

GENERAL SAFETY ISSUES
September 18, 2009

Is the 2009 H1N1 influenza vaccine safe?

- We expect the 2009 H1N1 influenza vaccine to have a similar safety profile as seasonal flu vaccines, which have a very excellent safety track record. Over the years, hundreds of millions of Americans have received seasonal flu vaccines. The most common side effects following flu vaccinations are mild, such as soreness, redness, tenderness or swelling where the shot was given.
- The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) will be closely monitoring for any signs that the vaccine is causing unexpected adverse events.

Is the H1N1 vaccine fast tracked.

- Vaccines against novel influenza A (H1N1) virus infection are being produced using methods similar to those used for seasonal influenza vaccines.
- Licensure of vaccines against novel influenza A (H1N1) virus is based on the same licensure standards used for seasonal influenza vaccines, as is done routinely each year when strains are changed in the seasonal vaccine.
- Both live, attenuated and inactivated influenza A (H1N1) 2009 monovalent vaccine formulations will be available initially; as with seasonal influenza vaccines, neither of these vaccines will contain adjuvants.

See US CDC's MMWR August 21, 2009

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr58e0821a1.htm>

Will the benefits of the 2009 H1N1 influenza vaccines outweigh the risks?

- Currently the 2009 H1N1 influenza virus (sometimes called "swine flu") virus seems to be causing serious health outcomes for:
 - healthy young people from birth through age 24;
 - pregnant women; and
 - adults 25 to 64 who have underlying medical conditions.
- Seasonal influenza vaccines are highly effective in preventing influenza disease. The expectation is that a vaccine against 2009 H1N1 influenza would probably work in a similar fashion to the seasonal influenza vaccines. CDC and FDA, state and local public health officials and medical professionals believe that the benefits of vaccination with the 2009 H1N1 influenza vaccine will far outweigh the risks.
- Vaccination is the best way to prevent influenza infection and its complications. This is the reason that CDC, national health organizations, and healthcare providers intensively promote vaccination for seasonal influenza, and the reason why so much work is being done to have a vaccine available in the fall for the 2009 H1N1 influenza virus.
- Influenza vaccines do not protect against other viruses that cause respiratory illnesses. Even after you are vaccinated, it is still important to wash your hands well and often, to cover your coughs and sneezes, and to stay home if you are sick.

- Public health officials encourage you to ask your healthcare provider any questions you may have about the 2009 H1N1 influenza vaccine and the seasonal influenza vaccines that will be available during the 2009-2010 influenza season. Your healthcare provider is an excellent source for information on the benefits and risks of vaccination for protection against 2009 H1N1 influenza for you, your children, and other family members.

Will the H1N1 vaccine be issued under an Emergency Use Authorization and not full FDA approval?

- No, it is being issued with the full FDA approval.

Are there any side effects to the 2009 H1N1 influenza vaccine?

- CDC expects that any side effects following vaccination with the 2009 H1N1 influenza vaccine would be rare. If side effects occur, they will likely be similar to those experienced following seasonal influenza vaccine.
- Mild problems that may be experienced include soreness, redness, or swelling where the shot was given, fainting (mainly adolescents), headache, muscle aches, fever, and nausea. If these problems occur, they usually begin soon after the shot and last 1-2 days. Life-threatening allergic reactions to vaccines are very rare. If they do occur, it is usually within a few minutes to a few hours after the shot is given.
- If any unusual condition occurs following vaccination, seek medical attention right away. Tell your doctor what happened, the date and time it happened, and when the vaccination was given. Ask your doctor, nurse, or health department to report the reaction by filing a Vaccine Adverse Event Reporting System (VAERS) form. Or you can file this report yourself through the VAERS Web site at www.vaers.hhs.gov. You may call 1-800-822-7967 to receive a copy of the VAERS form. VAERS is not able to provide medical advice.

Are there some people who should not receive this vaccine?

- People who have a severe (life-threatening) allergy to chicken eggs or to any other substance in the vaccine should not be vaccinated.

How and why are the CDC and FDA monitoring the vaccines for safety?

