

# Key Information Regarding Smallpox Vaccine\*

## General

- Smallpox vaccine is a live-virus vaccine composed of vaccinia virus—a virus closely related to the causative agent of smallpox, *variola major*.<sup>1</sup>
- Immunization with vaccinia virus causes a localized, self-limited infection that elicits an immune response which confers immunity to future infections with the related smallpox virus.<sup>1,2</sup>
- Exactly how long and to what extent immunity to smallpox infection lasts after vaccination is uncertain. The current hypothesis, based on epidemiologic data, is that an increased level of protection against smallpox persists for at least three years after primary vaccination and substantial but waning immunity may persist for  $\geq 10$  years.<sup>3</sup>

## Supply

- Recent studies have shown that existing stocks of smallpox vaccine—15 million doses of Dryvax® (Wyeth Laboratories) and 85 million doses of Glycerated Vaccine (Aventis-Pasteur)—can be diluted to provide sufficient doses to immunize the entire U.S. population should that become necessary.<sup>4-6</sup>
- Dryvax® is the only smallpox vaccine currently licensed by the FDA.<sup>7,8</sup> Licensure does not yet include diluting the vaccine beyond 1:1.<sup>8</sup>
- The U.S. government has ordered 209 million doses of new vaccine—ACAM 1000 & ACAM 2000 (Acambis-Baxter).<sup>9</sup> These vaccines are expected to become available in early 2003 and would need to be administered as investigational new drugs prior to FDA licensure (which is not expected until 2004).<sup>4,10</sup>

## Adverse Events

- Common reactions to smallpox vaccine include fever, redness, and soreness at the site of immunization.<sup>1</sup> Other usually non-life threatening adverse events include: inadvertent inoculation, erythematous or urticarial rashes, erythema multiforme, and generalized vaccinia. The most serious—potentially life-threatening—adverse events are: eczema vaccinatum, progressive vaccinia, and post-vaccinial encephalitis.<sup>1,2,11,12</sup>
- Adverse events occur at higher rates in primary vaccinees and in infants.<sup>11,12</sup> Immunosuppressed individuals also have a higher risk of complications because their compromised immune systems may not be able to con-

tain the normally localized infection caused by the live-virus vaccine.<sup>1,13</sup>

- It has been estimated that as many as 10 million individuals in the United States may be immunocompromised and at risk for severe complications from smallpox vaccination, including 184,000 solid-organ transplant recipients, 850,000 individuals living with HIV infection or AIDS, and approximately 8.5 million cancer patients.<sup>13</sup>
- Those who suffer from atopic dermatitis and eczema appear to have a higher risk of acquiring secondary vaccinia infection (i.e., infection with vaccinia virus as a result of close contact with someone who has been recently vaccinated) and developing complications—such as eczema vaccinatum—through contact vaccinia.<sup>14</sup>
- It has been estimated that if all persons with a history of eczema or atopic dermatitis and their household contacts were excluded from vaccination, approximately 50% of the U.S. population would be excluded from a preemptive, voluntary vaccination program.<sup>15</sup>
- Contraindications to smallpox vaccination are not absolute; the risk of developing a complication from vaccination must be balanced with the risk of developing smallpox after close contact with a contagious person with smallpox.<sup>2</sup>
- Historical data suggest that overall death rates from smallpox vaccination are one per million primary vaccinations and one per 4 million revaccinations.<sup>12</sup>

## Treatment of Adverse Events

- Vaccine immune globulin (VIG) is the only therapeutic product available to treat serious vaccine-related adverse events (excluding post-vaccinial encephalitis and vaccinia keratitis—conditions in which VIG is contraindicated).<sup>2</sup>
- Current supplies of VIG are limited—600–700 doses<sup>16</sup>; supplies are sufficient to treat the complications expected from 4–6 million vaccinations.<sup>17</sup>
- By the end of 2002, VIG supplies were estimated to be ~5,000 doses, sufficient to treat the complications from ~40 million vaccinations.<sup>18</sup>
- Unlike the current VIG formulation, which must be administered intramuscularly, the new supply of VIG will be administered intravenously (which will facilitate administration). However, the new supply must be given as an investigational new drug prior to FDA licensure (DA Henderson, personal communication).

