

### **3. Indications for Vaccination during a Smallpox Emergency**

By far, the most common mode of transmission of smallpox from person-to-person is from spread through direct deposit of infective droplets onto the nasal or oral mucosal membranes, or into the alveoli of the lungs of a susceptible person. This generally requires face-to-face contact of  $\leq 2$  meters ( $\leq 6.5$  feet) as the droplets do not travel more than a few meters in the air before settling out onto the ground. Much less commonly and under certain circumstances, smallpox can be spread by fine-particle aerosols that can travel in the air greater distances than droplets. This type of spread usually occurred in hospital settings where more severe cases of smallpox or cases with a cough were admitted and not isolated to areas of the hospital that had air supply and ventilation systems separate from other areas. In rare instances, smallpox has also been spread by contact with contaminated materials.

In a smallpox outbreak, the following high-risk groups should be prioritized for vaccination:

- 1) Persons who were exposed to the initial release of the virus.
- 2) Persons who had face-to-face, household, or close-proximity contact ( $\leq 2$  meters = 6.5 feet) with a confirmed or suspected smallpox patient after the patient developed fever and until all scabs have separated (no longer infectious).
- 3) Healthcare personnel, public health personnel, first responders, law enforcement personnel, and others whose jobs put them at increased risk of exposure to smallpox.
- 4) Laboratory personnel involved in the collection or processing of clinical specimens from confirmed or suspected smallpox cases.
- 5) Other persons with increased likelihood of contact with infectious materials from a smallpox patient, such as laundry or medical waste handlers for a facility where smallpox patients are admitted.
- 6) Other groups whose unhindered function is deemed essential to maintaining basic community needs (e.g., transportation, pharmacy, etc), response activities, and who are not otherwise involved in patient-care activities but who have a reasonable probability of contact with smallpox patients or infectious materials (e.g., law enforcement, emergency response, or military personnel).
- 7) Because of the potential for greater spread of smallpox in a hospital setting due to aerosolization of the virus from a severely ill patient, vaccination should be considered for those individuals present in the hospital during the time that a case was present and not yet isolated in an appropriate manner in a

room with ventilation separate from other areas of the hospital (see [Guide C— Infection Control Measures for Healthcare and Community Settings and Quarantine Guidelines](#)).

#### 4. Persons with contraindications for vaccination, but not in a situation likely to encounter a smallpox case

**In general, the risk of developing smallpox for face-to-face contacts with smallpox cases outweighs the risk of developing complications for those smallpox case contacts with 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.**

Persons with certain medical conditions are known to have a higher risk of developing severe complications following vaccination with vaccinia vaccine (smallpox vaccine). These include:

1. Persons who have **ever been diagnosed with eczema or atopic dermatitis**, even if the condition is mild or not presently active.

*A household member who has eczema, atopic dermatitis, or a history of eczema or atopic dermatitis who is exposed to a recently vaccinated household member is also at higher risk for developing a postvaccination complication from inadvertent inoculation with virus from the vaccination site of the vaccinated person.*

2. Persons with other acute, chronic, or exfoliative skin conditions such as, burns, impetigo, varicella zoster (shingles), herpes, severe acne, severe diaper dermatitis with extensive areas of denuded skin, or psoriasis should not be vaccinated until the condition resolves. Additionally, persons with Darier's disease should not be vaccinated.
3. Persons with **diseases or conditions which cause immunodeficiency**, such as HIV/AIDS, leukemia, lymphoma, generalized malignancy, agammaglobulinemia, or therapy with alkylating agents, antimetabolites, radiation, immunosuppressive medications, or large doses of corticosteroids (i.e.,  $\geq 2\text{mg/kg}$  body weight or  $20\text{ mg/day}$  of prednisone for  $\geq 2$  weeks). Persons with immunosuppression also include hematopoietic stem cell transplant recipients who are  $<24$  months posttransplant, and hematopoietic stem cell transplant recipients who are  $\geq 24$  months posttransplant, but have graft-versus-host disease or disease relapse. It is also reported that some patients with severe clinical manifestations of some autoimmune diseases

(e.g., systemic lupus erythematosus) may have some degree of immunocompromise as a component of the disease. While there are no data to indicate that an individual is at risk from live virus vaccines due to severe autoimmune disease in the absence of immunosuppressive therapy, individuals with immunodeficiency as a clinical component of their autoimmune disease should not receive the smallpox vaccine.