- The CDC and FDA closely monitor the safety of seasonal influenza and other vaccines licensed for use in the United States in cooperation with state and local health departments, healthcare providers, and other partners.
- The purpose of vaccine safety monitoring is timely identification of clinically significant adverse events following immunization that may be of public health concern. Adverse events, or possible side effects, following immunization may be coincidental to (meaning occurring around the same time but not related to vaccination) or caused by vaccination. The purpose of vaccine safety monitoring is timely identification of clinically significant adverse events following immunization that might be of public health concern.
- CDC and its partners will use multiple systems to monitor the safety of 2009 H1N1 influenza vaccine. Two of the primary systems that will be used to monitor the safety of these vaccines after they are in widespread use are: the Vaccine Adverse Event Reporting System (VAERS), which is jointly operated with FDA, and the Vaccine Safety Datalink (VSD) Project. These systems are used routinely to monitor effects from other vaccines.

If swine flu is mild and most will experience mild symptoms and fully recover, why do we need a vaccine?

- The vast majority of people with novel H1N1 do have mild disease. However, hospitalization and death rates are highest among young people and pregnant women. Preliminary data show that one-third of pregnant women with H1N1 are ill enough with respiratory distress that they have to be hospitalized. The average age for hospitalization with H1N1 is 22, and the average age for death is 37.
- If we don't try to stop this pandemic through vaccination, we risk this virus continuing to circulate without much to slow it down, and risk it evolving to a more serious infection.

We can't trust the pharmaceutical industry.

- We "trust" the pharmaceutical industry every time we take medicine to reduce a fever or antibiotics to treat an infection.
- There are a number of checks and balances in the system, including FDA oversight as well as the involvement of the NIH and other agencies.

What is the best source of information for 2009 H1N1 influenza vaccine safety?

- In addition to talking openly with your healthcare providers, people are also encouraged to stay informed by checking the following Web sites often for the most up-to-date news and information: www.cdc.gov/H1N1flu and www.flu.gov.

PRESERVATIVES/ADJUVANTS

Will the 2009 H1N1 vaccines that are currently recommended contain adjuvants?

- No. According to current federal plans, only unadjuvanted vaccines will be used in the United States during the 2009 flu season. This includes all of the 2009 H1N1 and seasonal influenza vaccines that will be available for children and adults in both the injectable and nasal spray formulations. None of these influenza vaccines will contain adjuvants.
- 2009 H1N1 vaccines with adjuvants are being studied to determine if they are safe and effective. Experts will review these data when they are available. There is no plan at this time to recommend a 2009 H1N1 influenza vaccine with an adjuvant.

Will the 2009 H1N1 influenza vaccine contain thimerosal?

- The 2009 H1N1 influenza vaccines that FDA is licensing (approving) will be manufactured in several formulations. Some will come in multi-dose vials and will contain thimerosal as a preservative. Multi-dose vials of seasonal influenza vaccine also contain thimerosal to prevent potential contamination after the vial is opened.
- Some 2009 H1N1 influenza vaccines will be available in single-dose units, which will not require the use of thimerosal as a preservative. In addition, the live-attenuated version of the vaccine, which is administered intranasally (through the nose), is produced in single-units and will not contain thimerosal.

What is thimerosal?

- Thimerosal is a mercury-based preservative that has been used for decades in the United States in multi-dose vials (vials containing more than one dose) of some vaccines to prevent the growth of microorganisms, such as bacteria and fungi, which may contaminate them.

What are preservatives and why are they used in vaccines?

- In vaccines, preservatives are used to prevent the growth of bacteria and fungi in the event that they get into the vaccine. This may occur when a syringe needle enters a vial as a vaccine is being prepared for administration. Contamination by germs in a vaccine could cause serious illness or death. In some vaccines, preservatives are added during the manufacturing process to prevent microbial growth.

I have concerns about the use of thimerosal. Is thimerosal still being used?

- People have a right to expect the vaccines they receive are safe and effective. CDC and FDA also hold vaccines to the highest standards of safety. That is why CDC and FDA continually evaluate new scientific information about the safety of vaccines. Since 2001, no new vaccine licensed by FDA for use in children has contained thimerosal as a preservative, and all vaccines routinely recommended by CDC for children under six years of age have been thimerosal-free, or contain only trace amounts, except for multi-dose formulations of influenza vaccine. This was done as a precautionary step and not because there was evidence confirming that thimerosal-containing vaccines were causing health problems. The most recent and rigorous scientific research does not support the hypothesis that thimerosal-containing vaccines are harmful.
- Thimerosal is an important preservative that protects vaccines against potential microbial contamination, which may occur in opened multi-dose vials of vaccine. Such contamination could cause serious illness or death. Since seasonal influenza vaccine is produced in large quantities for annual immunization campaigns, some of the vaccine is produced in multi-dose vials, and contains thimerosal to safeguard against possible contamination of the vial once it is opened.
- Three leading federal agencies (CDC, FDA, and NIH) have reviewed the published research on thimerosal and found it to be a safe product to use in vaccines. Three independent organizations [The National Academy of Sciences' Institute of Medicine, Advisory Committee on Immunization Practices (ACIP), and the American Academy of Pediatrics (AAP)] reviewed the published research and also found thimerosal to be a safe product to use in vaccines. The scientific community supports the use of thimerosal in influenza vaccines.

