INFORMATION PAPER

Military Vaccine Agency
22 October 2009

SUBJECT: Novel A(H1N1) Influenza Vaccine

1. Purpose. To describe Novel A(H1N1) Influenza infection and vaccines.

2. Facts.

a. Background. Novel A(H1N1) influenza is a new influenza virus of swine origin that first caused illness in Mexico and the United States in April, 2009. It is thought that novel A(H1N1) influenza spreads in the same way that regular seasonal influenza viruses spread, mainly through coughs and sneezes of people who are sick with the virus. It may also be spread by touching infected objects and then touching your nose or mouth. Novel A(H1N1) influenza infection has been reported to cause a wide range of flu-like symptoms, including fever, cough, sore throat, body aches, headache, chills, and fatigue. In addition, many people also have reported nausea, vomiting and/or diarrhea.

b. Microbiology. Influenza A viruses are negative-sense single-stranded RNA viruses and belong to the family Orthomyxoviridae and the genus Influenzavirus A. Enveloped virions consist of spike-shaped surface proteins, a partially host-derived lipid-rich envelope, and matrix (M) proteins surrounding a helical segmented nucleocapsid (6 to 8 segments). The virus envelope glycoproteins (hemagglutinin [HA] and neuraminidase [NA]) are distributed evenly over the virion surface, forming characteristic spike-shaped structures; antigenic variations in these proteins form the basis of the classification system for influenza A virus subtypes.

There are 16 different HA antigens (H1 to H16) and nine different NA antigens (N1 to N9) for influenza A. Human disease historically has been caused by three subtypes of HA (H1, H2, and H3) and two subtypes of NA (N1 and N2). More recently, human disease has been recognized to be caused by additional HA subtypes, including H5, H7, and H9 (all from avian origin). All of these subtypes have been found in birds, and birds are the primordial reservoir for influenza A viruses. Several subtypes have been found in pigs.

The 2009 novel A(H1N1) influenza virus appears to be of swine origin and contains a unique combination of gene segments that has not been identified in the past. The NA and M gene segments are in the Eurasian swine genetic lineage; they were originally derived from a wholly avian influenza virus and likely entered the Eurasian swine population in 1979. Until emergence of the current novel H1N1 strain, these gene segments had not been identified outside Eurasia. The HA, NP, and NS gene segments are in the classical swine lineage; they likely entered the swine population around 1918 and are common in North America. The PB2 and PA gene segments are in the swine triple reassortant lineage; viruses of this lineage entered pigs in North America around 1998. Viruses that seeded this lineage were originally of avian origin. The BP1 gene segment is in the swine triple reassortant lineage and was seeded in

pigs from humans also around 1998; this virus was also originally from an avian source. A recent molecular analysis of the novel H1N1 virus demonstrates that the virus possesses a distinctive evolutionary trait (genetic distinctness) that may be characteristic in pig-human interspecies transmission of influenza A.

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 estimated incubation period is unknown and could range from 1 to 7 days, although the incubation period for most cases will likely range from 1 to 4 days. Due to this short incubation period, influenza outbreaks may be explosive, especially in highly susceptible populations as can occur in a pandemic. The duration of shedding for the novel A(H1N1) influenza virus is unknown; therefore, until data are available, the estimated duration of viral shedding is based on seasonal influenza virus infection. Infected persons are assumed to be shedding virus from the day prior to illness onset until resolution of symptoms. Persons with novel A(H1N1) influenza infection should be considered potentially contagious for up to 7 days following illness onset. Persons who continue to be ill longer than 7 days after illness onset should be considered potentially contagious until symptoms have resolved. Children, especially younger children, and immunosuppressed or immunocompromised persons might be contagious for longer periods.

d. Epidemiology. The epidemiology of novel A(H1N1) influenza virus infection is under investigation, and epidemiologic characteristics might change as transmission continues. Outbreaks in settings in which young persons congregate have been a frequent source of community transmission. Transmission of novel A(H1N1) influenza virus infection in healthcare settings has been reported. Among 11 healthcare personnel (HCP) with probable or possible patient-to-HCP acquisition and available information on personal protective equipment use, only three HCP reported always using either a surgical mask or an N95 respirator in one case series. Acquisition of novel A(H1N1) influenza virus infection by HCP in community settings also has been identified, raising the possibility of introduction of novel A(H1N1) influenza viruses to patients in healthcare settings by infected HCP.

e. Vaccine. Both live, attenuated and inactivated novel A(H1N1) 2009 influenza monovalent vaccine formulations will be available initially; as with seasonal influenza vaccines, neither of these vaccines contain adjuvants. The Food and Drug Administration and the World Health Organization have selected A/California/07/2009

(H1N1) for use as the strain for the vaccines. 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. It is administered by intramuscular route, into the deltoid muscle.

(2) The intranasal influenza vaccine contains live attenuated influenza virus. Immunization involves spraying 0.1 ml of the vaccine into each nostril.

(3) One dose is required for those 10 years of age and up. For children 6 months to 9 years of age, 2 doses should be administered approximately one month apart.

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 should receive either type of vaccine. 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. Adverse events should be reported to the Vaccine Adverse Events Reporting System (VAERS).

h. DoD Policy. The goal is for all members of the DoD community who wish to be immunized, to receive the vaccine. See HA policy. (http://www.vaccines.mil/documents/1291DoD_H1N1_Policy_Sep2009.pdf)

i. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by Military Vaccine Agency: http://www.vaccines.mil/h1n1.

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