

## Chapter 10a

### Pandemic (H1N1) 2009

(formerly known as Swine flu or Influenza A (H1N1))

NOTIFIABLE

**Date: 04/12/2009**

**Version 1.3**

*This chapter has been developed to provide current information on pandemic (H1N1) 2009 influenza, on vaccines available for use in Ireland and on vaccination recommendations. It also provides links to further information sources.*

*The information contained in this chapter is subject to change as more information becomes available or recommendations change.*

*Please check for updates from the Royal College of Physicians in Ireland website, College publications section at <http://www.rcpi.ie/PressRoom/Pages/PressRoom.aspx>*

### Important updates on previous version

**On the basis of the most recent data in relation to Pandemrix, NIAC has updated the recommendation in relation to the number of doses required to the following:**

- for all people 6 months and above who are immunocompromised, 2 doses of Pandemrix are required
- for all other people 6 months and above (including pregnant women and women up to 6 weeks post partum) 1 dose of Pandemrix is required (including children 10-13 years of age who previously received a paediatric dose)

**Recommendations in relation to the dose volume remains unchanged from the last amendment version 1.2.**

### Introduction

Influenza pandemics occur when a new influenza virus (typically influenza A virus) appears, against which the human population has little or no immunity. Pandemic strains can result in a range of illness, from mild to severe, and a varying number of deaths associated with illness. The severity of a pandemic can change over the course of that pandemic. Three influenza pandemics occurred in the 20<sup>th</sup> century, in 1918-1919, 1957 and 1968. The pandemic in 1918-1919 was the most severe and is estimated to have been associated with between 20-40 million deaths worldwide.

Pandemic (H1N1) 2009, formerly known as swine flu or influenza A (H1N1), is a new type of flu virus that contains genes from pig, bird and human influenza viruses in a combination that has not been observed before. The virus was first recognised in April 2009 in Mexico and subsequently spread to all parts of the world. An influenza pandemic was declared by the World Health Organization (WHO) on June 11<sup>th</sup> 2009.

## Epidemiology

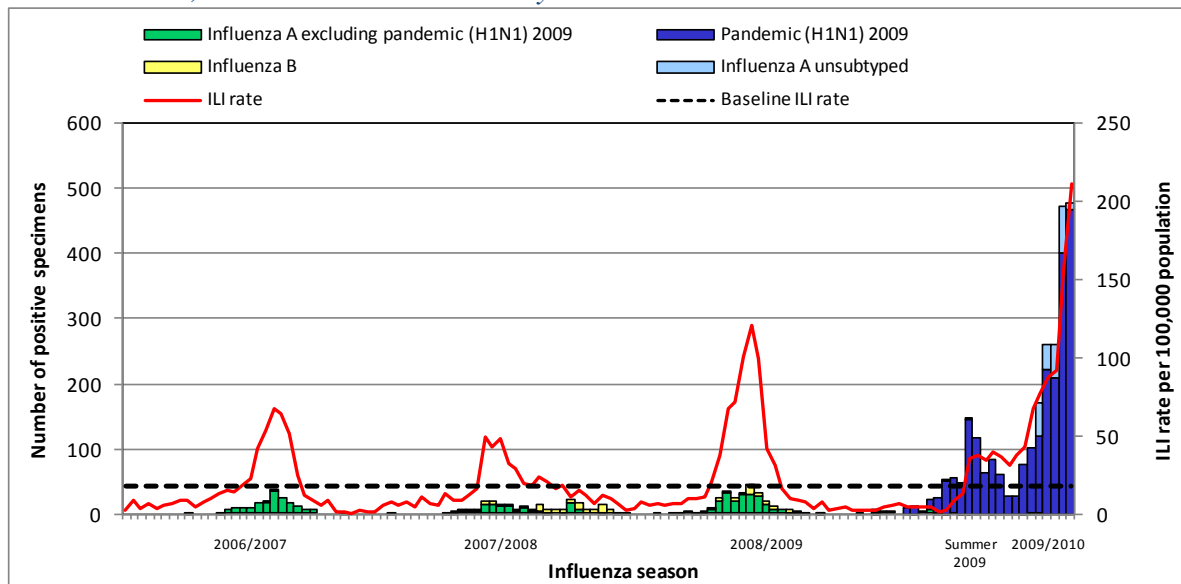
Note: please see [www.hpsc.ie](http://www.hpsc.ie) for the most recent information on the evolving epidemiology of pandemic (H1N1) 2009.