*(continued →)*

\*Data compiled on December 9, 2002, by Michael Mair, Senior Research Assistant, Center for Civilian Biodefense Strategies, Johns Hopkins University, and Luciana Borio, M.D., Clinical Fellow, Division of Infectious Diseases, Johns Hopkins University School of Medicine.

## REFERENCES

1. Henderson DA, Inglesby TV, Bartlett JG, et al. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA*. Jun 9 1999;281(22):2127-2137.
2. Goldstein JA, Neff JM, Lane JM, Koplan JP. Smallpox vaccination reactions, prophylaxis, and therapy of complications. *Pediatrics*. Mar 1975;55(3):342-347.
3. Plotkin SA, Orenstein WA. Chapter 6: Smallpox and Vaccinia. *Vaccines*. 3rd ed. Philadelphia: W.B. Saunders Co.; 1999.
4. Senior K. USA firms up smallpox vaccine plans. *Lancet Infect Dis*. Nov 2002;2(11):649.
5. Frey SE, Couch RB, Tacket CO, et al. Clinical responses to undiluted and diluted smallpox vaccine. *N Engl J Med*. Apr 25 2002;346(17):1265-1274.
6. Frey SE, Newman FK, Cruz J, et al. Dose-related effects of smallpox vaccine. *N Engl J Med*. Apr 25 2002;346(17):1275-1280.
7. Connolly C. FDA Grants License for Smallpox Vaccine; Debate Continues on How Much of U.S. Population Should Be Inoculated. *The Washington Post*. November 2, 2002: Section A; Page A13.
8. Product Approval Information—Licensing Action—Dryvax. Food and Drug Administration. November 6, 2002. Available at: <http://www.fda.gov/cber/products/smalwye-102502.htm>. Accessed November 22, 2002.
9. HHS Awards \$428 Million Contract To Produce Smallpox Vaccine. Department of Health & Human Services. Available at: <http://www.hhs.gov/news/press/2001pres/20011128.html>. Accessed November 9, 2002.
10. Altman LK, Gay Stolberg S. Threats and Responses: The Bioterror Menace; Smallpox Vaccine Backed for Public. *New York Times*. October 5, 2002: Section A; Page 1; Column 1; National Desk.
11. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. *J Infect Dis*. Oct 1970;122(4):303-309.
12. Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968. *N Engl J Med*. Nov 27 1969;281(22):1201-1208.
13. Kemper AR, Davis MM, Freed GL. Expected adverse events in a mass smallpox vaccination campaign. *Eff Clin Pract*. Mar-Apr 2002;5(2):84-90.
14. Neff JM, Lane JM, Fulginiti VA, Henderson DA. Contact vaccinia—transmission of vaccinia from smallpox vaccination. *JAMA*. Oct 16 2002;288(15):1901-1905.
15. Engler RJ, Kenner J, Leung DY. Smallpox vaccination: Risk considerations for patients with atopic dermatitis. *J Allergy Clin Immunol*. Sep 2002;110(3):357-365.
16. Grady D. Threats and Responses: The Side Effects; Medical Conditions Create Vulnerability to Vaccine. *New York Times*. September 24, 2002: Section A; Page 18; Column 11; National Desk.
17. Draft Supplemental Recommendations of the ACIP: Use of Smallpox (Vaccinia) Vaccine, June 2002. Advisory Committee on Immunization Practices. Available at: <http://www.bt.cdc.gov/agent/smallpox/vaccination/acip-guidelines.asp#vig>. Accessed November 9, 2002.
18. McNeil DG, Altman LK. Next Step in Smallpox Effort: Drug for Vaccine Side Effects. *New York Times*. November 12, 2002: Section F; Page 1; Column 3; Science Desk.

Address bulk reprint requests to:  
Mary Ann Liebert, Inc. publishers  
2 Madison Avenue  
Larchmont, NY 10538

Telephone: (914) 834-3100  
E-mail: [reprints@liebertpub.com](mailto:reprints@liebertpub.com)

Published online: December 19, 2002