Is thimerosal safe when used as a preservative in vaccines?

- CDC places a high priority on vaccine safety, surveillance, and research. CDC is aware that the presence of the preservative thimerosal in vaccines and suggestions of a relationship to autism has raised concerns. These concerns make the decisions surrounding vaccinations confusing and difficult for some people, especially parents. Numerous studies have found no association between thimerosal exposure and autism.

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- Unfortunately, we have not seen reductions in the numbers of children identified with autism indicating that the cause of autism is not related to a single exposure such as thimerosal.
- The federal government is committed to assuring the safety of vaccines. This is achieved by FDA oversight of rigorous pre-licensure trials and post-licensure monitoring by CDC and FDA. This commitment not only stems from our scientific and medical dedication, it is also personal – for most of us who work at CDC are also parents and grandparents. We too, place tremendous value on the health and safety of children.

PREGNANCY

Why does CDC recommend that pregnant women receive the 2009 H1N1 influenza vaccine?

- It is important for a pregnant woman to receive the 2009 H1N1 influenza vaccine as well as a seasonal influenza vaccine. A pregnant woman who gets any type of flu is at risk for serious complications and hospitalization. Pregnant women who are otherwise healthy have been severely impacted by the 2009 H1N1 influenza virus (formerly called “novel H1N1 flu” or “swine flu”). In comparison to the general population, a greater proportion of pregnant women infected with the 2009 H1N1 influenza virus have been hospitalized. In addition, severe illness and death has occurred in pregnant women. Six percent of confirmed fatal 2009 H1N1 flu cases thus far have been in pregnant women while only about 1% of the general population is pregnant. While hand washing, staying away from ill people, and other steps can help to protect pregnant women from influenza, vaccination is the single best way to protect against the flu.

Is there a particular kind of flu vaccine that pregnant women should get? Are there flu vaccines that pregnant women should not get?

- There are two type of flu vaccine. Pregnant women should get the “flu shot”— an inactivated vaccine (containing fragments of killed influenza virus) that is given with a needle, usually in the arm. The flu shot is approved for use in pregnant women.
- The other type of flu vaccine — nasal-spray flu vaccine (sometimes called LAIV for “live attenuated influenza vaccine)—is not currently approved for use in pregnant women. This vaccine is made with live, weakened flu viruses that do not cause the flu). LAIV (FluMist®) is approved for use in healthy* people 2-49 years of age who are not pregnant.

Is the 2009 H1N1 influenza vaccine safe for pregnant women?

- Influenza vaccines have not been shown to cause harm to a pregnant woman or her baby. The seasonal flu shot (injection) is proven as safe and already recommended for pregnant women. The 2009 H1N1 influenza vaccine will be made using the same processes and facilities that are used to make seasonal influenza vaccines.

What safety studies have been done on the 2009 H1N1 influenza vaccine and have any been done in pregnant women?

- A number of clinical trials which test 2009 H1N1 influenza vaccine in healthy children and adults are underway. These studies are being conducted by the National Institutes of Allergies and Infectious Diseases (NIAID). Studies of 2009 H1N1 influenza vaccine in pregnant women are expected to begin in September.

Does the 2009 H1N1 influenza vaccine have preservative in it?

- There is no evidence that thimerosal (used as a preservative in vaccine packaged in multi-dose vials) is harmful to a pregnant woman or a fetus. However, because some women are concerned about exposure to preservatives during pregnancy, manufacturers will produce preservative-free seasonal and 2009 H1N1 influenza vaccines in single dose syringes for pregnant women and small children. CDC recommends that pregnant women may receive influenza vaccine with or without thimerosal.

Can the family members of a pregnant woman receive the nasal spray vaccine?

- Pregnant women should not receive the live nasal spray influenza vaccine but family and household members and other close contacts of pregnant women (including healthcare personnel) who are 2 through 49 years old, healthy* and not pregnant may receive live nasal spray vaccine.

Can a pregnant healthcare worker administer the live nasal influenza vaccine?

