Fed Purchase of Avian Flu Vaccine Suggested

Advisors want the government to purchase all doses and prioritize their use in a pandemic.

BY HEIDI SPLETE
Senior Writer

ROCKVILLE, MD. — Should the United States face an influenza pandemic, the federal government should buy all the vaccine, members of the National Vaccine Advisory Committee agreed at a joint meeting with the Advisory Committee on Immunization Practices.

The committees met to review the work of the Pandemic Influenza Working Group and vote on several points in the Department of Health and Human Services' current draft Pandemic Influenza Preparedness Plan.

During deliberations of the National Vaccine Advisory Committee (NVAC), members preferred the government vaccine purchase option over three others, including the current standard purchase of vaccines by a mix of public and private groups. However, they emphasized that the universal government vaccine purchase applied only in the event of a pandemic.

The NVAC also voted to accept the recommendations of the working group's antiviral subgroup. These recommendations included creation of an antiviral drug stockpile sufficient to reduce the public health impact of a flu pandemic. At least 40 million courses of antiviral drugs are needed to provide critical response support in the event of a pandemic, said Andrew Pavia, M.D., of the University of Utah, Salt Lake City, who presented the recommendations.

At least 40 million courses of antiviral drugs are needed to provide critical response during a pandemic event.

DR. PAVIA

The NVAC voted that oseltamivir should be the primary drug stockpiled for a flu pandemic, with zanamivir stockpiled as a backup. Although vaccination is the most formidable weapon against a flu pandemic, antiviral drugs are effective when used early in the disease if vaccines are not available, Dr. Pavia noted.

In addition, NVAC members voted to accept the recommendation of the antiviral subgroup on the approximate numbers of drug courses needed for priority target groups including hospitalized patients, health care workers with direct patient contact, pandemic health responders, public safety officials, and government decision makers. They also approved the subgroup's recommendations that additional research to support the use of antivirals in the event of a flu pandemic should include the safety of oseltamivir in infants less than 1 year of age, the sensitivity of rapid diagnostic tests for flu strains with pandemic potential, such as H5N1, the impact of antiviral treatment of a flu pandemic on hospital admissions, the testing of an optimal treatment dose and schedule in a ferret model with H5N1 and other flu strains, and the investigation of the potential for use of other antiviral agents.

The NVAC and the Advisory Committee on Immunization Practices (ACIP), both of which advise the Centers for Disease Control and Prevention, also met jointly and voted in favor of a "prioritization table" of people who would be the first to receive vaccines in the event of a flu pandemic.

The supply of vaccine will likely be limited, and identification of priority groups will help decrease the overall health impact of a pandemic while limiting economic disruption and reducing the overall societal impact, said Ben Schwartz, M.D., of the National Vaccine Program Office at the Department of Health and Human Services. The draft prioritization table, created by the Joint ACIP/NVAC Working Group on Pandemic Influenza Vaccine Prioritization, established four tiers.

Tier 1 is subdivided to include persons with direct patient contact and critical support staff, patients in the highest risk group based on the standard ACIP criteria, household contacts of children younger than 6 months, pregnant women, and critical government leaders and pandemic responders.

Tier 2 includes other high-risk patients, followed by those in critical community infrastructure, such as public health emergency responders, public safety, utility, and telecommunications workers.

Tier 3 includes other important government health care decision makers, and mortuary service personnel.

Tier 4 includes healthy people aged 2-64 years who are not in any other group.

"We in clinical care need to have very explicit guidelines as to which patients can be identified upfront [for vaccine priority] by the use of things like administrative databases, coding, and demographic information," commented Jonathan Temte, M.D., the American Academy of Family Physicians' liaison to ACIP.

"We need to develop lists now that correspond to the priority groups, rather than trying to do that on the fly," he said. Explicit definitions given to those in charge of clinics can avoid disruption with staff over situations such as, "you work in the file room, so you don't get a shot."

The draft of the Pandemic Influenza Preparedness Response Plan has been sent to the Department of Health and Human Services for review, with additional revisions possible later this year. ■

U.S. Government Requests 22 Million Avian Flu Vaccine Doses

The U.S. government aims to buy millions of doses of avian influenza vaccine, which preliminary data have shown produces a robust immune response against the A (H5N1) virus in some doses.

"We have been asked to provide up to 20 million doses of the vaccine, in addition to the 2 million we have already agreed to supply," Len Lavenda, spokesman for Sanofi-Pasteur, Swiftwater, Pa., told FAMILY PRACTICE NEWS. The contract would be contingent on the vaccine being approved after thorough testing in clinical trials. Currently, only preliminary information is available about immunogenicity in adults, and trials in children and the elderly have yet to start.

If the vaccine is approved, the 22 million doses will be added to the Strategic National Stockpile of drugs, and distributed only in the event of an H5N1 pandemic.

Although the first clinical trial of 452 healthy adults aged 18-64 years is ongoing, early data show immune response in the 113 subjects for whom serology is available, John Treanor, M.D., said in an interview. The trial is testing four doses of the vaccine (7.5 mcg, 15 mcg, 45 mcg, and 90 mcg). Subjects received an initial vaccination plus a booster of the same dose given about a month later.

All doses produced some response, but only two 90-mcg doses gave a response robust enough to inspire confidence about immunity, said Dr. Treanor, principal investigator of the trial conducted at the University of Rochester (N.Y.).

With the 90-mcg doses, "We're confident the immune response would be protective against the H5 virus," he said. "There was definitely a dose-response reaction."

But the large dose required to produce optimal response could put a strain on manufacturing, making it tough for the government to meet its preliminary quota of 22 million doses, said Anthony Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases.

"This will put an extra strain on the production issue—which has been an issue of concern even before this," he told this newspaper. "We've been talking about the lack of ability to manufacture a global vaccine for a long time. This underscores the issue. It's a problem that will only be solved by getting more companies involved."

Several factors affect vaccine production capacity, said Mr. Lavenda. The concentration of antigen in each dose is one factor.

However, he said, the company recently began construction of a new influenza vaccine facility, which will more than double its U.S. capacity. The facility will probably come online by 2008. An overhaul of the company's French facility, which will double its capacity, is in the works as well.

Researchers will be searching for ways to decrease the antigen load in each dose, Dr. Treanor said. "We'll be looking at reducing the dose but achieving the same response, maybe by adding adjuvants or going a different route of administration."

The vaccine must also still be tested in children and the elderly, he noted. But the preliminary results in adults are raising hopes for similarly good responses in other age groups. The quick turnaround on the development of this vaccine also shows that vaccines against other emergent strains could be produced rapidly, Dr. Treanor said.

Work on the vaccine began in early 2004, when the initial viral sample was isolated in Southeast Asia. Proceeding from virus isolation to vaccine clinical trials in little more than 1 year is unprecedented, Dr. Treanor and Dr. Fauci said.

"The most important part of this study is that for the first time we have gone through the whole process of identifying the virus, making a genetically engineered seed virus, producing the vaccine, and then getting immune results 4 months from vaccination," said Dr. Treanor.

Having such a process in place gives some assurance that researchers would be able to respond quickly to any antigenic drift the H5 virus might experience, Dr. Fauci said. "The virus might change so significantly that this vaccine would offer much less protection. This exercise that we have gone through is an important dry run in being able to produce a vaccine as quickly as possible."

—Michele G. Sullivan

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'As long as research sponsored by [the National Center for Complementary and Alternative Medicines] and private foundations continues, advocates of alternative treatments can claim that a state of equipoise exists when, in fact, the issues should have been settled on the basis of previous knowledge.'

Dr. Wallace Sampson, p. 34