WHO has called the new influenza A strain “Pandemic (H1N1) 2009”. This new strain appears to be more infectious than seasonal influenza, and has spread rapidly worldwide, particularly among young children, and those aged 10 to 45 years. As a result of this increased transmissibility the virus can spread rapidly in schools and closed institutions, causing rapidly escalating outbreaks in these settings. The severity of the disease ranges from very mild symptoms to severe illnesses that can result in death. The majority of people who contract the virus experience mild disease and recover without antiviral treatment or medical care.

In Ireland, the impact of the pandemic has been marked. By week 43 of 2009, the rate of influenza-like-illness (ILI) as reported through the sentinel surveillance network has exceeded the highest ILI rates ever seen in Ireland since reporting began in 2000 (Figure 10a.1).

**Figure 10a.1 ILI GP consultation rates per 100,000 population, baseline ILI threshold rate, and number of positive influenza specimens, by influenza week and season<sup>1</sup>**

Source: NVRL, CUH & UCHG laboratory data and ICGP clinical ILI data

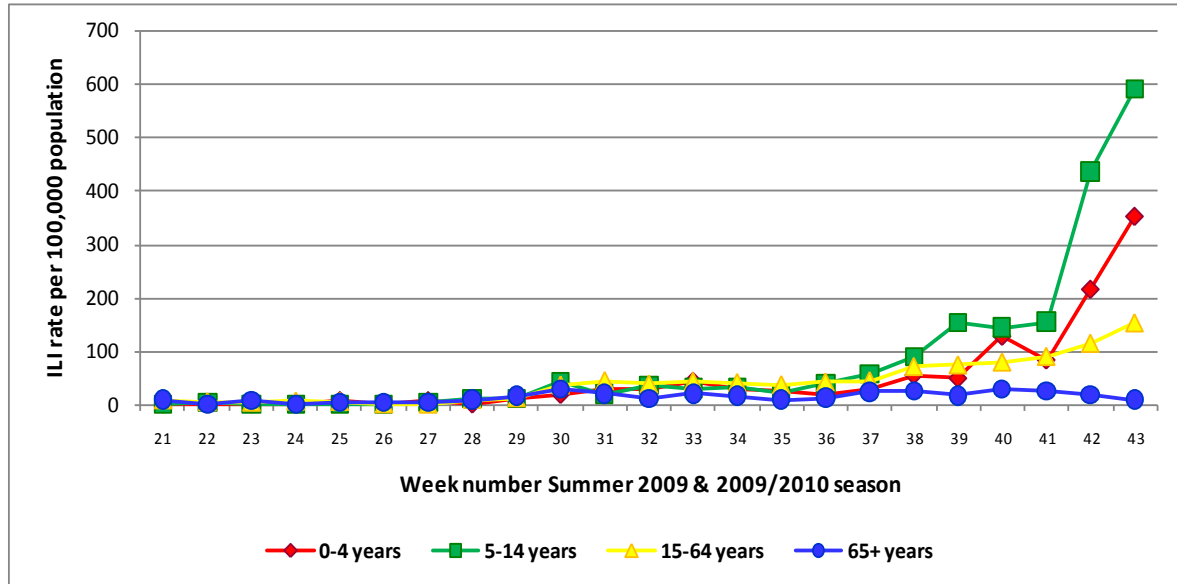


<sup>1</sup> Please note that virological data up to week 38, 2009 refers to NVRL data only. Virological data from week 39 2009 onwards refers to data from NVRL, CUH & UCHG. Virological data from CUH includes 187 influenza A untyped detections which are awaiting confirmation as pandemic (H1N1) 2009.

Similar to the global situation, in Ireland the pandemic has predominantly affected young adults and children (Figure 10a.2) and the numbers hospitalised and those requiring intensive care has increased as the virus spreads (Figure 10a.3). By the end of October 2009 (week 42), 16% of H1N1 confirmed cases had been hospitalised, of whom 8.7% were admitted to ICU; 42.7% of hospitalised cases had pre-existing clinical conditions including chronic heart, liver, renal, respiratory and neurological disease, asthma, haemoglobinopathy, immunosuppression, diabetes mellitus, severe obesity ( $BMI \geq 40$ ) and pregnancy.

