Primary Vaccination

A primary vaccination which is successful should show a typical Jennerian vesicle (see "Clinical Pharmacology") and may be accompanied by fever, regional lymphadenopathy, and malaise persisting for a few days. If the typical vesicle is not observed, vaccination procedures should be checked and vaccination repeated with another lot of vaccine on a different area of skin until a successful result is obtained.

##### Revaccination

Following revaccination, two responses are defined by the WHO Expert Committee on Smallpox, eliminating use of older terms such as "accelerated," "vaccinoid," and "immune."

##### a. "Major Reaction"

A vesicular or pustular lesion or an area of definite palpable induration or congestion surrounding a central lesion which may be a crust or ulcer. This reaction indicates that virus multiplication has most likely taken place and that the revaccination is successful. Major reactions, especially when there has been an interval of many years since the last successful vaccination, may be accompanied by fever, regional lymphadenopathy, and malaise persisting for a few days.

##### b. "Equivocal Reaction"

Any other reaction should be regarded as equivocal. These responses may be the consequence of immunity adequate to suppress virus multiplication or may represent only allergic reactions to an inactive vaccine. If an equivocal reaction is observed, revaccination procedures should be checked and revaccination repeated with another lot of vaccine.

#### How Supplied

Combination package of 1 vial of Dried Smallpox Vaccine, 1 container of Diluent (0.25 mL, sufficient for 100 vaccinations), and 100 sterile bifurcated needles.

#### Storage

Store DRYVAX in the refrigerator (2-8° C, 35-46° F). RECONSTITUTED DRYVAX may be used for 3 months if stored below 4° C (39° F), preferably below 0° C (32° F), when not in actual use. At time of reconstitution, record date in space provided on vial label. DRYVAX should not be used after the expiration date regardless of whether it is in the dry or reconstituted form.

#### References

1. MMWR 34:341, 1985.
2. MMWR 33:37, 1984.
3. MMWR 34:182, 1985.
4. LANE, J. & MILLAR, J. Risks of smallpox vaccination complications in the United States. *Am. J. Epidemiol.* 93:238, 1971.
5. NEFF, J. et al: Complications of Smallpox Vaccination, *NEJM* 276(3): 426, 1967.
6. LANE, J. et al: Complications of Smallpox Vaccination, 1968: Results of Ten State-wide Surveys. *J. Inf. Dis.* 722:303, 1970.
7. LANE, J. et al: Complications of Smallpox Vaccination, 1968. *National Surveillance in the United States. NEJM* 281(22): 1201, 1969.