Candidate H1N1 Vaccines Enter Clinical Trials

BY DOUG BRUNK

Physicans preparing to deal with the anticipated spread of the novel influenza A(H1N1) virus are awaiting the results of a series of U.S. clinical trials aimed at gathering critical data about two candidate vaccines.

The studies which were initiated under the directorship of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health, got underway at the institutes's eight Vaccine and Treatment Evaluation Units (VTEUs).

The goal was to quickly evaluate pilot vaccine lots from two manufacturers, Sanofi Pasteur and CSL Biotherapies, to determine vaccine safety and efficacy in inducing protective immune responses.

"It's an exciting event," Dr. Robert B. Belshe, an internist who directs the VTEU at St. Louis University School of Medicine, said of the trials. "We don't have a major antigenic change very often for flu. This year we are clearly in the midst of the early pandemic. But this pandemic is going to be much different than other pandemics."

In contrast to their counterparts during previous pandemics, today's clinicians have good diagnostics at their disposal.

"We know how to make vaccines, and we know how to treat influenza with antivirals. The race is on right now to make as much vaccine as possible and get it into the highest risk population, which for this particular virus is children," he said.

According to a written statement issued by the NIH, initial studies at the VTEUs were designed to examine whether one or two 15-mcg doses of H1N1 vaccine would be needed to induce a potentially protective immune response in healthy adults (aged 18-64 years old) and elderly people (aged 65 and older). They studies also were aiming to assess whether one or two 30-mcg doses would be needed. Doses would be given 21 days apart. If early data indicate that the vaccines are safe, similar trials in healthy children (aged 6 months to 17 years) will begin.

'The race is on right now to make as much vaccine as possible and get it into the highest risk population.'

DR. BELSHE

Another set of trials was planned to examine the safety and immune response in healthy adult and elderly volunteers given the seasonal flu vaccine plus a 15-mcg dose of novel H1N1 vaccine. The H1N1 vaccine would be given to different sets of volunteers either before, after, or at the same time as the seasonal flu vaccine. If early data indicate that these combinations are safe, similar trials in healthy children will start.

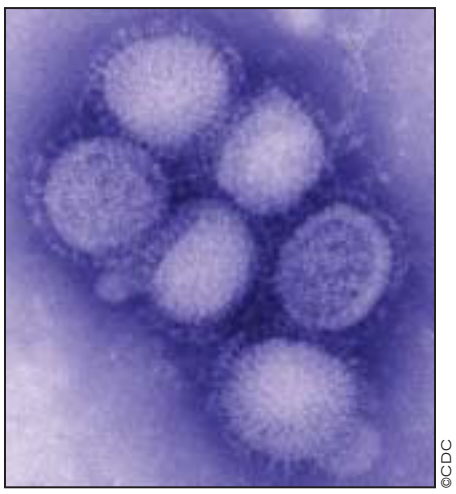
"I would anticipate that the monovalent H1N1 vaccine will behave exactly like the seasonal flu vaccine in terms of safety and adverse events, meaning it will probably cause some local pain, but nothing else," said Dr. Belshe, professor of infectious diseases and immunology at St. Louis University.

"The biggest challenge is, how do we get vaccine to as many high-risk people as possible? What's going to happen next year? Is this new virus going to replace the previous circulating H1 virus? I wouldn't be surprised if it did. If so, we will change the seasonal vaccine next year to include the new H1 and drop the old H1."

In previous years, Dr. Belshe has enrolled in vaccine clinical trials as a volunteer, but said he won't be doing so this time around. "We discourage investigators from vaccinating themselves. There is a time-honored tradition of physicians experimenting on themselves, but under the current system of institutional review boards and regulatory standards, that would be frowned upon," he said.

Dr. Belshe was quick to note, however, that he will take the vaccine as soon as it's available for general use. "I am certainly not afraid of the vaccine," he said. Health care workers are a high-priority group to receive immunization against the novel H1N1 virus, according to recommendations issued recently by the Centers for Disease Control and Prevention.

In the meantime, he said, being part of the national discussion on how to respond to the current pandemic "is very exciting, and to be able to provide advice and experience from our many years of clinical trials on how to successfully design a trial and answer the critical questions [has] been very rewarding."



©CDC

The newly identified H1N1 virus (above) could replace the previous H1 virus.