*A household member who has an immunodeficiency disease or is undergoing one of the therapies listed who is exposed to a recently vaccinated household member is also at risk of developing a post vaccination complication from potential inadvertent inoculation with virus from the vaccination site of the vaccinated person.*

4. Persons with inflammatory eye disease being treatment with steroids.
5. Women who are pregnant or breast-feeding.
6. Persons < 1 year of age.
7. Persons with serious, life-threatening allergies to the antibiotics polymyxin B, streptomycin, tetracycline, or neomycin (risk of anaphylactic reaction to vaccine component, but otherwise no increased risk from the live vaccinia virus unless requires suppressive doses of steroids to control allergic reaction).

In general, individuals with the above conditions should not be vaccinated **unless** they have been exposed to smallpox virus. When there is uncertainty as to the level of exposure to the virus, the risks versus benefits of vaccination must be evaluated.

## **5. Reconstitution, Administration, and Storage of Vaccinia Vaccine**

**Vaccine preparations utilized in response to an outbreak of smallpox may not be licensed and must be administered under an IND protocol as a diluted preparation of an existing vaccine (Dryvax® or Aventis Pasteur vaccines) or as a newly developed cell culture vaccine (Acambis and Baxter vaccines). Studies have shown that the existing vaccines can be diluted without affecting the ability of the vaccine to produce the expected vaccine skin reaction (vaccine take). Newer cell culture vaccines are made with a vaccinia virus strain similar to the one present in the Dryvax® and Aventis Pasteur vaccines and would be expected to have similar protection and vaccine take rates.**

### **Reconstitution of Vaccine with Commercially Packaged Diluent**

Diluent is required for the reconstitution of the lyophilized smallpox vaccine **Dryvax®** prior to administration. The Aventis Pasteur vaccine is already in liquid form but may require the addition of extra diluent if diluted formulations of the vaccine are utilized. Instructions on the reconstitution and preparation of vaccine prior to use for immunizations are vaccine specific and will be provided within the vaccine packaging or accompanying IND protocols. The diluent preparation utilized for reconstituting or diluting vaccines is a 50% glycerin solution with a small amount of phenol as a preservative. Dryvax® also contains trace amounts of polymyxin B, neomycin sulfate, chorotetracycline hydrochloride, and streptomycin sulfate. The Aventis-Pasteur smallpox vaccine does not contain any antibiotics. Information regarding the composition of the different vaccine formulations will also be provided with the vaccine.

NOTE: The vaccine vial, its stopper, the diluent syringe, the needle used for diluent reconstitution of the vaccine, and any gauze or cotton that came in contact with the vaccine should be disposed of as biohazardous waste.

### **Administration of Reconstituted Vaccine**

Sterile, bifurcated needles are used to administer smallpox immunization. The needles are designed to hold the designated dose of vaccine (2.5µl) between the needle prongs to allow delivery to the skin surface. Once on the skin, the needle is used to make superficial punctures at the vaccination site to permit percutaneous penetration of the vaccine. Trace amounts of blood at the vaccination site are visual evidence of successful vaccine delivery.

