

Pandemic (H1N1) Influenza Vaccine

Questions and Answers for Health Care Providers

October 21, 2009

The following Questions and Answers are intended to provide information on the Pandemic (H1N1) influenza vaccine.

NEWLY AVAILABLE INFORMATION ABOUT PANDEMIC (H1N1) INFLUENZA VACCINES

Q1. What Pandemic (H1N1) influenza vaccines are available in Canada?

In Canada, there will be two types of Pandemic (H1N1) influenza vaccines as follows:

Arepanrix™:

- Adjuvanted vaccine for everyone 6 months of age and older who is not pregnant;
- Can be used for healthy women in the second half of pregnancy (over 20 weeks of gestation) or women with underlying medical conditions at any stage of pregnancy if Pandemic (H1N1) influenza is circulating in their community and the unadjuvanted vaccine is unavailable.

Influenza A (H1N1) 2009 Monovalent Vaccine (without adjuvant):

- For pregnant women

Q2. When will the Pandemic (H1N1) influenza vaccine be available?

Arepanrix™ is now available in Canada. It is being distributed across the country in small allotments depending on manufacturing capacity. Initial shipments will focus on high risk individuals who are defined as:

- People less than 65 years of age with chronic medical conditions (see Question 3)
- Children from 6 months of age to less than 5 years of age
- Health care providers (see Question 4)
- Household contacts or caregivers of children less than 6 months of age or immunocompromised individuals
- Pregnant or within four weeks post-partum (see Question 5)
- People from remote or isolated communities

The first shipment in Middlesex London will be 19,500 doses and is expected towards the end of the week of October 19, 2009. As this will not be sufficient vaccine for all the high risk groups, first priority will be given to:

- Health care providers
- Children from 6 months of age to less than 5 years of age
- Household contacts of children less than 6 months of age
- Pregnant women in the second half of pregnancy (over 20 weeks gestation) or women with underlying medical conditions at any stage of pregnancy

As additional vaccine becomes available it will be provided to the other risk groups, including people with underlying medical conditions who are less than 65 years of age (see Question 3). Once high priority groups have been offered vaccine, anyone 6 months of age and over will be able to receive their vaccination(s).

Influenza A (H1N1) 2009 Monovalent Vaccine (without adjuvant) is not expected to be available until about November 9, 2009.

Q3. What medical conditions are considered high risk in people 65 years of age and under?

- chronic respiratory disease, including asthma
- cardiac disease
- diabetes mellitus and other metabolic diseases
- cancer
- immunodeficiency or immunosuppression (due to underlying therapy and/or disease including HIV/AIDS)
- renal disease
- anemia or hemoglobinopathy
- morbid obesity
- children less than 18 years of age on long term aspirin therapy
- conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration, such as neurologic conditions or cognitive disorders

Q4. Which health care providers should receive the vaccine when first available?

Health care providers who should receive the vaccine when first available include the following:

- All staff members who work in the following locations:
 - hospitals;
 - long term care facilities;
 - community health care provider offices;
 - Community Care Access Centres (CCAC);
 - contract nursing agencies;
 - Emergency Medical Services;
- Doctors and nurses
- Pharmacists and pharmacy assistants;
- Mental health workers; and
- Emergency personnel who respond to health emergencies.

Vaccine will be provided to hospitals and long term care facilities for administration to staff. Other health care providers should attend the community clinics listed in the attached schedule or other clinics that will be announced shortly and over the coming weeks. Some health care providers' offices will be receiving vaccine for staff members on the understanding that they administer it to 10 staff members without wasting vaccine from the mixed 10 dose vial. Clinic schedules will be posted on our web site www.healthunit.com/h1n1info .

Q5. Which vaccine is recommended for pregnant women?

Influenza A (H1N1) 2009 Monovalent Vaccine (without adjuvant) is the recommended product for pregnant women. However, it will not be available until about November 9, 2009 and currently Pandemic (H1N1) influenza is circulating widely in our community. Pregnant women in the second half of pregnancy are at increased risk for complications from influenza compared to other adults. As well, pregnant women with underlying medical conditions, like others with underlying medical conditions, have higher complication rates.

Seasonal influenza vaccine is widely used in pregnant women without any safety concerns. Arepanrix™ differs from seasonal influenza vaccine because of the addition of the adjuvant, which has not been specifically studied in pregnancy. However, given increasing disease in our community and the delay in the arrival of the unadjuvanted vaccine, the risk-benefit assessment favors vaccinating pregnant women with underlying medical conditions regardless of their stage of pregnancy or healthy pregnant women in the second half of pregnancy with Arepanrix™. This vaccine, under the trade name Pandemrix, is also being used in Europe to vaccinate pregnant women.

Q6. Which vaccine is recommended for children?