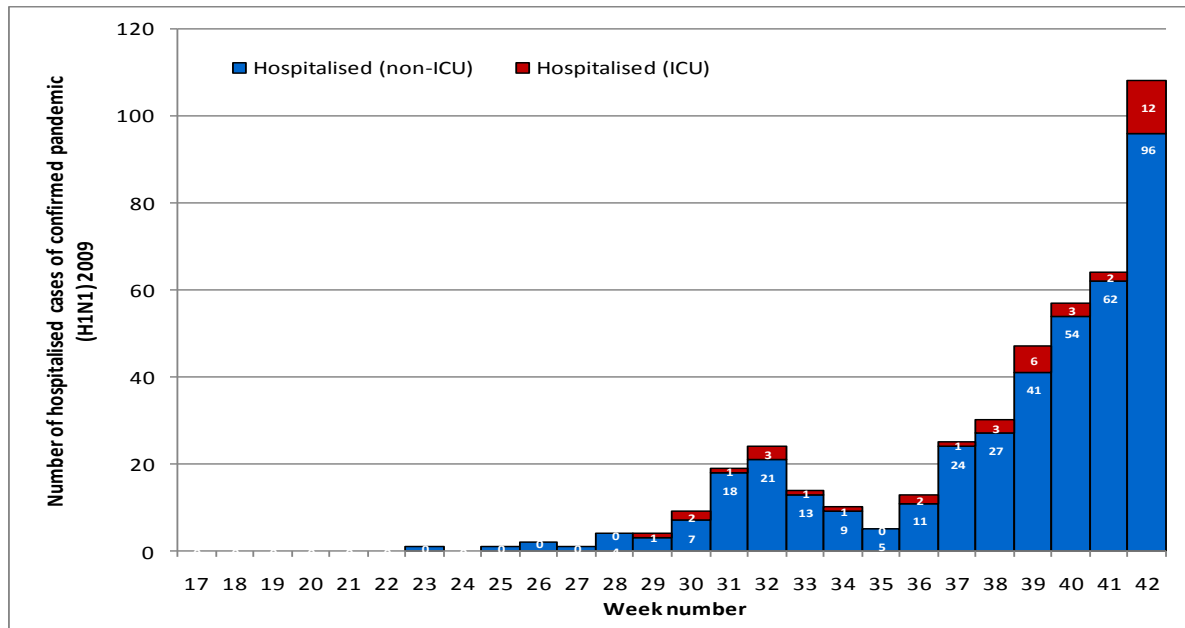
**Figure 10a.2: Age-specific sentinel GP consultation rate for ILI per 100,000 population by week during the Summer 2009 and 2009/2010 influenza seasons**

Source: ICGP ILI clinical data



**Figure 10a.3: Number of hospitalised cases of confirmed pandemic (H1N1) 2009 by week number<sup>2</sup>**

Source: CIDR



WHO has recently reported that teenagers and young adults continue to account for the majority of cases, with rates of hospitalisation highest in very young children. Between 1% to 10% of

<sup>2</sup> Week number in Figure 10a.3 is based on infectious disease notification week number, which is one week behind the international influenza week number. Therefore week 41 above is equivalent to week 42 on the influenza system

patients with clinical illness require hospitalisation. Of hospitalised patients, from 10% to 25% require admission to an intensive care unit, and from 2% to 9% have a fatal outcome. From 7% to 10% of hospitalised patients are pregnant women in their second or third trimester of pregnancy. Pregnant women are ten times more likely to need intensive care compared to the general population (WHO briefing note 14).

### **Transmission**

Pandemic (H1N1) 2009 is spread from person to person by direct contact, by droplet infection or by contact with materials recently contaminated by nasopharyngeal secretions. Airborne spread can also occur. It is very contagious, especially in younger children in close contact environments such as day schools, and particularly residential schools or institutions. Virus can be detected in respiratory secretions from about one day before the onset of clinical illness to 7 days or longer after symptom onset. Shedding can be more prolonged in young children and in the immunocompromised.

### **Effects of pandemic influenza A (H1N1) 2009**

*For the most recent information on global epidemiology please refer to WHO website [www.who.int](http://www.who.int).*

The pandemic strain (H1N1) 2009 causes an acute illness of the upper and/or lower respiratory tracts similar to seasonal influenza in the majority of cases. It affects all age groups but the highest age-specific rates are in children and adults < 45 years of age.

The illness is characterised by the abrupt onset of fever, headache, myalgia, cough, sore throat and malaise. For most people the illness is relatively mild and self-limited, with recovery in 2-7 days, but it can be severe. Individuals with pre-existing serious underlying illness are at increased risk of developing severe disease. Of the more serious cases who have been hospitalised, between one-third to more than half have had underlying health conditions.

Small subsets of patients develop very severe progressive pneumonia either rapidly or over a period of days after the initial ILI. The severe viral pneumonia is often associated with failure of other organs, or marked worsening of underlying asthma or chronic obstructive airway disease. Many of the most severe cases develop an acute respiratory distress syndrome (ARDS) requiring high pressure ventilation and intensive care.

