FDA Panel Backs Approval of 'Stopgap' Vaccine for Avian Flu

BY ELIZABETH MECHCATIE
Senior Writer

GAITHERSBURG, MD. — An inactivated H5N1 influenza virus vaccine that a federal advisory panel has recommended for approval would, if approved, become the first vaccine for avian influenza licensed in the United States.

At a meeting of the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee, the panel agreed that that there were sufficient data to support the safety and effectiveness of the investigational vaccine during an avian flu pandemic or in situations of potential high-risk exposure. The vaccine is based on an A/Vietnam strain of the H5N1 avian influenza virus.

The proposed indication for the vaccine, manufactured by Sanofi Pasteur, is for active immunization against influenza disease caused by the H5N1 A/Vietnam/1203/2004 influenza virus and for primary vaccination of healthy adults aged 18-64. Two 90-mcg doses of the vaccine would be administered intramuscularly, 28 days apart.

The vaccine is made using the same process as the seasonal influenza vaccine, which panel members said provided reassurance of its safety.

If approved, the vaccine would not be available commercially but would be part of the prepandemic vaccine stockpile in the United States.

This "is an important step in the development of a pandemic influenza vaccine," said panel chair Dr. Ruth A. Karron, professor in the department of international health, Johns Hopkins School of Hygiene and Public Health, Baltimore.

Throughout the meeting, panelists and FDA officials referred to the vaccine as an "interim" or "stopgap" vaccine. Many other vaccines are being developed that are potentially better than this vaccine, said Dr. Norman Baylor, director of the FDA's office of vaccines research and review.

Panelist Robert Webster, Ph.D., chair of the department of virology and molecular biology at St. Jude Children's Research Hospital, Memphis, said it would not be clear how well the current vaccine works unless it were used in an actual pandemic. Nevertheless, if the H5N1 influenza virus does acquire human-to-human transmissibility, there will not be enough time to produce enough vaccine, so "we need this stockpile," he said.

The vaccine is manufactured with the same process used for the seasonal influenza virus vaccine, which several panel members said provided reassurance about its safety.

The vaccine contains a much higher amount of antigen than the seasonal flu vaccine, however, which raised some concerns about the potential for adverse effects.

Safety and efficacy data came from a prospective, multicenter randomized double-blind phase I/II trial launched in 2004 and conducted by the National Institute of Allergy and Infectious Diseases. Investigators measured hemagglutinin inhibition (HAI) immunogenicity in 452 adults, aged 18-64, who received two injections of different vaccine doses 28 days apart.

The response rate—at least a fourfold increase in the HAI titer 28 days after the injection—among those who received the 90-mcg dose was 23% after the first dose and 45% after the second dose, with a waning of the response rate to about 18% 6 months after the second dose, said Dr. Andrea James of the FDA's division of vaccines and related product applications.

The immunogenicity in this study is less than that usually seen in studies of seasonal influenza vaccine, she pointed out.

Dose-related injection site reactions were the most common side effects, with 85% of those receiving 90-mcg doses having at least one such reaction. Systemic events were less frequent, with about 40% developing headache and 30% developing malaise with the 90-mcg dose, Dr. James said.

The vaccine is also being investigated in a study of 259 elderly adults and a study of 125 children aged 2-9. Once the FDA makes a decision about licensing of the vaccine for people ages 18-64, the company will initiate discussions about expanding the age range for approval, according to Sanofi Pasteur. ■

Containment Should Be Top Priority in Case of Flu Pandemic

BY MARY ELLEN SCHNEIDER
New York Bureau

BOSTON — In the event of an avian influenza pandemic, old-fashioned containment strategies will need to be the first line of defense to limit exposure, David Heyman, a terrorism expert, said at the annual meeting of the American Public Health Association.

The best countermeasure in the case of a pandemic is vaccine, but vaccine is unlikely to be available for at least 4-6 months after the onset of the outbreak.

