INFORMATION PAPER

DHA-IHB
16 August 2017

SUBJECT: Smallpox Disease and Smallpox Vaccine

1. Purpose. To describe Smallpox disease and the Smallpox vaccine.

2. Facts.

   a. Microbiology. Variola virus causes the contagious disease smallpox in humans. Variolavirus is a poxvirus of the genus *Orthopoxvirus*. *Orthopoxviruses* are large, complex, brick- shaped, double-stranded DNA viruses that cause infections characterized by a rash. Poxviruses have highly specialized modes of replication and pathogenesis allowing them to replicate in the cytoplasm of infected cells. Because it doesn't replicate in the host cell's nucleus, the poxvirus has no access to the host cell's transcription and DNA replication apparatus, and therefore, has a large genome to support all of its nuclear-replication processes.

   b. Disease. Smallpox was a serious, contagious, and sometimes fatal infectious disease. Typical smallpox disease (variola major) was characterized by fever followed by the development of pocks (raised bumps) through various stages (macules, papules, vesicles, and pustules) on the face and body of the infected person. The word 'pox' comes from the Latin word for 'spotted', referring to the raised bumps that occur during infection with these viruses. The pustules progress from being filled with fluid to umbilication (shrinking in the center), scabbing over, and falling off. After these scabs fall off and the skin underneath is healed, a person is then considered no longer contagious. It is important to know the key differences between smallpox and chickenpox. Smallpox spreads from the extremities towards the center of the body; chickenpox spreads from the center of the body outward. During smallpox infection, lesions usually appear 1-2 days after a high fever and are all in the same stage of development. Chickenpox lesions also appear a few days after a high fever, but emerge in various stages or crops, and typically are more concentrated on the trunk. Historically, smallpox infection killed an average of 30% of those infected, with higher mortality rates among the young. Death often occurred from respiratory or cardiac arrest or hemorrhage as complications of the disease. Smallpox survivors were often scarred and, less often, blinded. A milder case of smallpox was called variola minor. The mortality rate for variola minor was under 1%. There is no Food and Drug Administration (FDA)-approved treatment for smallpox and the only prevention is vaccination. Rigorous use of the

smallpox vaccine resulted in the global eradication of smallpox disease in 1980. Although smallpox has been eradicated in nature, there are concerns smallpox could be used as a bioterror weapon.

c. Epidemiology. Naturally occurring smallpox was highly contagious, and was transmitted from an infected person to a susceptible (unvaccinated) person by respiratory secretions or through contact with infected skin. Transmission usually occurred after prolonged face-to-face contact with a contagious person for three or more hours at a distance of ≤ 6.5 feet. Although less common, transmission through contact with infected skin or inanimate objects (e.g., clothing, towels, bed linens) occurred. Once infected, a person usually began to experience symptoms in 7 to 17 days and was most contagious during the early rash stage following a fever that typically exceeded 101°F (38.3°C). On average, each contagious person infected about 3 to 5 other close contacts such as household members. When smallpox disease was circulating the only known reservoir for the virus was humans; no known animal or arthropod reservoirs existed.

d. Vaccine. The current smallpox vaccine, ACAM2000™, manufactured by Sanofi Pasteur, contains live vaccinia virus derived from the only other smallpox vaccine licensed by the FDA, Dryvax®, which is no longer manufactured. The vaccinia virus used in both vaccines cross-protects against the variola virus by causing a mild infection that stimulates an immune response to smallpox without actually causing the disease. About 95% of primary vaccine recipients are protected for 3 to 10 years or more depending on product and exposure. Individuals at high risk for exposure, such as research laboratory personnel handling variola virus, or in the event of an outbreak, revaccination is recommended every 3 years. For individuals deemed to be at an increased risk, such as segments of the military, revaccination is recommended every 10 years.

e. Vaccine Handling. ACAM2000™ is shipped and stored in the refrigerator at 2-8°C (36-46°F). Once ACAM2000™ is removed from long-term storage at the Centers for Disease Control and Prevention's (CDC) Strategic National Stockpile (SNS), the vials will be labeled with an 18-month expiration date. Un-reconstituted ACAM2000™ should not be exposed to room temperature conditions (23-27°C or 73-81°F) for more than 48 hours. Use vaccine within 30 days of reconstitution. Place vaccine back in the refrigerator (2°C - 8°C, 36°F - 46°F) after each use. ACAM2000 vaccine may be administered during a 6 to 8 hour workday at room temperature but placing the reconstituted vaccine at room temperature for a period of time, and then placing it back in refrigeration (2°C - 8°C) regardless of total of number of cycles or cumulative time out of refrigeration, constitutes thermal cycling the product. If the vaccine is reconstituted and left at room temperature, it should be discarded at the

end of the day or when a maximum of 8 hours at room temperature has been reached. To prevent vaccine from spraying out of the vial during reconstitution, the vial's vacuum seal should be released with a 21 gauge (or smaller) needle inserted into the vial's rubber stopper prior to adding diluent. Gloves should be worn when reconstituting or administering the vaccine. Change gloves in between patients.