Arepanrix™ is the recommended vaccine for all children 6 months of age and over, including children between 6 months of age and less than 3 years of age. This vaccine is being recommended because it is anticipated that the adjuvant will enhance the immune response in these children, who generally mount less than optimal responses to seasonal influenza vaccines without an adjuvant.

Although the adjuvant in Arepanrix™ has not been specifically studied in children less than 3 years of age, a vaccine for avian influenza (H5N1) with the same adjuvant has been studied in a limited number of children 3 to 9 years of age with no safety concerns. A seasonal influenza vaccine with an adjuvant that is similar to, but not the same as, the adjuvant in Arepanrix™ (squalene-based adjuvant, see Question 17), has been studied in some children 6 months to less than 3 years of age with no safety concerns. In both studies, the adjuvant resulted in increased local reactions at the injection site. Arepanrix™ (under the trade name Pandemrix) is being used to vaccinate children 6 months of age and over in Europe.

Children from 6 months of age to less than 10 years of age require two doses of Arepanrix™, given at least 21 days apart. Unadjuvanted vaccine can be administered in children 6 months of age to less than 3 years of age (0.25 ml IM at least 21 days apart) but this is not recommended since Arepanrix™ is expected to induce a better immune response after the first injection. Given this better immune response, the fact that Pandemic (H1N1) influenza is currently circulating widely in Middlesex-London, and the delay in the unadjuvanted vaccine's arrival, parents should be strongly encouraged to vaccinate their young children with Arepanrix™.

Q7. What is the dose of Arepanrix™?

Age	Dose	Number of doses
6 months to 9 years of age (inclusive)	0.25 ml IM	Two doses at least 21 days apart
10 years of age and older	0.5 ml IM	One dose

In pregnant women receiving Influenza A (H1N1) 2009 Monovalent Vaccine (without adjuvant), one injection of 0.5 ml IM is recommended.

Q8. How is Arepanrix™ mixed?

The adjuvant will come in a separate vial from the antigen. The adjuvant will need to be withdrawn from its smaller vial and added to the larger vial containing the antigen. Once mixed, the multi-dose vial contains 10 doses. The mixed product must be used within 24 hours of mixing or failing that, must be discarded.

Q9. Will information sheets and consent forms be available from the Health Unit?

The Health Unit is working to develop an information sheet and consent form that will be used at our community clinics and can also be used by health care providers in their offices. This will be distributed to health care providers when complete.

Q10. Can seasonal influenza vaccine and Pandemic (H1N1) influenza vaccine be given at the same visit? What about Pandemic (H1N1) influenza vaccine and other vaccines?

Pandemic (H1N1) influenza vaccines (adjuvanted or unadjuvanted) can be administered at the same visit as any other vaccine including the seasonal influenza vaccine. A separate needle, syringe and injection site should be used. If only Pandemic (H1N1) and seasonal influenza vaccines are being given, they should be administered in opposite arms.

If the Pandemic H1N1 influenza vaccine is being given with both the seasonal influenza vaccine and pneumococcal vaccine, the seasonal influenza vaccine and the pneumococcal vaccine should be given in the same arm at least one inch apart, and the Pandemic (H1N1) influenza vaccine should be given in the opposite arm because of its increased reactogenicity. The location that each vaccine was given should be clearly documented in the medical record.

If not administered at the same time, there is no minimum interval between the Pandemic (H1N1) influenza vaccine and any other vaccine.

It should be noted that initially only the Pandemic (H1N1) influenza vaccine will be offered at the Pandemic (H1N1) Clinics. It is possible that at clinics later in November or in December, seasonal influenza vaccine may also be offered.

Q11. Do people who have had influenza-like illness need to have the Pandemic (H1N1) influenza vaccine?

People who have had laboratory confirmation of the Pandemic (H1N1) influenza infection do not need to receive the Pandemic (H1N1) vaccine. As well, people who had influenza A infections diagnosed by a swab from their nose over the summer or early fall, and were not subsequently tested to confirm that it was the H1N1 strain, likely do not need to receive the Pandemic (H1N1) influenza vaccine. No other seasonal influenza strains were circulating over the summer and early fall, so influenza A diagnosed by laboratory tests over the summer and early fall was almost certainly Pandemic (H1N1). The same is not true for influenza A diagnosed by laboratory tests in the spring, since other seasonal strains of influenza circulated in the late spring.

People who did not have laboratory confirmation of influenza A or Pandemic (H1N1) should receive the Pandemic (H1N1) vaccine even if they had symptoms compatible with influenza, since there are many other viruses that can cause similar symptoms. Vaccinating people who have already had Pandemic (H1N1) influenza infection will not be harmful.

Q12. How is the Pandemic (H1N1) influenza vaccine being distributed?