- Yes. No special precautions are (such as gloves) are necessary. Hands should be washed or cleaned with waterless hand sanitizer before and after administering the vaccine or having any direct contact with patients in a health care setting.

GUILLAIN-BARRE SYNDROME and 1976 SWINE FLU

Will there be a possibility of Guillain-Barré Syndrome (GBS) cases following the 2009 H1N1 vaccine?

- Guillain-Barré syndrome (GBS) is a rare disease in which the body damages its own nerve cells, causing muscle weakness and sometimes paralysis. It is not fully understood why some people develop GBS, but it is believed that stimulation of the body's immune system may play a role in its development. Infection with the bacterium [Campylobacter jejuni](#), which can cause diarrhea, is one of the most common risk factors for GBS. People can also develop GBS after having the flu or other infections (such as cytomegalovirus

and Epstein Barr virus). On very rare occasions, they may develop GBS in the days or weeks following receiving a vaccination.

- In 1976, there was a small risk of GBS following influenza (swine flu) vaccination (approximately 1 additional case per 100,000 people who received the swine flu vaccine). That number of GBS cases was slightly higher than what is normally seen in the population, whether or not people were vaccinated. Since then, numerous studies have been done to evaluate if other flu vaccines were associated with GBS. In most studies, no association was found, but two studies suggested that approximately 1 additional person out of 1 million vaccinated people may be at risk for GBS associated with the seasonal influenza vaccine. FDA and CDC will be closely monitoring reports of serious problems following the 2009 H1N1 influenza vaccines, including GBS.

Background on 1976 swine flu:

- In early 1976, the novel A/New Jersey/76 (Hsw1N1) influenza virus caused severe respiratory illness in 13 soldiers with 1 death at Fort Dix, New Jersey.
- Since A/New Jersey (H1N1) was similar to the 1918–1919 pandemic virus (also a H1N1 strain), rapid outbreak assessment and enhanced surveillance were initiated.
- Up to 230 soldiers were infected with the A/New Jersey virus.
- Cases of “swine flu” strain of H1N1 were found only among the Fort Dix Army personnel and in January and early February of 1976. No other evidence of transmission was found.

What is Guillain-Barré syndrome (GBS)?

- Guillain-Barré syndrome (GBS) is a rare disorder in which a person’s own immune system damages the nerve cells, causing muscle weakness and sometimes paralysis. GBS can cause symptoms that last for a few weeks or several months. Most people recover fully from GBS, but some people have permanent nerve damage. In rare cases, people have died of GBS, usually from difficulty with breathing. In the United States, for example, an estimated 3,000 to 6,000 people develop GBS each year on average, whether or not they received a vaccination. This is about 1 to 2 cases of GBS per 100,000 people.

What causes GBS?

- Scientists do not fully understand what causes GBS, but it is believed that stimulation of the body’s immune system may play a role in its development.
- Here’s what scientists know for sure: About two-thirds of people who develop GBS symptoms do so several days or weeks after they have been sick with a diarrheal or respiratory illness. Infection with the bacterium [Campylobacter jejuni](#) is one of the most common risk factors for GBS. People can also develop GBS after having the flu or other infections (such as cytomegalovirus and Epstein Barr virus). On very rare occasions, they may develop GBS in the days or weeks following receiving a vaccination. It is believed that infection from flu may be more highly associated with GBS than vaccination from the flu.

Who is at risk for developing GBS?

- Anyone can develop GBS, but it is more common among adults than children. The incidence of GBS increases with age, and people over age 50 are at greatest risk for

developing GBS. Each year, on average, about 3,000 to 6,000 people in the United States develop GBS whether or not they received a vaccination – that's 1 to 2 people out of every 100,000 people.

Do vaccines cause GBS?

- It is not fully understood why some people develop GBS, but it is believed that the nerve cells are damaged by a person's own immune system. Many types of infections, and in very rare cases vaccines, may activate the immune system to cause damage to the nerve cells.

How common is GBS, and how common is it after people are vaccinated for seasonal influenza?

- GBS is rare. Each year, about 3,000 to 6,000 people in the United States develop GBS whether or not they received a vaccination – that's 1 to 2 people out of every 100,000 people. This is referred to as the background rate.
- In 1976, there was a small risk of GBS following influenza (swine flu) vaccination (approximately 1 additional case per 100,000 people who received the swine flu vaccine). That number of GBS cases was slightly higher than the background rate for GBS. Since then, numerous studies have been done to evaluate if other flu vaccines were associated with GBS. In most studies, no association was found, but two studies suggested that approximately 1 additional person out of 1 million vaccinated people may be at risk for GBS associated with the seasonal influenza vaccine. It is important to keep in mind that severe illness and possible death can be associated with influenza, and vaccination is the best way to prevent influenza infection and its complications.