f. Precautions. ACAM2000™ contains live vaccinia virus. All vaccinees (whether primary or revaccinee) must be screened for contraindications prior to vaccination using the most current DoD Smallpox Vaccination Screening Form. As a superficially applied live virus vaccine, the virus can be transferred to other parts of the vaccinee's body or transmitted to persons who have close contact with the vaccinee. The risks in contacts are the same as those stated for vaccinees. Individuals at high risk for adverse events identified by the screening process should be deferred from vaccination. Smallpox vaccinations should be deferred during pregnancy and post-pregnancy period, and until a woman has returned to full duty. Screening for contraindications is required by DoD. Children younger than 12 months of age should not get or be exposed to the vaccine. In addition, those allergic to the vaccine or any of its components should not receive the vaccine. Also, people who have been diagnosed by a doctor as having a heart condition with or without symptoms, stroke or transient ischemic attack (a "mini-stroke" that produces stroke-like symptoms but not lasting damage), chest pain or shortness of breath with activity should not get the vaccine. Also, individuals who have 3 or more of the following risk factors should not get the vaccine: high blood pressure; high blood cholesterol; diabetes; a first degree relative (for example, mother, father, brother or sister) with a heart condition before the age of 50; and/or, currently a cigarette smoker. In the event of a smallpox outbreak, weigh the risks of vaccination with the risks of exposure.

g. Immunization. Screen all potential vaccine recipients for eligibility for vaccination using standardized screening form available from the DHA-Immunization Healthcare Branch at www.health.mil/smallpox. Provide all eligible vaccinees a medication guide before vaccination to help educate them about proper care of the vaccination site and to minimize risks associated with the vaccine. For both primary (naïve) vaccinees and re-vaccinees, administer a droplet of ACAM2000™ by percutaneous route (scarification) using 15 jabs with a bifurcated needle into the skin of the arm usually mid-upper arm (just above the insertion of the deltoid muscle) so that if the patient has a tape-sensitivity, a coban-like wrap can be used to secure the dressing. Jabs should be vigorous enough to cause a redness and blood to appear when the skin is broken at the vaccination site. After vaccination, individuals must follow specified site-care

guidelines listed in the DoD implementation policy and the Medication Guide ACAM2000™ approved by the FDA.

h. Adverse Events. There are side effects and risks associated with the smallpox vaccine. Most people experience normal, usually mild reactions that include inoculation site pain, redness, warmth, and itching. Lymphadenitis, malaise, fatigue, fever, myalgia, and headache also occur. However, other people experience reactions involving the skin, nervous system, and heart ranging from serious to life-threatening. Inadvertent inoculation of other body sites such as the face, nose, mouth, lips, genitalia, and anus is a frequent complication. Rare serious adverse events, such as myocarditis and pericarditis, encephalitis, encephalomyelitis, encephalopathy, progressive vaccinia, generalized vaccinia, severe vaccinial skin infections, erythema multiforme major, eczema vaccinatum, ocular complications, and fetal death, have occurred. These adverse events occur less frequently in revaccinated persons than persons receiving the vaccine for the first time. All personnel should report to a healthcare provider immediately if they inadvertently inoculate themselves or others or if they develop any of the above serious adverse events. The Immunization Healthcare Branch staff is available 24 hours a day at 877-438-8222, Option 1, to answer questions from vaccinees or the healthcare team.

i. DoD Policy. Because of concerns about the potential for deliberate use of variola virus as a bioterror weapon, the DoD requires smallpox vaccination of designated at-risk military personnel, DoD civilian personnel classified as emergency-essential, and members of smallpox response teams (e.g., smallpox epidemic response teams, treatment teams, and public health teams). See “Clarifying Guidance for Smallpox and Anthrax Vaccine Immunization Programs” (https://health.mil/Policies/2015/11/12/Clarifying-Guidance-for-Smallpox-and-Anthrax-Vaccine-Immunization-Programs) for more.

j. Special Considerations. Vaccinia virus can be spread from the vaccination site to other parts of the body or to nearby people through close physical contact. This can happen for up to 30 days after vaccination and until the site is healed. Do not touch a smallpox vaccination site or let others touch the site and bandages; this is the best way to avoid spreading the virus. Frequent hand washing also helps prevent spreading the virus if the vaccination site is touched by accident. Dispose of used bandages in a sealed plastic bag with a little bleach or in a sealed double plastic bag.

3. References.

a. Centers for Disease Control and Prevention. Vaccinia (Smallpox) Vaccine.Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2001; 50 (RR10):1-25.

b. Centers for Disease Control and Prevention. Supplemental recommendations for using smallpox vaccine in a pre-event vaccination program. Recommendations of the Advisory Committee on Immunization Practices. MMWR 2003;52(RR-7):1-16

c. Brooks GF, Carroll KC, Butel JS, Morse SA. Poxviruses. In Jawetz, Melnick, & Adelberg's Medical Microbiology. The McGraw-Hill Companies, 24th (ed.) 2007.

d. Control of Communicable Diseases Manual. David L. Heymann.Washington DC, USA: American Public Health Association, 18th (ed.) 2004.

e. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by the Immunization Healthcare Branch: www.health.mil/Smallpox

National Capital Region Regional Vaccine Safety Hub/877-438-8222
Approved: Chief, Immunization Healthcare Branch