The Pandemic (H1N1) influenza vaccine will be provided at public health clinics. The first six clinics on October 27, 28 and 29 have now been scheduled and additional clinics will be scheduled shortly as more vaccine becomes available. The clinic schedule can be found on the Health Unit's web site at: www.healthunit.com/h1n1info.

Vaccine for hospital staff and staff of long term care facilities will be available the week of October 26 and will be provided to these facilities for staff vaccinations. Health care providers who ordered influenza vaccine for high risk groups, will also begin receiving vaccine as soon as there is more certainty about the amount and timing of vaccine to be received at the Health Unit. This may be as early as the week of October 26, 2009. Initial shipments may be smaller than originally ordered because of limited supply, with more to follow based on increased availability of the vaccine. It should be noted that vaccine cannot be returned to the Health Unit once it is sent to health care providers' offices.

Health care providers administering influenza vaccine are asked to comply with the high risk sequence being used by the Health Unit as identified above in Question 2. As well, they will need to be sure that once the adjuvant and antigen are mixed together, the whole multi-dose vial is used within 24 hours of mixing. The required tally sheets of administered doses should be faxed to the Health Unit (519-663-8241) on a weekly basis.

BACKGROUND INFORMATION ABOUT PANDEMIC (H1N1) INFLUENZA VACCINES

Q13. Who is producing the Pandemic (H1N1) influenza vaccine for Canada?

The Pandemic (H1N1) influenza vaccine for Canadians is being produced by GlaxoSmithKline at its manufacturing plant in Quebec.

Q14. How much Pandemic (H1N1) influenza vaccine will be available?

The federal government has purchased 50.4 million doses of the Pandemic (H1N1) influenza vaccine. Of these, 19.5 million doses are for Ontario, which is sufficient to vaccinate the entire population. The vaccine is expected to be produced at a rate of about 3,000,000 doses per week for Canada, which may mean that Middlesex-London will receive approximately 30,000 doses per week. Our first shipment is however only 19,500 and is expected at the end of the week of October 19, 2009. A second shipment with a similar amount is expected shortly thereafter.

Q15. How is the Pandemic (H1N1) influenza vaccine made?

The Pandemic (H1N1) influenza vaccine is being grown in hens' eggs, inactivated and split apart to release the antigen, which is the usual mechanism for manufacturing influenza vaccines used in Canada. The Pandemic (H1N1) influenza vaccine will differ from seasonal influenza vaccine as it will contain an adjuvant.

Q16. What are adjuvants?

Adjuvants are substances designed to increase the host's immune response to vaccines. This allows smaller quantities of antigen to be used for each dose (dose sparing). Adjuvants may also broaden the immune response so that if the strain changes (drifts), the vaccine can still provide some protection. Seasonal influenza vaccines used in Canada do not contain an adjuvant. Other vaccines, like tetanus-containing vaccines, Prevnar™, hepatitis A, B and meningococcal vaccines, contain the commonly used adjuvant, alum or aluminium. The adjuvant being used in the GlaxoSmithKline Pandemic (H1N1) influenza vaccine is called ASO3. ASO3 is an oil-in-water suspension that contains squalene, α -tocopherol (Vitamin E) and polysorbate 80 (see Question 17 for additional information).

Novartis, another vaccine manufacturer, is using an adjuvant called MF59 in their Pandemic (H1N1) influenza vaccine. MF59 is also referred to as an oil-in-water or squalene-based adjuvant. MF59 is currently used in a licensed seasonal influenza vaccine called Fludax®. Fludax® has been used in Europe for seasonal influenza vaccination since 1997 and has been given to 40 million people without any safety concerns.

Q17. What is ASO3?

ASO3 is the adjuvant being used by GlaxoSmithKline. It is an oil-in-water suspension with the oil component consisting of α -tocopherol and squalene. The substance used to maintain the oil in suspension is polysorbate 80 which is found in other vaccines.

ASO3 is also the adjuvant used by GlaxoSmithKline in a vaccine called Prepandrix™, which was developed to protect against a possible pandemic of H5N1 (avian influenza). Prepandrix™ has been approved for use in the European Union and some Asian countries. It has been studied in adults and a smaller number of children 3 years of age and over. Immunologic tests showed that Prepandrix™ induced an immune response against drifted strains of H5N1 influenza.¹

The ASO3 adjuvant has been studied in 45,000 people. Its use has resulted in increased local reactions at the injection site but no serious safety concerns have been noted.²

References:

1. Leroux-Roels I and Leroux-Roels G, Current status and progress of prepandemic and pandemic influenza vaccine development. *Expert Review Vaccines*. 2009; 8(4),401-423.
2. WHO Virtual Consultation on the Safety of Adjuvanted Influenza Vaccines (3 June 2009). http://www.who.int/vaccine_research/InfluenzaMeeting/en/index.html Accessed September 13, 2009.