The other VTEUs are Baylor College of Medicine, Houston; Children's Hospital Medical Center, Cincinnati; Emory University, Atlanta; Group Health Cooperative, Seattle; University of Iowa, Iowa City; University of Maryland School of Medicine, Baltimore; and Vanderbilt University, Nashville, Tenn.

Dr. Belshe has been a consultant to several manufacturers of vaccines, including MedImmune, Sanofi Pasteur, GlaxoSmithKline, and Novartis. ■

Five Populations Targeted for Priority H1N1 Vaccination

BY MIRIAM E. TUCKER

ATLANTA — Initial vaccination efforts against the novel influenza A(H1N1) should focus on immunizing as many people as possible in five target groups, while smaller subsets of some of those groups should be targeted if demand for vaccine exceeds supply. As more supply becomes available, the rest of the population should be targeted for vaccination.

Those recommendations were made by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention. Primary targets for novel influenza A(H1N1) immunization efforts include the following five groups, which together total approximately 159 million individuals in the United States. Current seasonal influenza coverage among these groups is only 20%-50%, said Dr. Anthony J. Fiore of the CDC's Influenza Division.

► **Group 1—Pregnant women.** They have been found to be at higher risk for complications from seasonal influenza in past pandemics, and several deaths have been reported among pregnant women during the current 2009 pandemic. The vaccination of pregnant women also is seen as a way to potentially protect infants who cannot be vaccinated, via transfer of maternal antibodies to newborns.

► **Group 2—Household contacts and caregivers for infants younger than 6 months of age.** The aim is to provide a possible "cocooning effect," providing indirect protection for young infants who cannot be vaccinated but are at higher risk for influenza-related complications.

► **Group 3—Health care personnel and emergency medical personnel** (including emergency medical technicians, firefighters, and others whose jobs involve routinely providing emergency medical care in communities). These individuals are seen as a potential source of infection for vulnerable patients. In addition, increased absenteeism could reduce the health care capacity.

► **Group 4—Children and adults from 6 months through 24 years of age.** Children have the highest incidence of illness, and "explosive" outbreaks in schools have been a prominent feature of the spring 2009 epidemiology of the novel influenza A(H1N1). Children younger than 5 years of age are at the highest risk for hospitalization, and are sources of infection for the community and in schools. Moreover, illness in children keeps parents home from work. Young adults also have high attack rates and are seen as vectors.

► **Group 5—Adults aged 25-64 years with certain medical conditions that place them at greater risk for influenza-related complications.** These include chronic pulmonary, cardiovascular, renal, hepatic, cognitive, neuromuscular, hematologic, and metabolic disorders, as well as immunosuppression caused by medications or HIV infection. About 70% of adults hospitalized thus far with novel H1N1 infections had one of these conditions.

If vaccine demand exceeds availability, subgroups of the larger group, totaling 42 million people, should receive priority. The first subgroups—pregnant women and household and caregiver contacts for infants younger than 6 months of age—remain unchanged as a priority. The next subgroups include health care and emergency personnel in direct contact with patients; children aged 6 months through 4 years; and children with chronic medical conditions.

When vaccine availability is sufficient at the local level to routinely vaccinate initial target populations, a decision should be made in cooperation with state and local health authorities to vaccinate healthy adults aged 25-64 years first, then individuals aged 65 years and older. The last recommendation, in contrast to seasonal influenza vaccination recommendations, reflects the fact that older individuals thus far have been at lower risk for the novel influenza A(H1N1) virus.

New recommendations were needed, Dr. Fiore said, because the federal government's 2007 pandemic vaccine priority guidance had been developed for the scenario of a severe pandemic with the potential for social disruption of critical infrastructure. ACIP's Influenza Working Group concluded that current epidemiologic and immunologic evidence, combined with updated information on vaccine supply and availability, indicated a need to revise recommendations that had been made during prepandemic planning.

In drafting the document that ACIP voted on, the working group assumed the following: The severity of illness and groups at higher risk for infection or complications will be similar to what has already been observed; the safety profile and antigen content of novel H1N1 vaccines will be similar to that of seasonal vaccine; and adequate supplies of licensed unadjuvanted vaccine can be produced for all by approximately February 2010 but that enough vaccines for all will not be available before the next pandemic wave, expected this fall. ■