1. Gloves should be worn when handling opened vaccine vials or used bifurcated needles, also when administering the vaccine, or evaluating a vaccination site. Care should be taken to prevent bacterial contamination of the opened vaccine vial or vaccination site, or self-inoculation of virus to other sites (see Recognition of Adverse Events, below).
2. The site of vaccination should be one that is easily accessible for vaccination and evaluation of the vaccine take on postvaccination days 6 to 8. The outer aspect of the **upper arm** over the insertion of the deltoid muscle should be used as the standard vaccination. Vaccine should not be administered at the same site of a previous vaccination.
3. Cleaning the vaccination site is not necessary unless grossly contaminated. If cleaning is deemed necessary, clean the site with soap and water. If another chemical agent such as alcohol is used, the site should be allowed to **dry thoroughly**. It is essential the site be allowed to dry thoroughly in order to avoid inactivation of the vaccine deposited on the skin.
4. Dip the bifurcated point of a **sterile** bifurcated needle into the vial of reconstituted vaccine in a perpendicular fashion and withdraw the needle

maintaining its position perpendicular to the floor. Do not dip more than one needle into a vaccine vial at a time.

5. **Do not** redip a needle into the vaccine vial if the needle has touched the skin or any other surface outside of the vaccine vial. This will help prevent contamination of the multi-dose vaccine vial.

**Prevention of cross-contamination.** Patient-to-patient transmission of bloodborne viruses has been associated with contamination of multi-dose vials. To prevent an opportunity for such transmission, a contaminated needle should **never** be allowed to re-enter a vaccine vial. Furthermore, surfaces where vaccine is being handled should be free of visible blood, body fluids or other organic soil.

**If a contaminated needle is inadvertently redipped into a vaccine vial, that vial should immediately be discarded to prevent further use.**

Holding the skin of the upper arm taut, the vaccinator should place his/her wrist firmly on the arm. Holding the needle at a 90° angle (perpendicular) to the skin, rapidly (within about 3 seconds) puncture the skin within a 5 mm diameter area (Figure 1). Vaccinators should refer to the materials that accompany the vaccine shipment for instructions on the number of required punctures. Refer to the package insert for licensed vaccines, or the Investigational New Drug (IND) protocol for unlicensed vaccines. The strokes should be sufficiently vigorous to illicit a **trace** of blood at the vaccination site that appears 15-20 seconds later. If no trace of blood is visible after vaccination, additional insertions (see package insert or IND protocols for number) should be made using the same bifurcated needle without reinserting the needle into the vaccine vial. Any remaining vaccine should be wiped off with sterile dry gauze and the gauze disposed of in a biohazard container. If no evidence of vaccine take is apparent after 7 days, the individual may be vaccinated again.

6. Vaccinia virus may be recovered from the site of vaccination beginning at the time of development of a papule (2 to 5 days postvaccination) until the scab separates from the skin (14 to 21 days postvaccination). **The vaccination site can be covered with a porous bandage such as gauze until the scab has separated and the underlying skin has healed, in order to prevent inadvertent contact transmission of the virus to unvaccinated persons or inadvertent inoculation of another body site (see Adverse Events below).** Vaccinees should be instructed about site care and bandaging. The site should be kept dry, however normal bathing can occur. If available, a waterproof bandage can be used to prevent accidental transfer of the virus from the site to other mucosal surfaces when washing. The waterproof bandages should be changed back to a porous bandage after bathing is completed.

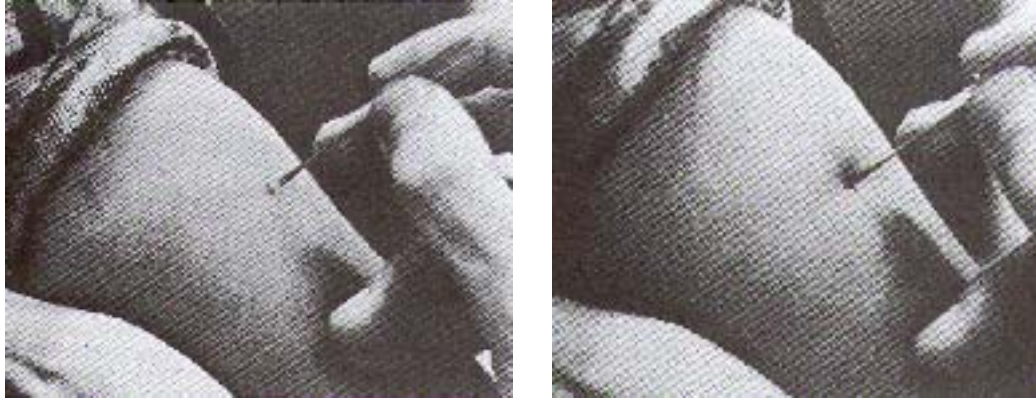


Figure 1. Needle held at a 90° angle to skin then rapid, up-and-down perpendicular strokes are used to administer the vaccine. [Fenner F, Henderson, DA, et al. Smallpox and its eradication. WHO. 1988, Reprinted with permission of WHO]

