

Swine Flu Shot in U.S. May Rely on Emergency Use of Additives

By Tom Randall and Gary Matsumoto

July 29 (Bloomberg) -- Swine flu vaccine makers may rely on a U.S. emergency declaration to use experimental additives made by GlaxoSmithKline Plc and Novartis AG to boost a limited supply of shots that will be available to fight the pandemic.

The ingredients, known as adjuvants, may be added for the first time to flu shots in the U.S. Health officials, meeting today at the U.S. Centers for Disease Control and Prevention in Atlanta, plan to discuss use of the additives, and may also recommend who should be first to receive the limited amount of vaccines drugmakers say they will begin delivering in October.

The U.S. Health and Human Services Department declared a public health emergency over swine flu in April, and the Food and Drug Administration has the power to allow the use of unapproved medical products during such a crisis. The U.S. has been slow to approve the use of adjuvants because of safety concerns, and for fear of giving Americans an excuse to avoid getting the shots, said John Treanor, a University of Rochester researcher.

"The question is, do you really feel comfortable throwing this new thing into the mix and do you really need to?" said Treanor, a professor of medicine, microbiology and immunology at the school in Rochester, New York. "I myself, if I had to do it, would really wrestle with that decision."

The CDC agreed to pay London-based Glaxo and Novartis, based in Basel, Switzerland, more than \$415 million for adjuvants that could be added to the swine flu vaccines, according to a July 13 statement.

Mice Studies

A safety concern was raised in 2004 when researchers at the University of Florida in Gainesville reported that mice injected with oils used in the adjuvants developed conditions of the type that occur when the body's immune system produces an excessive protective reaction. Similar reactions haven't been seen in humans.

MF59, made by Novartis, has been given to more than 40 million people, mostly adults, to prevent seasonal flu, according to the company. Glaxo's adjuvant has proven safe and effective in clinical trials with 39,000 people, said Lisa Behrens, a spokeswoman for the company, in an e-mail. Glaxo will conduct more studies and continue to monitor safety after the vaccines are in use, she said.

Under the U.S. health emergency, the FDA may authorize the use of unlicensed vaccines, according to Peper Long, an agency spokeswoman. The FDA convened an advisory committee July 23 to consider what trials are necessary for the vaccines' approval. Advisory committees consist of medical experts who provide guidance to the agency.

Race to Make Shots

Swine flu's full force may reach the U.S. earlier than the typical flu season, according to the CDC. Vaccine makers are racing to make shots by mid-October, when cases are expected to rise in the northern hemisphere, fueled by cooler temperatures and the return of pupils to close quarters of classrooms.

The World Health Organization, based in Geneva, has said the H1N1 influenza, as the pandemic flu is known, is moving with "unprecedented speed." The flu spread farther globally in less than six weeks than previous pandemics have in more than six months, the Geneva-based agency said on its Web site on July 17. Global health authorities have stopped counting the number of cases and the CDC says more than 1 million people Americans have been sickened by the virus.

The vaccine makers have found it difficult to cultivate the quantities of virus needed for vaccine, as the strain yields 50 percent to 75 percent less antigen, the substance that induces immunity, compared with a typical seasonal flu strain, according to the WHO. The strain doesn't grow well in eggs, the principal medium used by the industry, vaccine makers said.

Mixing Oil, Water

The adjuvants are mixes of oil and water that -- by stimulating the immune system -- offer a way to boost the body's response to antigen. Adjuvants, whose effectiveness vary by flu strain, may boost the strength of the antigen as much as 10-fold, as was the case with a bird flu vaccine approved in Europe, said Treanor, of the University of Rochester. By adding an adjuvant the same amount of antigen can be used to treat more people, he said.

"Until GlaxoSmithKline and Novartis can show me it won't harm a rat or guinea pig, I think it's a bad idea to give it to humans," Vicky Debold, a registered nurse with a Ph.D. in public health, who is a member of the FDA's advisory committee for reviewing vaccines, said July 27 in an interview.

'Tremendously Well'

The U.S. never had to consider the risks of an adjuvant because regular flu vaccines were deemed to have "worked so tremendously well," said Lone Simonsen, research director in the department of global health at George Washington University in Washington.

"We have had a safe experience with the MF59-adjuvanted vaccine in Italy and Spain for many years now," Simonsen said. "That experience we can lean on. That's going to be the best data we have in time for using adjuvanted vaccines."

CSL Ltd., which has a \$180 million order to supply bulk H1N1 antigen to the U.S. government, decided against boosting its vaccine with an adjuvant, preferring to use a formulation more closely resembling the seasonal flu shot, said Mary Sontrop general manager of the Melbourne-based company's biotherapies unit.

The U.S. has contracts with five companies to provide flu shots. Novartis, based in Basel, Switzerland, is responsible for 45 percent of the supply, while Sanofi will provide 26 percent and CSL will make 19 percent, said Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, in an interview last week.

The remaining doses will be made by Glaxo and London-based drugmaker AstraZeneca Plc.

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Last Updated: July 29, 2009 00:01 EDT