INFORMATION PAPER

Military Vaccine Agency
31 July 2009

SUBJECT: Influenza Infection and Influenza Vaccines

1. Purpose. To describe influenza disease and the influenza vaccines.

2. Facts.

a. Background. In the United States, analyses during the 1990s estimated an average of 36,000 annual deaths related to influenza, resulting in large part from an aging U.S. population. The average annual number of hospitalizations associated with influenza in the U.S has been estimated at 226,000.

b. Microbiology. Influenza viruses are divided into three genera, *Influenzavirus* A, *Influenzavirus* B, and *Influenzavirus* C based on antigenic differences in two major structural proteins. Influenza A viruses are further classified by subtype on the basis of the two main surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA). HA is the major antigen against which the host's protective antibody response is directed and is responsible for attachment of influenza viruses to the cell surface during early stages of infection. NA is less abundant on the viral surface and facilitates release of mature virus from infected cells. Antibody to NA is believed to restrict virus spread and reduce severity of the influenza infection. The capacity of influenza A and B viruses to undergo gradual antigenic change in their two surface antigens, the HA and NA, complicates vaccination against the disease. This ongoing process of antigenic drift ensures a constantly renewed pool of susceptible hosts and the repetitive occurrence of epidemics, necessitating annual review of strains to be included in the vaccine and frequent changes in vaccine strains. The strains prevalent in laboratory samples submitted each year are described by the virus type, geographic site where it was first isolated, a strain number, the year of isolation, and the virus subtype (e.g., A/Sydney/5/97(H3N2)). Scientists use this information to estimate which types and strains of influenza virus will circulate during the next influenza season, and then identify these strains for use in the annual influenza vaccine formulation.

c. Disease. Influenza is spread through aerosolized respiratory droplets during close contact with an infected person or animal or through contact with a contaminated object. Primary influenza illness is characterized by the abrupt start of fever, sore throat, headache, myalgia, chills, anorexia, and extreme fatigue with major symptoms lasting an average of 7 days. The presence of cough and temperature are generally the best predictors of influenza illness in adults and children during periods of influenza circulation. Fever usually ranges between 38°C and 40°, but may be higher and usually lasts for 3-5 days. Illness typically improves within a week, but cough and malaise may persist for 2 or more weeks. The incubation period for influenza is commonly 2 days,

but ranges from 1-4 days. Due to this short incubation period, influenza outbreaks may be explosive, especially in highly susceptible populations as can occur in a pandemic.

d. Epidemiology. In temperate climates, influenza activity occurs during the late autumn and winter months. However, in tropical climates, influenza can occur year round. Influenza B viruses have been documented to be in continuous circulation in the human population since their first isolation in 1940; whereas influenza A (H3N2) viruses have been in circulation since their emergence in 1968. During influenza seasons, an estimated 5-20% of the U.S. population can develop influenza, but 40-50% within institutions such as nursing homes is not unusual. In communities, influenza cases often appear first among school-age children. Attack rates usually are the highest in this group and lowest among the elderly whereas rates of serious disease are highest among the elderly, the very young, and those with certain underlying chronic conditions.

e. Vaccine. Two forms of influenza vaccine are distributed in the United States. An inactivated, protein derived vaccine, given by intramuscular injection, and a live attenuated (weakened) vaccine sprayed into the nose. Both the injectable and intranasal vaccines prepared for the 2009-2010 season include A/Brisbane/59/2007 (H1N1)-like virus, A/Brisbane/10/2007 (H3N2)-like virus, and B/Brisbane/60/2008-like antigens. All influenza vaccine must be stored in a refrigerator between 2-8°C (35-46°F) upon receipt and until use before the expiration date on the vial/sprayer label.

(1) Injectable influenza vaccines contain inactivated viruses that have been broken into pieces and then purified. *Fluzone*® is indicated for immunization in people 6 months of age and older. *Afluria*® has not been evaluated in the pediatric population. This vaccine is only indicated for adults 18 years of age or older.

(2) The intranasal influenza vaccine, *FluMist*®, contains live attenuated influenza viruses. Immunization involves spraying 0.1 ml of the vaccine into each nostril. *FluMist*® is indicated for healthy people 2 to 49 years of age.

f. Immunization. CDC's Advisory Committee on Immunization Practices (ACIP) states that injectable and intranasal vaccines should be used to reduce the risk for influenza virus infection and its complications. Healthy, non-pregnant persons aged 2-49 years may choose to receive either type of vaccine; however, ACIP makes specific recommendations for which vaccine are most appropriate for other populations.

g. Adverse Events. The most common serious complications of influenza include exacerbation of underlying chronic pulmonary and cardiopulmonary diseases, such as chronic obstructive pulmonary disease, asthma, and congestive heart failure, as well as development of bacterial pneumonia. Influenza vaccines should not be administered to people with sensitivities to egg proteins (eggs or egg products), chicken proteins or any component of the vaccine. Influenza vaccine should also not be administered to

anyone with an active nervous system disorder or a history of Guillain-Barrẽ syndrome. Report any adverse events to the Vaccine Adverse Events Reporting System (VAERS).

h. DoD Policy. Influenza vaccination is required for military personnel. In accordance with HA Policy 08-005, military treatment facilities are directed to require all civilian healthcare personnel (HCP) who provide direct patient care in DoD MTFs be immunized against seasonal influenza infection each year as a condition of employment, unless there is a documented medical or religious reason not to be immunized. Injectable vaccine will be reserved for people in whom the intranasal vaccine is medically contraindicated or not logistically feasible. Vaccination of other populations is in accordance with ACIP recommendations.

3. References.

a. Advisory Committee on Immunization Practices, Prevention and Control of Influenza, MMWR, 2009; 58; (31 July 2009) [revised annually]. www.cdc.gov/mmwr/preview/mmwrhtml/rr5808a1.htm.

b. Vaccine Adverse Event Reporting System filing instructions and forms are available at www.vaers.hhs.gov.

c. ASD (HA) Memorandum, Subject: Policy Guidance for the Use of Influenza Vaccine for the 2009-2010 Influenza Season, XX Aug 09: www.ha.osd.mil/policies/default/cfm.

d. HA Policy 08-005, Policy for Mandatory Seasonal Influenza Immunization for Civilian Health Care Personnel Who Provide Direct Patient Care in Department of Defense Military Treatment Facilities, 4 April 2008: www.vaccines.mil/documents/1169HCPFluHAPolicy_08_005.pdf.

e. Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases.* Atkinson W, Hamorsky J, McIntyre L, Wolfe S, eds. 11th ed. Washington DC: Public Health Foundation, 2009. The Pink Book. www.cdc.gov/vaccines/pubs/pinkbook/default.htm.

f. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by Military Vaccine Agency: www.vaccines.mil/influenza.

Mr. Don Dutra/(703) 681-0623

Approved: LTC Garman