7. Dispose of the bifurcated needle in a medical waste sharps container.
8. If vaccine is to be stored for subsequent use, recap the vial with the rubber stopper and store the vial according to the manufacturer's recommendations in the package insert or IND protocol instructions that accompany the vaccine.

## 6. Recognition of Expected Vaccine Reactions/Take

Successful vaccination is normally associated with tenderness, redness, swelling, and a lesion at the vaccination site. Primary vaccination may also be associated with fever for a few days and enlarged, tender lymph nodes in the axilla of the vaccinated arm. These symptoms are more common in persons receiving their first dose of vaccine (15 to 20%) than in persons being revaccinated (0 to 10%).

A primary (major) reaction results from successful primary vaccination of a non-vaccinated individual. It is expected that the majority of individuals will exhibit this type of reaction as most have never received vaccination or were vaccinated over 20 years ago. Reactions other than a primary or major reaction in an individual receiving their first vaccination or revaccination after many years should be interpreted as an unsuccessful vaccination, and the individual should be revaccinated.

1. **Primary (major) reaction** – The inoculation site becomes reddened and pruritic 3-5 days after vaccination. The papule becomes vesicular (approximately day 5-8), then pustular, and usually enlarges to reach maximum size in 8-10 days. The pustule dries from the center outward and forms a scab, which separates 14-21 days after vaccination, usually leaving a pitted scar (Figure 2).

A “take” or “major reaction” indicates successful vaccination and is characterized by a pustular lesion or an area of definite induration or congestion surrounding a central lesion, which can be a scab or an ulcer. All other responses are “non-takes” or may also be called “equivocal reactions.” “Non-takes” can be caused by improper vaccination technique, use of vaccine that has lost its potency, or residual vaccinia immunity among previously vaccinated persons. Persons with a “non-take” cannot be presumed to be immune to smallpox, and revaccination is recommended.

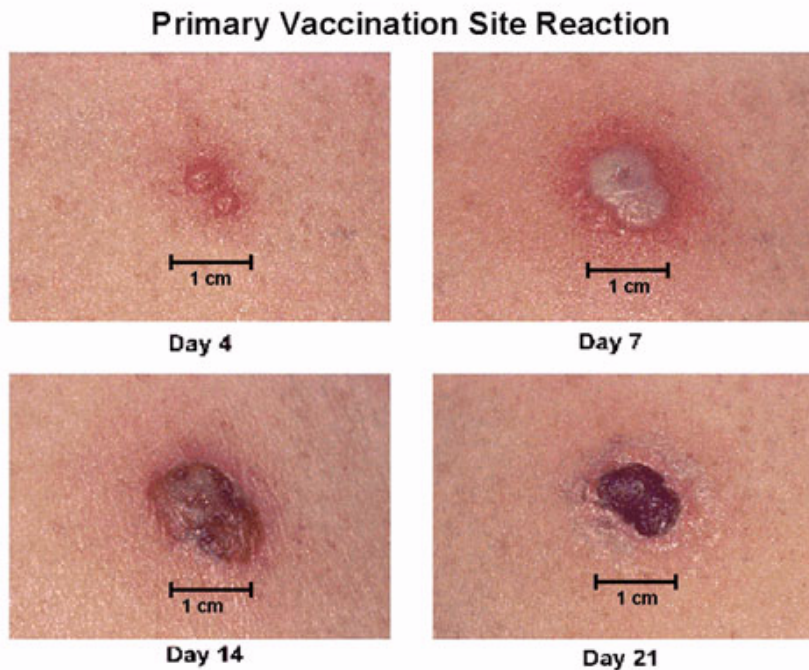


Figure 2. Major (primary) reaction: Expected vaccine site reaction and progression following primary smallpox vaccination or revaccination after a prolonged period between vaccinations. Multiple pressure vaccination technique used. Source: CDC.