Antiviral treatment could help improve outcomes but has been shown to have only a modest effect on transmission and may also be in short supply in the event of an influenza pandemic, said Mr. Heyman, director and senior fellow for the Center for Strategic and International Studies' Homeland Security Program in Washington.

The U.S. strategy for responding to an avian influenza pandemic has so far centered on vaccine production and development, stockpiling of antiviral medications, and state plans for distribution.

Although it is important to focus on vaccines and antivirals, those treatments are unlikely to be ready in time for the first wave of a pandemic, he said.

"There are a number of tools in our toolbox. The strategy needs to be figured out. We don't have a specific strategy right now," Mr. Hewitt said.

The key to bringing a pandemic under control will be to slow transmission until vaccines and other medicines become available.

Some possible elements of a disease-containment strategy being considered by the U.S. government include closing schools, encouraging social distancing, voluntary household quarantines, and masking and good infection control.

It is important that the least restrictive measures necessary are used, and the public must be engaged as a partner in the response, he said. "They need to be educated, starting today."

However, implementing such containment strategies would be a challenge because many people are resistant to strategies that involve quarantine because of "the historical use of quarantines that led to deprivation of rights and privacy," he said.

FDA Advisory Panel Selects 2007-2008 Influenza Vaccine Strains

BY ALICIA AULT
Associate Editor, Practice Trends

GAITHERSBURG, MD. — The 2007-2008 trivalent influenza vaccine should retain two strains from the current vaccine and change one strain, a Food and Drug Administration advisory panel has concluded.

The Vaccines and Related Biological Products Advisory Committee followed the lead of the World Health Organization, which made its recommendations for a Northern Hemisphere winter vaccine a week earlier.

In most cases, the FDA follows its panel's advice.

The decision gives the green light to manufacturers to go ahead with production. It generally takes until July or August for vaccine makers to complete testing, acquire FDA approval, and begin packaging their product.

Distribution usually starts in September and ends by Nov. 1.

Based on surveillance reports, the availability of seed stock to grow viruses, and reagents to test potency, vaccine makers already had begun production of most of the strains that ultimately were selected, said Albert Thomas, a Sanofi Pasteur representative who spoke at the FDA meeting. The manufacturers take the early production risk in order to speed up the process, he explained.

If the FDA committee had chosen different strains, vaccine makers likely would have had to reduce their ultimate production by 20%, Mr. Thomas said.

That potential production loss pushed the committee to vote against changing one component, the influenza A (H3N2) strain, even though the most recent surveillance data suggest that a different H3 strain currently is emerging.

The WHO recommended keeping the current H3N2 strain, which is the A/Wisconsin/67/2005-like virus. The 2006-2007 flu season had been dominated mostly by influenza A (H1N1) strains, said Nancy J. Cox, Ph.D., director of the Centers for Disease Control and Prevention's influenza division. But in February, it appeared that H3N2 strains were starting to dominate. It wasn't clear yet which of those might be the predominant H3 strain, Ms. Cox said.

Even though panelists were concerned about the emergence of a new H3N2 subtype, 11 of 13 members voted to keep the current H3 strain. "At this point, I feel like we don't have any choice," said Dr. Melinda Wharton, deputy director of the CDC's National Immunization Program and a temporary voting member of the committee. She noted that manufacturers already had started production on the current H3 strain.

Two committee members said they wanted to defer a decision until more surveillance data were available.

The panel voted unanimously to change the current H1N1 strain from A/New Caledonia/20/99-like virus with A/Solomon Islands/3/2006. The WHO had recommended that change.

The FDA committee also voted unanimously to retain the current B strain—B/Malaysia/2506/2004-like virus—mirroring the WHO recommendation.

The 2006-2007 season has been fairly mild, Ms. Cox said. As of Feb. 17, widespread flu activity was reported in 24 states, 14 states reported regional activity, 10 reported local activity, and 2 reported sporadic activity.

For adults, the death rate from pneumonia and influenza—at 6.9%—was below the epidemic threshold of 7.9%. There were 3 pediatric deaths during that week, bringing the total to 15 deaths since the season began Oct. 1, 2006. ■