Primary viral pneumonia is the most common finding in severe cases and a frequent cause of death. Secondary bacterial infections have been found in approximately 30% of fatal cases. Respiratory failure and refractory shock have been the most common causes of death.

The clinical picture in severe cases is very different from that seen during epidemics of seasonal influenza. While people with certain underlying medical conditions, and pregnancy, are known to be at increased risk, many severe cases occur in previously healthy young people. In these patients, predisposing factors that increase the risk of severe illness are not currently understood.

In severe cases, patients generally begin to deteriorate around 3 to 5 days after symptom onset. Deterioration is rapid, with many patients progressing to respiratory failure within 24 hours, requiring immediate admission to an intensive care unit. Most of these patients need mechanical ventilation. Some do not respond well to conventional ventilatory support, further complicating the treatment.

Prompt treatment with the antiviral drugs, oseltamivir or zanamivir, reduces the severity of illness and improves the chances of survival. Early treatment with these drugs for people at risk of severe disease is recommended, even in the absence of a positive confirmatory test.

In addition to viral pneumonia, co-infection with bacteria can also contribute to a severe, rapidly progressive illness. Bacteria frequently reported include *Streptococcus pneumoniae* and *Staphylococcus aureus*, including methicillin-resistant strains in some cases. Infection with meningococcal disease is a recognised complication of influenza infection, and may appear in the weeks following infection.

### **Pandemic influenza outbreaks – Ireland 2009**

By the end of October 2009, 93 general outbreaks of pandemic (H1N1) 2009 and ILI have been reported in Ireland since week 23. More than 2,000 people have been affected. Most outbreaks have occurred in educational settings. Outbreaks in residential institutions, crèches, social gatherings, workplace settings, a community hospital/long-stay unit, an hotel and an intellectual disability unit have also been reported.

### **Pandemic H1N1 2009 vaccine**

A number of vaccine manufacturers have produced pandemic vaccines for worldwide use. The licensing of vaccines to date by the European Medicines Agency (EMA) in conjunction with the Irish Medicines Board (IMB), including those used in Ireland (Celvapan and Pandemrix), was based on safety and immunogenicity data of similar vaccines developed with a strain of influenza virus other than that responsible for the current pandemic (the H5N1 strain). Clinical trials are on-going in adults and children with pandemic H1N1 2009 vaccines and the product information is expected to be updated regularly as data become available and these updates can be accessed on the IMB website at [www.imb.ie](http://www.imb.ie). In line with this, the recommendations provided here on dosing are interim and may be subject to revision.

Both pandemic H1N1 2009 vaccines are monovalent inactivated vaccines and a summary of their features is given in Table 10a.1 below.

**Table 10a.1 Summary of the features of the two pandemic vaccines available in Ireland**

	<b>Celvapan (Baxter)</b>	<b>Pandemrix (GSK)</b>
Antigen	Whole virion influenza vaccine, inactivated containing antigen* of pandemic strain A/California/07/2009 (H1N1)v 7.5 micrograms haemagglutinin per 0.5 ml dose	Split influenza virus, inactivated, containing antigen* equivalent to: A/California/7/2009 (H1N1)v-like strain (X-179A) 3.75 micrograms haemagglutinin per 0.5 ml dose (after mixing)
Manufacturing process	Propagated in vero cells (continuous cell line of mammalian origin)	Propagated in eggs
Main differences in constituents	Non adjuvanted No preservative	Adjuvanted with AS03 Has thiomersal as preservative
Contraindications	History of an anaphylactic (i.e. life-threatening) reaction to any of the vaccine constituents or trace residues e.g.	
	Formaldehyde, benzonase, sucrose	Egg and chicken protein, ovalbumin, formaldehyde, gentamicin sulphate and sodium deoxycholate
	History of Guillain-Barré Syndrome (GBS) within 6 weeks of influenza vaccination	History of Guillain-Barré Syndrome (GBS) within 6 weeks of influenza vaccination
Precautions	Acute severe febrile illness; defer until recovery.	Acute severe febrile illness; defer until recovery.
	Caution re IM injection in bleeding disorder e.g. clotting factor deficiency or severe thrombocytopenia	Caution re IM injection in bleeding disorder e.g. clotting factor deficiency or severe thrombocytopenia
	History of sporadic Guillain-Barré Syndrome (GBS) within previous 12 months	History of sporadic Guillain-Barré Syndrome (GBS) within previous 12 months
Reconstitution	Does not require reconstitution	Requires reconstitution
Pack size	200 doses	500 doses <b>or</b> 20 doses
Presentation	1 box with 20 multidose vials	1 box with 50 multidose vials of antigen and 25 x 2 boxes of multidose vials of adjuvant <b>or</b> 1 box with 2 multidose vials of antigen and 2 multidose vials of adjuvant
Shelf life once vial is opened	3 hours	24 hours

### Adjuvants

Adjuvants are substances that enhance the immune response in vaccines and can make them more effective. They have been used for many years in some vaccines. Scientific data support the safety of adjuvants in pandemic influenza vaccine production.

