



Arkansas Department of Health

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Governor Mike Beebe

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May 6, 2010

Influenza Testing Update: Total number of samples tested last month= 150. There were 5 positive samples, all were H1N1.

Licensure of a High-Dose Inactivated Influenza Vaccine for Persons Aged ≥ 65 Years (Fluzone High-Dose) and Guidance for Use - United States, 2010, *MMWR*, April 30, 2010 / 59(16);485-486

Persons aged ≥ 65 years are at greater risk for hospitalization and death from seasonal influenza compared with other age groups (1,2), and they respond to vaccination with lower antibody titers to influenza hemagglutinin (an established correlate of protection against influenza) compared with younger adults (3). On December 23, 2009, the Food and Drug Administration (FDA) licensed an injectable inactivated trivalent influenza vaccine (Fluzone High-Dose, Sanofi-Pasteur) that contains an increased amount of influenza virus hemagglutinin antigen compared with other inactivated influenza vaccines such as Fluzone. Fluzone High-Dose is licensed as a single dose for use among persons aged ≥ 65 years and will be available beginning with the 2010-11 influenza season. The Advisory Committee on Immunization Practices (ACIP) reviewed data from prelicensure clinical trials on the safety and immunogenicity of Fluzone High-Dose and expressed no preference for the new vaccine over other inactivated trivalent influenza vaccines (4). This report summarizes the FDA-approved indications for Fluzone High-Dose and provides guidance from ACIP for its use.

Standard dose inactivated trivalent influenza vaccines contain a total of 45 μg (15 μg of each of the three recommended strains) of influenza virus hemagglutinin antigen per 0.5mL dose (5). In contrast, Fluzone High-Dose is formulated to contain a total of 180 μg (60 μg of each strain) of influenza virus hemagglutinin antigen in each 0.5mL dose. Like other inactivated influenza vaccines, Fluzone High-Dose is administered as an intramuscular injection (6). Fluzone High-Dose is available as a single-dose prefilled syringe formulation and is distinguished from Fluzone by a gray syringe plunger rod. As with other 2010--11 influenza vaccines, Fluzone High-Dose will contain antigens of the three recommended virus strains: A/California/7/2009 (H1N1)-like, A/Perth/16/2009 (H3N2)-like, and B/Brisbane/60/2008-like (7).

Immunogenicity data from three studies among persons aged ≥ 65 years indicated that, compared with standard dose Fluzone, preparations of Fluzone High-Dose elicited significantly higher hemagglutination inhibition (HI) titers against all three influenza virus strains that were included in seasonal influenza vaccines recommended during the study period (8--10). In one study, prespecified criteria for superiority, defined as when the lower 95% confidence limit of 1) a ratio

of geometric mean HI titers is >1.5 for at least two strains and 2) the difference in fourfold rise of HI titers is $>10\%$ for at least two strains, were demonstrated for persons aged ≥ 65 years who received Fluzone High-Dose compared with Fluzone for influenza A(H1N1) and influenza A(H3N2) antigens. Prespecified criteria for noninferiority to Fluzone were demonstrated for the influenza B antigen (6,9). Whether the higher postvaccination immune responses observed among Fluzone High-Dose vaccine recipients will result in greater protection against influenza illness is unknown.

Solicited injection site reactions and systemic adverse events were more frequent after vaccination with Fluzone High-Dose compared with standard Fluzone, but typically were mild and transient (8--10). In the largest study, 915 (36%) of 2,572 persons who received Fluzone High-Dose, compared with 306 (24%) of 1,275 persons who received Fluzone, reported injection site pain ≤ 7 days after vaccine administration. In the same study, significantly more Fluzone High-Dose recipients (1.1%) reported moderate ($>100.4^{\circ}\text{F}$ -- $\leq 102.2^{\circ}\text{F}$ [$>38^{\circ}\text{C}$ -- $\leq 39^{\circ}\text{C}$]) to severe ($>102.2^{\circ}\text{F}$ [$>39^{\circ}\text{C}$]) fever, compared with Fluzone recipients (0.3%)(9).

ACIP Guidance for Use of Fluzone High-Dose

Fluzone High-Dose may be used for persons aged ≥ 65 years. All persons aged ≥ 6 months are recommended for annual influenza vaccination beginning with the 2010--11 influenza season. ACIP has not expressed a preference for any specific licensed inactivated trivalent influenza vaccine, including Fluzone High-Dose, for use in persons aged ≥ 65 years (4). Data demonstrating greater protection against influenza illness after vaccination with Fluzone High-Dose are needed to evaluate whether Fluzone High-Dose is a more effective vaccine for persons aged ≥ 65 years. A 3-year postlicensure study of the vaccine effectiveness of Fluzone High-Dose compared with standard dose inactivated influenza vaccine (Fluzone) was begun in 2009 and should be completed in 2012. As with other inactivated influenza vaccines, Fluzone High-Dose should not be administered to anyone with a known hypersensitivity to egg proteins or influenza vaccine. Adverse events after receipt of any vaccine should be reported to the Vaccine Adverse Event Reporting System at <http://vaers.hhs.gov>.

If you have any questions please feel free to contact Dr. Sandy Snow at 501-661-2169 or fax to 501-661-2300 or e-mail to Sandra.snow@arkansas.gov