Q18. How is the safety of the Pandemic (H1N1) influenza vaccines being assessed?

The Pandemic (H1N1) influenza vaccines are assessed according to the usual regulatory processes. Each country where the vaccine is to be used has similar but independent review processes. Before a vaccine can be used in Canada, it is thoroughly reviewed by the Biologics and Genetic Therapies Directorate (BGTD) of Health Canada. The review process conducted by scientists at BGTD involves assessing data from animal studies and immunogenicity studies in humans, inspecting the manufacturing plant and independently testing each lot of vaccine before it can be released for use. For some vaccines, efficacy data are also required. GlaxoSmithKline has indicated that it intends to study their Pandemic (H1N1) influenza vaccine in 16 clinical trials

involving 9,000 individuals in Canada, the United States and Europe.³ Results of these studies are being released as they become available.

After the vaccine is authorized for use, post-marketing surveillance occurs in many countries. This is important to detect rare adverse events that could not be detected in the numbers of people included in clinical trials. In Canada, the system for post-marketing surveillance is called the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS). Under this system, health care providers report adverse events that appear in patients following vaccination. The reports are then analyzed to assess if there are adverse events being reported at a greater frequency than would be expected in the general population. As CAEFISS only generates signals of possible adverse events, further studies may be indicated based on the analyses of CAEFISS. A similar system exists in the United States; this system is called the Vaccine Adverse Event Reporting System (VAERS). Unlike CAEFISS, patients can also directly report adverse events to VAERS.

Reference:

3. GlaxoSmithKline Pandemic (H1N1) 2009 influenza update, Issued: Friday 14 August. 2009
http://www.gsk.com/media/pressreleases/2009/2009_pressrelease_10084.htm Accessed: September 13, 2009

Q19. Why is there discussion about Guillain-Barré Syndrome?

In January and February 1976, a new strain of influenza A of swine origin appeared among military personnel on a military base at Fort Dix, New Jersey. Although the strain of influenza did not spread beyond the base and cases ceased within a few weeks, in October 1976 officials began a mass immunization campaign to prevent the circulation of this New Jersey strain. In total, 45 million doses of vaccine were administered in the United States between October and December 1976. The program was stopped when it was realized that 500 cases of Guillain-Barré Syndrome (GBS) had arisen after vaccination, resulting in 25 deaths. It was estimated that in the 6 to 8 weeks after vaccination, vaccinated individuals had a 4 to 8 times increased risk of GBS compared to non-vaccinated individuals. It is estimated that slightly less than 1 in 100,000 vaccinated people developed GBS in 1976. The cause of this increased risk was never determined.⁴

In subsequent vaccination seasons, studies have shown either a non-existent risk of GBS after influenza vaccine or an increased risk of approximately 1 per 1,000,000 doses of influenza vaccine administered.⁴ To ensure its safety with respect to rare diseases such as Guillain-Barré Syndrome, post-marketing reporting of adverse events following receipt of Pandemic (H1N1) influenza vaccine will be monitored closely.

Reference:

4. Haber P et al. Vaccines and Guillain-Barré Syndrome. *Drug Safety* 2009;(32)4:309-323.

Q20. What is Guillain-Barré Syndrome?

Guillain-Barré Syndrome (GBS) is a rapidly evolving, bilateral, ascending flaccid motor paralysis, with variable sensory changes. The prognosis is generally good, although some patients require mechanical ventilation and some fatalities occur, particularly in the elderly. It is a relatively rare condition that occurs at a rate of ~1-2 / 100,000; the incidence increases with age. GBS is believed to be immune mediated and results due to the production of antibodies that cross react with the peripheral nerve. In about two-thirds of cases, it occurs after a bacterial or viral infection such as *Campylobacter jejuni*, *Mycoplasma pneumonia*, HIV, Epstein-Barr virus, cytomegalovirus or possibly influenza infection itself.⁴

Q21. What is thimerosal?

Thimerosal is a mercury product added to multi-dose vials of vaccines to prevent bacterial and fungal contamination of these products. It has been used in vaccines since the 1930's and is found in both the adjuvanted and unadjuvanted Pandemic (H1N1) influenza vaccines. Thimerosal is not methyl mercury, which is found in fish and can be toxic at high levels in people. Thimerosal is ethyl mercury which does not accumulate in the body and has not been known to cause any adverse effects. There have been numerous studies and comprehensive reviews of the safety of thimerosal and there is no evidence that thimerosal is related to autism or any neurologic or health problems.

If you have any questions, please do not hesitate to contact the Middlesex-London Health Unit at 519-663-5317 ext. 2330. Please also visit our web site frequently, as updated information and clinic schedules will be posted there at www.healthunit.com/h1n1info .