The squalene-based adjuvant used in Pandemrix (the GSK vaccine used in Ireland) is AS03. It is an oil-in-water emulsion. The oil phase contains two oils, squalene and DL- $\alpha$ -tocopherol (vitamin E). WHO and EMEA have reviewed the safety of adjuvanted influenza vaccines in 2009 and reported that there were no significant concerns regarding using adjuvanted H1N1 vaccine.

Celvapan does not contain an adjuvant.

### **Thiomersal**

Thiomersal is present in Pandemrix. It has been used in vaccine production since the 1930s to protect against bacterial contamination of vaccines. It is broken down in the body and one of the products is ethyl mercury. There is no evidence that ethyl mercury in vaccines has any adverse effects apart from minor reactions such as swelling and redness at the site of injection.

Ethyl mercury should not be confused with methyl mercury. Methyl mercury can accumulate if consumed regularly over time, whereas ethyl mercury is rapidly excreted. Everybody in the population (including pregnant women) is likely to be exposed to small amounts of methylmercury via food, especially fish.

WHO has concluded that there is no evidence of mercury toxicity in infants, children or adults exposed to thiomersal in vaccines. The EMEA has acknowledged that the presence of thiomersal in some vaccines is necessary, including its use as a preservative in multidose vials. After evaluation of the scientific evidence, the EMEA has concluded that immunisation with vaccines containing thiomersal continues to offer benefits to the general population.

While there are differences between the two vaccines in terms of their manufacture and constituents, the EMEA has concluded in licensing both vaccines that they are equally safe and effective.

### **Indications**

Pandemic influenza vaccines are recommended for everyone over six months of age including those with a history of “swine flu”. Although sufficient vaccines will be procured over the winter months to meet the needs of the whole population, the Pandemic Influenza Expert Group (PIEG) and the National Immunisation Advisory Committee (NIAC) have recommended that those individuals most likely to develop severe illness and death following infection with pandemic (H1N1) 2009 be prioritised for vaccination in the first phase. The Health Service Executive has proposed the methods of delivery of the pandemic vaccination campaign to the priority groups (see Table 10a.2 below).

**Table 10a.2 Priority groups for vaccination**

<b>Group order</b>	<b>Priority group</b>
Group 1	At-risk groups aged 6 months up to 65 years of age  Pregnant women in 2 <sup>nd</sup> and 3 <sup>rd</sup> trimester and up to 6 weeks post partum or in 1 <sup>st</sup> trimester with an additional risk factor  Immunosuppressed individuals* and household contacts of individuals with immunosuppression**  Residents of disability units regardless of whether they are in one of the medically at risk groups  Individuals with significant physical or intellectual disability (including neurodevelopmental conditions)†
Group 2	Healthcare staff
Group 3	Children aged 6 months -18 years Household contacts of children under 6 months
Group 4	Adults aged 65 years and over
Group 5	All others

\* There are individuals with conditions that may not be immunosuppressant by nature, but the individuals may be on immunosuppressant medication to control the condition- and individual risk assessment is needed

\*\*Household contacts of people who are immunosuppressed should be vaccinated. This group includes people undergoing active chemotherapy or receiving immunosuppressive treatment that makes them unable to respond to vaccination, and for 6 months following treatment.

†if prone to recurrent respiratory tract infections

### **Priority group 1**

*Those aged 6 months to 64 years (inclusive) with the following chronic illness requiring regular medical follow-up:*

- Chronic respiratory disease (including asthma and cystic fibrosis)
- Chronic heart disease
- Chronic renal disease
- Chronic liver disease
- Chronic neurological disease
- Immunosuppression due to disease or treatment including asplenia or splenic dysfunction
- Household contacts of these immunosuppressed people
- Diabetes mellitus
- Haemoglobinopathies (including thalassaemia, sickle cell disease)
- Morbid obesity (BMI  $\geq$  40)
- Residents of disability units regardless of whether they are in one of the medically at risk groups

- Individuals with significant physical, intellectual or neurological condition if prone to recurrent respiratory tract infections (including cerebral palsy, Down syndrome, muscular dystrophy)

*Pregnant women:*

- All pregnant women in the 2nd and 3rd trimester (from 14 weeks gestation) and those in the first 6 weeks postpartum.
- Pregnant women in the 1st trimester (less than 14 weeks gestation) with another risk factor (chronic illness requiring regular medical follow-up, as above).

