

## Manufacturers Ramp Up Supply

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during 2002-2003, the combined rates of laboratory-confirmed influenza outpatient clinic visits and emergency room visits were identical for these age groups, at 60 per 1,000. During 2003-2004, a more severe influenza season, the rates were 164/1,000 for the 6- to 23-month-olds and 111/1,000 for those aged 24-59 months.

Similar outpatient visit rates also were seen in children older than 5 years, of which 80% were associated with antibiotic use, Dr. Poehling noted.

Influenza vaccine manufacturers have indicated that they plan to produce between 100 million and 120 million doses for the 2006-2007 flu season, which should be enough to cover the additional 5.3 million healthy children aged 2-5 years in the United States.

In a separate vote, ACIP also advised against "tiering" of influenza risk groups in the absence of a supply decrease or delay, as has been done in previous seasons in anticipation of such problems.

Dr. Baker pointed out that expanding

the age of universal influenza immunization up to age 5 years will reduce rates in the overall population, given data suggesting that these children are the vectors of influenza transmission to their contacts. While the ACIP did include household contacts in their recommendation, their immunization rates are typically far lower than for groups designated as high risk.

Dr. Baker also announced during the meeting a new "Call to Action" initiative of the National Foundation for Infectious Diseases that will be aimed at improving influenza immunization rates among the 6 million children in the United States with asthma. Currently, only one-third of that high-risk group is immunized against influenza, despite long-standing recommendations that they receive a flu shot annually, said NFID president-elect Baker, of Baylor College of Medicine, Houston.

The NFID initiative, which is supported by a list of other professional societies including the AAP, the CDC, the American College of Emergency Physicians, the

American Medical Association, and the American Thoracic Society, will provide guidance for physicians in increasing patient demand for the vaccine, enhancing access to it, and overcoming practice barriers. More information is available at [www.nfid.org](http://www.nfid.org).

While these latest measures should help reduce the burden of influenza in the United States in the near future, ACIP's Prevention and Control of Influenza statement for the 2006-2007 season will contain a statement of the committee's intention to move toward a universal recommendation for influenza vaccine for the entire U.S. population.

That decision came after a strong endorsement of the concept from panel member Dr. Gregory A. Poland, of the Mayo Clinic.

"Health care workers and the public are immensely frustrated and confused regarding who should get vaccinated. 'It seems every year you guys add another risk group' is a refrain I continually hear. Do we really want a policy of 'creeping incrementalism'? It's time to be bold."

The committee fell just short of voting to "encourage" influenza vaccine for everyone, with a nearly tied vote. ■



Only one-third of child asthmatics are immunized, despite long-standing recommendations, said Dr. Carol J. Baker (right).

## FDA Panel Votes to Follow WHO on Key Influenza Strains

BY DEEANNA FRANKLIN  
Associate Editor

BETHESDA, MD. — A federal advisory panel unanimously voted to change two of the three strains slated to comprise the 2006-2007 influenza vaccine.

The Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee recommended the changes based on shifts seen in viral activity, according to data culled from surveillance sites in Japan, England, Australia, and the United States.

The recommended vaccine changes correlate with the World Health Organization's suggested vaccine composition for the Northern Hemisphere for the 2006-2007 winter season.

The FDA advisory panel recommended that the trivalent vaccine retain the influenza A(H1N1) strain—A/New Caledonia/20/99(H1N1)-like virus—due to evidence of continued resilience.

However, they suggested replacing the A/California/7/2004(H3N2)-like virus with A/Wisconsin/67/2005(H3N2)-like virus. Also, the influenza B/Shanghai/361/2002-like virus should be replaced with the B/Malaysia/2506/2004-like virus.

According to Dr. Zhiping Ye, senior investigator for the division of viral products with the FDA's Center for Biologics Evaluation and Research, influenza A infections were inadequately covered by the 2005-2006 vaccine. It's estimated that in the pediatric population there was an overall 50% reduction in the hemagglutination inhibition (HI) reaction to the H3N2 component of the vaccine.

A similar reduction in coverage of the A/Wisconsin strain was noted in adult populations in Europe, Japan, and the United States.