At the end of the first week between the vesicular and pustular phases, there may be a variable amount of fever, malaise, and regional lymphadenitis. These symptoms usually subside within 1 to 2 days and are more likely to occur in older children and adults than in infants. Some individuals have a robust primary reaction (i.e., >10 cm in diameter) that peaks between 8-12 days following vaccination (Figure 3). This reaction can consist of painful lymphadenitis, a greater amount of erythema and swelling at the vaccination, and occasional fever. This robust primary reaction should be distinguished from complicating bacterial cellulites of the vaccine site through clinical and laboratory evaluation.



Figure 3. (Left) Robust take with lymphangitis; extensive erythema and induration with a linear streak posteriorly on day 9. (Right) Same patient – full view indicating vaccination site

Revaccination of a person who has been vaccinated within the last 10 years (a partially immune person) is usually followed by an attenuated primary vaccine site reaction with the following characteristics:

- absence of fever or constitutional symptoms,
  - papule by 3<sup>rd</sup> day that becomes vesicular by 5 to 7<sup>th</sup> day, and dries shortly thereafter,
  - a relatively small vesicle and areola, and
  - the scar, if present, is usually insignificant and disappears within 1 to 2 years.
2. A delayed type of skin sensitivity consisting of **erythema only** within 24 to 48 hours may occur following killed as well as live vaccine. Under these circumstances, it represents a response to inert protein in a previously sensitized person. This type of reaction can occur in a highly immunized person or in individuals with little or no immunity and is indistinguishable from the immediate or immune reaction. These persons will appear to have **no take** on vaccination reading days (days 6-8 postvaccination). Therefore, persons exhibiting this type of reaction should be revaccinated (Figure 4).

### Confirmation of Successful Vaccine Take

Successful take of vaccination should be contingent upon the presence of a pustular lesion in a previously unvaccinated person and a pustular lesion or an area of definite induration or congestion surrounding a central lesion, 6-8 days following revaccination in a previously vaccinated person. Vaccinees who do not exhibit the type of “major” reaction at the vaccination site on day 7 illustrated in Figure 4 should be revaccinated. Additional information about evaluation of vaccination take can be found on the CDC Smallpox Web site.



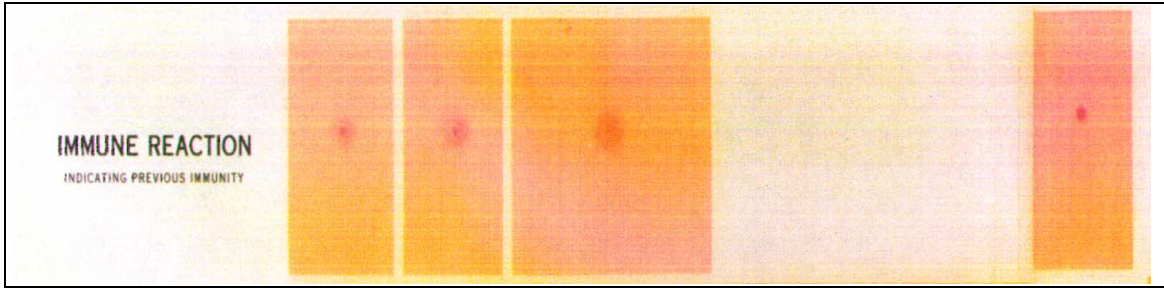


Figure 4. Attenuated reaction in an immune person that can also represent a response to an inert protein without development of immunity. Individuals with this reaction should be revaccinated.

**(Document continues in Guide B – Part 3 of 3)**