## **Priority group 2**

*Healthcare staff:*

Healthcare workers are a priority both for their own protection – as these are a group likely to come in contact with the virus during this pandemic – and for the protection of their patients.

## **Priority group 3**

*Children aged 6 months to 18 years:*

The incidence and transmission is highest in children. Although for most children the disease is mild, hospitalisation rates are high in this age group. Premature infants should be vaccinated as soon as they reach six months.

*Household contacts of children aged less than 6 months:*

Immunisation of household contacts of these infants may provide some protection to them.

## **Priority group 4**

*Adults aged 65 years and over:*

People aged 65 years and over seem to have some immunity to pandemic (H1N1) 2009 infection and have a lower incidence of illness. However, if they become infected they are at higher risk of complications as they are more likely to have co-existing diseases and their immune system is less effective.

## **Priority group 5**

*All others:*

So far most people have experienced a mild to moderate illness. However, some previously healthy adults have had severe disease and some of them have died.

## **Pregnancy and breast-feeding**

NIAC recommends that all pregnant women in the second and third trimester and up to 6 weeks post delivery should receive pandemic (H1N1) 2009 vaccine. The first trimester of pregnancy is not a contraindication to vaccination. Women in the first trimester who require vaccination due to their occupation or a medical condition other than pregnancy that places them at high risk of severe outcomes from pandemic (H1N1) 2009 should receive the vaccine.

Breastfeeding is not a contraindication to vaccination. Breastfeeding is beneficial to the child, particularly as the mother may transfer antibodies to protect the baby if she is immunised with pandemic (H1N1) 2009 vaccine.

### **Premature infants and infants under six months**

It is important that premature infants who have clinical risk factors are protected as early as possible and therefore have all their immunisations at the appropriate age. Premature infants should be vaccinated with pandemic (H1N1) 2009 vaccine after the child has reached six months of age.

Children less than 6 months of age are not recommended vaccine. However, immunisation of household contacts of these infants may provide some protection to them.

### **Vaccination after influenza-like-illness (ILI)**

Most people with respiratory illnesses or ILI since the pandemic began were not laboratory confirmed and disease may have been caused by another virus. For this reason, all individuals without laboratory-confirmed pandemic (H1N1) 2009 disease are recommended to get the pandemic (H1N1) 2009 vaccine. Individuals with laboratory-confirmed disease are most probably immune and there is unlikely to be any benefit from vaccination.

Individuals with a recent history of ILI (unconfirmed pandemic (H1N1) 2009 disease) should defer vaccination until recovery. An arbitrary time period of two weeks between onset of illness and vaccination is suggested as it will decrease the likelihood of associating symptoms of infection with vaccination.

### **Contraindications**

There are very few people who cannot receive the pandemic (H1N1) 2009 vaccine.

- Anaphylactic reaction to a preceding dose or any of the constituents or trace residues of the vaccine. Pandemrix should not be given to persons with known anaphylactic hypersensitivity to eggs.
- Anaphylactic hypersensitivity to eggs is not a contraindication to Celvapan as it is not propagated in eggs.
- History of Guillain-Barré Syndrome (GBS) within 6 weeks of influenza vaccination.

### **Precautions**

- Acute severe febrile illness, defer until recovery.
- Caution is required if vaccines are given intramuscularly to those with a bleeding disorder or receiving anticoagulant treatment as ecchymosis at the injection site is common, particularly in those with severe bleeding diatheses.
- History of sporadic Guillain-Barré Syndrome (GBS) within previous 12 months. However, the need for immunisation requires evaluation of the risks and benefits on an individual basis. The risk of GBS post pandemic vaccination should be considered in the context of the possible risk of GBS associated with influenza and the risk of severe illness and possible death from pandemic influenza.

**Individuals with a history of allergic hypersensitivity to egg protein or chicken are advised to have Celvapan (non-egg derived) instead of Pandemrix (egg derived).**

**Since there are two pandemic vaccines available, if there are any concerns about allergic hypersensitivity to any constituent of one vaccine, then use the other.**

### **Dose and route of administration**

Both vaccines are licensed for adults and for children 6 months of age and older. There are no immunogenicity, efficacy or safety data to support interchangeability of Celvapan and Pandemrix. If two doses of the vaccine are required the second dose should be the same vaccine as the first dose. Based on available data, Pandemrix may be more immunogenic than Celvapan after a single initial dose, hence the differences in the number of doses recommended.