"If we use Wisconsin as a vaccine, then we probably will get better coverage," Dr. Ye said. "But this is only one piece of the puzzle." Surveillance studies show that several other strains in the same lineage as A/Wisconsin also were inadequately covered by the current vaccine. However, there would likely be residual coverage of these strains by targeting the A/Wisconsin strain.

The current vaccine still appeared effective against the influenza A(H1N1) strain, A/New Caledonia/20/99(H1N1)-like virus, according to data from surveillance sites in North and South America, Europe, Asia, Africa, and Australia.

Data from the United States and Europe showed that several strains were inadequately covered by the influenza B component of the current vaccine, and the B/Malaysia/2506/2004-like virus was one of them, Dr. Ye noted.

The vote on the 2006-2007 vaccine composition was unanimous, but the panel members had some reservations.

Although influenza A strains are responsible for most U.S. influenza cases, in recent years the selection of an influenza B strain has been more difficult to accurately pin down. "This winter the B/Victoria has been dominant in North America, but our vaccine was the B/Yamagata strain," said panelist Dr. Robert B. Couch, professor of medicine, microbiology, and immunology at Baylor College of Medicine, Houston.

"We do the best we can to predict the likely epidemic virus, but for roughly the last 3 years, it's been a little too much of a guess with the influenza B. If it's going to continue this way, then we need to discuss how to address this problem," Dr. Couch said in an interview.

Despite these misgivings, he voted in favor of the B/Malaysia strain, which is part of the B/Victoria/2/87 lineage. ■

## New Methods, Adjuvants May Boost Flu Vaccine Production

BY JEFF EVANS  
Senior Writer

WASHINGTON — Methods are now available to produce influenza virus vaccines in a greater number of doses and with more up-to-date coverage of relevant strains than what is currently available, Peter Palese, Ph.D., said at a biodefense research meeting sponsored by the American Society for Microbiology.

In most instances, these methods can be applied to both killed (inactivated) and live (attenuated) vaccines, said Dr. Palese, chair of microbiology at Mount Sinai Medical Center, New York.

Viruses that are used in killed vaccines are grown in embryonated eggs, purified, inactivated with formaldehyde, and usually then treated with a detergent to make the vaccine less pyrogenic.

The recently approved live vaccines are grown in tissue culture at a lower temperature (25° C) and in embryonated eggs, which makes the virus temperature-sensitive and attenuated; this limits the virus to a few replication cycles in the upper respiratory tract, he said.

New adjuvants should help to reduce the amount of antigenic viral material in each vaccine dose that is necessary to induce protective immunity, Dr. Palese said.

If adjuvants were used, the antigenic mass in each vaccine dose could be reduced to 10%-20% of its current amount. Alum is the only adjuvant approved by the Food and Drug Administration to be given in combination with some vaccines.

"This is an area where we really have to improve," he said.

Each February, the FDA decides which strains should be included in vaccines for the next influenza season. Only the viruses that are circulating until the end of January can be considered in the decision.

The FDA would make better decisions about which influenza isolates should be included in the vaccine if the decision could be delayed until May or June, Dr. Palese said.

Vaccines used in the 2005-2006 season were trivalent with surface antigens from an influenza A H3N2 isolate from 2004, an older influenza A H1N1 isolate from 1999, and an influenza B isolate from 2002. One or two of the three components changes each flu season, Dr. Palese said.

A new technique may allow researchers to adjust the viral antigens in vaccines and produce vaccines more quickly. It would work by inserting a combination of DNA copies of specific genes from a laboratory viral strain and genes for the hemagglutinin and neuraminidase antigens on currently circulating viruses into cells in a tissue culture.

The resulting recombinant seed viruses could then be generated in a 1- to 2-week period for distribution to manufacturers for annual vaccine production. This process allows more time to select the appropriate antigenic seed strains, he said.

Vaccine developers also may be able to use this process to engineer the influenza virus genome to express an altered version of nonstructural protein 1 (NS1). NS1 normally inhibits the interferon response of a host cell; viruses that lack NS1 cannot block interferon and, as a result, cannot replicate. ■