

**National Institutes of Health (NIH)
H1N1 2009 Influenza Research Key Points
September 23, 2009**

Key Points are divided into the following sections:

Clinical Trials of H1N1 Influenza Vaccines
 Background
 Clinical Trials Design
Early Results from the Adult Trials
Early Safety Information from the Adult Trials Enabled Research to Begin in Children and Pregnant Women
Early Results of Pediatric Trials

Clinical Trials of H1N1 Influenza Vaccines

Background:

- On July 22, 2009, the National Institute of Allergy and Infection Diseases (NIAID), NIH announced the start of a series of clinical trials to test pilot lots of two manufacturers' versions of 2009 H1N1 influenza vaccine.
- The trials are designed to help quickly evaluate the pilot lots to determine whether the vaccines are safe and to assess their ability to induce protective immune responses.
- Information from these studies in healthy people will help public health officials develop recommendations for immunization schedules, including the optimal dosage and number of doses for multiple age groups, including adults, the elderly, and children.
- Data from all these trials are being factored into decisions about how to implement a 2009 H1N1 flu immunization program this fall and guidance for people at high risk for severe illness from flu.
- NIAID tapped its longstanding vaccine clinical trials infrastructure— a network of medical centers known as the Vaccine and Treatment Evaluation Units— to enroll these trials quickly while meeting highest standards for clinical care. This network is an important part of our country's preparations to respond to emerging infectious diseases such as 2009 H1N1 influenza.
- Close collaboration among NIAID, the U.S. Food and Drug Administration (FDA) and the Biomedical Advanced Research and Development Authority (a component of the Department of Health and Human Services) was key to launching the trials quickly while ensuring high clinical standards. Following initial discussions between the agencies on trial design, NIAID prepared the protocols and submitted them to the FDA for review. FDA rapidly completed the necessary reviews and approved the trial protocols.

Clinical Trials Designs

- Like inactivated seasonal influenza vaccines, the vaccine in these NIAID-sponsored trials contains a purified part of a killed 2009 H1N1 influenza virus and cannot cause flu.

- All clinical trials are being closely monitored by the trial physicians and staff as well as by an independent safety monitoring committee.
- The first trials were in healthy adult and elderly volunteers. Because there were no red flags from review of early safety data from these trials, trials were allowed to begin in other groups, including children and pregnant women.
- Initial studies are looking at whether one or two 15-microgram doses of H1N1 influenza vaccine are needed to induce a potentially protective immune response in healthy adult volunteers (aged 18 to 64 years old) and elderly people (aged 65 and older).
- The doses in the first trial were given 21 days apart, testing two manufacturers' vaccines (Sanofi Pasteur and CSL Biotherapies).
- A concurrent set of trials is designed to determine safety and immune response in healthy adult and elderly volunteers who are given the seasonal flu vaccine along with a 15-microgram dose of 2009 H1N1 vaccine. The H1N1 vaccine was given to different sets of volunteers before, after, or at the same time as the seasonal flu vaccine.
- The healthy adult and elderly trials are evaluating pilot vaccines by Sanofi Pasteur and CSL Biotherapies, Ltd. Trials in pregnant women and children are evaluating Sanofi Pasteur's pilot vaccine.

Early Results from the Adult Trials

- NIAID trials are testing two different dosages (15 micrograms versus 30 micrograms) and evaluating the immune response to one and two doses of these vaccines.
- More than 2,800 people are participating in ongoing NIAID trials of these vaccines.
- Preliminary analyses of early data from the NIAID trials showed that both vaccines studied induced what is likely to be a protective immune response in most adults following a single dose in the same amount (15 micrograms) used in seasonal flu vaccines.
- Specifically, in blood samples obtained 8 to 10 days after vaccination

Among healthy adults who received a single 15-microgram dose of the Sanofi Pasteur vaccine, a robust immune response was measured in 96 percent of adults aged 18 to 64 and in 56 percent of adults aged 65 and older.

Similarly, among healthy adults who received a single 15-microgram dose of the CSL Limited vaccine, a robust immune response was measured in 80 percent of adults aged 18 to 64 and in 60 percent of adults aged 65 and older.

- Additional data from the NIAID trials are forthcoming. However, on the basis of these strong early data, our results are consonant with other reports from manufacturers that a single 15-microgram dose of unadjuvanted 2009 H1N1 influenza vaccine is well tolerated and induces a robust immune response in healthy adults between the ages of 18 and 64.

- For adults aged 65 and older, the immune response to 2009 H1N1 influenza vaccine is somewhat less robust, as is the case with seasonal influenza vaccines.

Early Safety Information from the Adult Trials Enabled Research to Begin in Children and Pregnant Women

- Early information from the adult trials indicated that these vaccines are safe, so similar trials in healthy children (aged 6 months to 17 years old) began August 19 and 20, 2009 and in healthy pregnant women on September 9, 2009.
- These trials are testing 2009 H1N1 influenza vaccines that do not contain thimerosal or an immune booster, known as an adjuvant.

Early Results of H1N1 Influenza Vaccine in Children

- The ongoing trials in children 6 months to 17 years in age began in mid-August at five sites nationwide. The dosing trials are assessing the safety and immune responses to one and two doses of either 15 micrograms or 30 micrograms of vaccine. A concurrent set of trials is designed to determine the safety and immune response in children who are given the seasonal flu vaccine along with a 15-microgram dose of 2009 H1N1 vaccine. The H1N1 vaccine was given to different sets of volunteers before, after, or at the same time as the seasonal flu vaccine. Early results from the dosing trial testing only 2009 H1N1 influenza vaccine in children look promising.
- As we had hoped, responses to the 2009 H1N1 influenza vaccine have been very similar to what we see with routinely used seasonal influenza vaccines made in the same way.
- The 2009 H1N1 influenza virus is causing widespread infections among children, so these are welcome results.
- Preliminary analysis of blood samples from a small group of trial participants showed that a single 15-microgram dose of 2009 H1N1 influenza vaccine – the same dose that is in the seasonal flu vaccine – generates an immune response that is expected to be protective against 2009 H1N1 influenza virus in the majority of 10- to 17- year-olds, 8 to 10 days following vaccination.
- Younger (6 months to 9 years old) children generally had a less robust early response to the 2009 H1N1 influenza vaccine than older children (10 to 17 years old). This is very similar to what we see with routinely used seasonal influenza vaccines.
- It seems likely that the H1N1 flu vaccine will require just one 15-microgram dose for children 10 to 17 years of age.
- Data from the trial is being compared for three age groups: children 6 months to 35 months old; 3 to 9 years old; and 10 to 17 years old.

- Immune responses were strongest among the oldest children, those 10 to 17 years old. In this group of 25 children, a strong immune response was seen in 76 percent who received one 15-microgram dose of vaccine.
- The immune responses in children 9 years old and younger were not as strong. Among 25 volunteers aged 3 to 9 years old, a strong immune response was seen in 36 percent of those given 15 micrograms of vaccine.
- In the youngest group, 20 children between 6 months to 35 months old, a single 15-microgram dose of vaccine produced a strong immune response in 25 percent of recipients.
- The preliminary results are based on blood samples taken 8 to 10 days after the first vaccination. Study investigators are also collecting blood samples from the volunteers about three weeks after both the first and second injections. These samples will provide researchers with more data about how children respond to the vaccine.
- The H1N1 influenza vaccine being tested in the NIAID pediatric trials is manufactured by Sanofi Pasteur in Swiftwater, Pa., in the same manner as its licensed seasonal vaccine.

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