**This is an interim guidance and may be revised in light of new evidence regarding the persistence of an adequate immune response.**

All people over 6 months who are immunocompromised are recommended two doses of either vaccine as their ability to mount an immune response is likely to be impaired.

#### ***Celvapan***

For Celvapan, two doses of vaccine, at an interval of at least three weeks, are currently recommended for all individuals receiving the vaccine.

#### ***Pandemrix***

On the basis of the most recent immunogenicity data from GSK in relation to Pandemrix, the EMEA (and IMB) recommend:

##### *Children aged 10 years and older, and adults*

One dose of 0.5 ml (adult dose) at an elected date. A second dose is not indicated unless immunocompromised.

##### *Children aged from 6 months to 9 years*

One dose of 0.25 ml (paediatric dose) at an elected date. A second dose is not indicated unless immunocompromised.

Preliminary immunogenicity data obtained at three weeks after administration of a single dose of 0.25 ml to a limited number of healthy children aged 6-35 months old are available and demonstrate that an immune response is elicited. This data has been extrapolated to children aged 36 months and older. The need for any further dose of Pandemrix, in terms of persistence of immunogenic response, will be kept under review. This recommendation includes children aged 10-13 years of age who previously received a paediatric dose of Pandemrix.

**Table 10a.3 Dose and number of doses of the two pandemic vaccines available in Ireland**

	Dose of Celvapan	Dose of Pandemrix
Children 6 months to 9 years	0.5mls	0.25mls
Adults and children aged 10 years and older	0.5mls	0.5mls
	Number of doses of Celvapan	Number of doses of Pandemrix
All those 6 months and over who are immunocompromised	2 doses	2 doses
All those 6 months and over (including pregnant women and women up to 6 weeks post partum) who are NOT immunocompromised	2 doses	1 dose

Either vaccine can be used in all groups.

*These recommendations are based on best current international and Irish evidence of risk and best international evidence on vaccine efficacy and are subject to change as new evidence is available.*

### **Route of administration**

The deltoid muscle is the recommended site for adults and older children and the anterolateral thigh for infants and young children.

Both vaccines are recommended for administration by intramuscular (IM) injection. There are no data with pandemic vaccines using the subcutaneous route. Immunogenicity of vaccines recommended for IM administration may not be as long-lasting if they are given subcutaneously. The patient or parent should be advised of this.

### ***Bleeding disorders***

In those with bleeding disorders it is prudent to use a 23-gauge needle, and to apply pressure to the vaccine site for 1-2 minutes after the injections. In those with a severe bleeding disorder (e.g. clotting factor deficiency or severe thrombocytopenia) vaccination can be scheduled shortly after administration of clotting factor replacement or similar therapy. Individuals with bleeding disorders are under the care of a specialist who can be consulted about vaccinations. The risks of pandemic influenza versus risks of IM injection should be considered. There are no data on subcutaneous administration of pandemic influenza vaccine and if this route is used consideration should be given to possible reduction of immunogenicity. The patient or parent should be advised of this.

Patients on warfarin should be having regular blood tests to check INR. It may be useful to ask when INR was last checked and if it was acceptable. If INR has not been checked for some time or was very high at the most recent test or warfarin dose was increased then the individual can be referred to their own GP for review. The usual precaution of applying pressure for 1-2 minutes and checking that bleeding has stopped before removing pressure should be sufficient for patients on warfarin.

### Co-administration with other vaccines

Both vaccines are inactivated and can be administered at the same time as other vaccines, but in separate limbs.

- Both vaccines may be co-administered with the seasonal influenza vaccine and other routine childhood vaccines.

### Storage and use of multidose pandemic vaccine vials

Both vaccines should be stored in the original packaging in a refrigerator at +2°C to +8°C and protected from light.

Pandemrix must be used within 24 hours after reconstitution. Once reconstituted Pandemrix should be stored at a temperature of +2°C to +25°C.

Celvapan must be used within 3 hours once the vial has been removed from the fridge. Once Celvapan has reached room temperature it should **not** be returned to the fridge but kept at a temperature of up to 25°C and used within 3 hours or discarded.

Pandemrix vaccine must be reconstituted before administration.

Both vaccines are provided in multi-dose vials. Appropriate infection control precautions should be taken at all times. Specific guidelines have been developed and are available on the NIO website at [www.immunisation.ie](http://www.immunisation.ie).