What happened in 1976 with GBS and the swine flu vaccine?

- Scientists first reported a suspected link between GBS and vaccinations in 1976, during a national campaign to vaccinate people against a swine flu virus. The investigation found that vaccine recipients had a higher risk for GBS than those who were not vaccinated (about 1 additional case occurred per 100,000 people vaccinated). Given this association, and the fact that the swine flu disease was limited, the vaccination program was stopped.
- Since then, numerous studies have been done to evaluate if other flu vaccines were associated with GBS. In most studies, no association was found, but two studies suggested that approximately 1 additional person out of 1 million vaccinated people may be at risk for GBS associated with the seasonal influenza vaccine.

Why did some people develop GBS after they received the 1976 swine flu vaccine?

- The Institute of Medicine (IOM) conducted a thorough scientific review in 2003 and concluded that people who received the 1976 swine influenza vaccine had a slight increased risk for developing GBS. Scientists have multiple theories on why this increased risk may have occurred, but the exact reason for this association remains unknown.

Do you expect that the 2009 H1N1 vaccine will be associated with GBS?

- We expect the 2009 H1N1 vaccine to have a similar safety profile as seasonal flu vaccines, which have very good safety track records. The seasonal influenza vaccine has not been consistently associated with GBS. Although we do not expect GBS cases to

occur after vaccination with the 2009 H1N1 vaccine, we will be closely monitoring for any cases out of an abundance of caution.

How will public health authorities investigate cases of GBS?

- Ensuring the safety of vaccines is a high priority for CDC. CDC and its partners have an aggressive plan to actively monitor the 2009 H1N1 vaccine to ensure its safety. Several systems are in place to monitor vaccine safety. One of these systems is the [Vaccine Adverse Event Reporting System \(VAERS\)](#).
- CDC and FDA co-manage VAERS, which serves as an early warning system to collect voluntary reports about possible side effects that people experience following vaccinations. CDC and FDA scientists review all VAERS reports and store the information in a computerized database that is monitored to detect new, unusual, or rare health events that could be possible side effects of vaccines.
- In addition to the normal vaccine safety monitoring systems, CDC is proactively putting additional monitoring systems in place to ensure safety after licensing. Some of these systems include: actively observing persons in defined geographic areas, collaborating with professional organizations for reports of any adverse events after vaccination, and conducting thorough investigations when severe adverse events occur to determine whether they may have been associated with the vaccine. Through these numerous approaches, we will be able to detect any possible risk of GBS that might be associated with the 2009 H1N1 vaccine early in the vaccination campaign and take appropriate action.

How will the federal government determine whether people who receive the 2009 H1N1 vaccine have an increased risk for GBS?

- GBS cases occur every year in the general population for many different reasons. To monitor whether people who receive the 2009 H1N1 vaccine have an increased risk for GBS, U.S. public health officials will determine if the number of GBS cases reported among people who receive the 2009 H1N1 vaccine is higher than the number of cases reported in the general population.
- If there is an increase in the number of reported cases, public health officials will conduct intensive investigations. If any problems are detected with this 2009 H1N1 vaccine, they will be reported to health officials, healthcare providers, and the public, and health officials will take needed action to ensure the public's health and safety.

Some Sources:

Guillain-Barre Syndrome Fact Sheet

<http://www.ninds.nih.gov/disorders/gbs/gbs.htm>

Swine Influenza A Outbreak, Fort Dix, NJ 1976; January, 2006

<http://www.cdc.gov/ncidod/EID/vol12no01/05-0965.htm>

Reflections of the 1976 Swine Flu Vaccination Program by former directors of US CDC and National Influenza Immunization Program, January, 2006

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GBS Following Influenza Vaccine 2004 JAMA

<http://jama.ama-assn.org/cgi/content/full/292/20/2478>

American Journal of Epidemiology 2008 article on GBS and ILI and influenza vaccine
<http://aje.oxfordjournals.org/cgi/content/abstract/169/3/382>

Emerging Infectious Disease article on association between Influenza A and other infections with GBS, 2006
<http://www.cdc.gov/ncidod/Eid/vol12no12/05-1032.htm>

Journal of Infectious Disease, 2008 article on GBS and Influenza Vaccine
<http://www.journals.uchicago.edu/doi/abs/10.1086/589624>