### Adverse reactions

At the time of licensing of the vaccines, data on adverse effects came from studies on the mock-up vaccines which used H5N1 influenza virus as well as preliminary results from trial data of the vaccines. Adverse effects were similar to those from seasonal flu vaccines. Since licensing, post-marketing surveillance data are available from mass-vaccination programmes in a number of EU Member States and to-date the adverse effects seen are those which were anticipated from clinical trials.

**Local:** local reactions are common and include pain, redness, swelling, or bruising at the injection site.

**General:** the more common generalised reactions include: headache, fever, fatigue, malaise, myalgia, arthralgia, vertigo, nasopharyngitis and lymphadenopathy. These reactions usually last 1 to 2 days.

Allergic reactions and anaphylaxis are rare. As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available.

Encephalomyelitis, neuritis, and Guillian-Barré syndrome have on very rare occasions been temporally associated with some seasonal influenza vaccines. Convulsions, transient thrombocytopenia and vasculitis have also been reported rarely. To date, there is no evidence of any association between sporadic GBS or encephalitis and pandemic vaccines.

For more details on potential side-effects please see the specification of product characteristics (SPC) for each vaccine which is available on the Irish Medicines Board (IMB) website [www.imb.ie](http://www.imb.ie).

### Post-market surveillance

The IMB will be evaluating and assessing all suspected adverse reactions reported and will continue to monitor experience from other countries. This assists the IMB to make informed decisions and take measures as it deems appropriate to continue to safeguard public health safety in relation to medicines.

Suspected adverse reactions can be reported to the IMB by:

- Completing the online report on the IMB website ([www.imb.ie](http://www.imb.ie))
- Downloading an adverse report form available on: <http://www.imb.ie/EN/Safety--Quality/Online-Forms/Human-Medicine-Adverse-Drug-Reaction.aspx>. Complete the form and send it to the IMB Pharmacovigilance Department
- Contacting the IMB's Pharmacovigilance Department on 01-676 4971.

### Antiviral drugs

Anti-viral medicines are used for the early treatment of influenza infection. Early treatment is recommended for any patient who has severe symptoms, and for patients in defined risk groups (see below). Use clinical judgement. Treatment should be started as early as possible (preferably within 48 hours of onset) but may be started at any time if clinically indicated. Some of these patients may require hospitalisation.

*Defined risk groups:*

- Chronic respiratory, heart, kidney, liver or neurological disease
- Immunosuppression (whether caused by disease or treatment)
- Diabetes mellitus
- People aged 65 years and older
- Children <5 years (children <2 years are at higher risk for severe complications)
- People on medication for asthma
- Severely obese people (BMI  $\geq$  40)
- Pregnant women
- Haemoglobinopathies (including thalassaemia, sickle cell disease).

Antiviral treatment can reduce the severity and duration of symptoms of influenza if started within 48 hours of illness onset, and limited data from observational studies among hospitalised patients with pandemic (H1N1) 2009 infection indicate that oseltamivir can reduce mortality, even when started > 48 hours after illness onset. The drug of first choice in the management of influenza pandemic (H1N1) 2009 is oseltamivir (Tamiflu®). Zanamivir (Relenza®) is available when clinically indicated. Both drugs have been used in young children, pregnant women and other individuals with risk conditions and have been shown to be safe, effective and associated with improved outcomes.

Chemoprophylaxis is no longer generally recommended for contacts except for exceptional individual cases or settings where it may be appropriate (e.g. nursing homes or special education residential centres – following discussion with local public health staff).

Guidelines on the use of antivirals are available from the Irish Medicines Board at [www.imb.ie](http://www.imb.ie) and HPSC at [www.hpsc.ie](http://www.hpsc.ie).

### **Managing Outbreaks**

In general, immunisation as a control measure has been shown to be effective in preventing ongoing transmission in outbreaks. If an outbreak occurs in an institution vaccination should be considered for all unvaccinated individuals.

The benefit of vaccinating individuals who have already had laboratory-confirmed disease is unclear.

### **Pandemic Surveillance**

A number of surveillance activities are being implemented to monitor the impact of pandemic (H1N1) 2009 on the population. These include sentinel surveillance of ILI consultation rates, ILI calls to GP out-of-hour deputising services, hospitalised patient surveillance, surveillance of patients admitted to intensive care units, virological surveillance (NVRL), mortality surveillance of acute respiratory illness (General Register's Officer; GRO). Reports on the outcome of these surveillance activities are routinely published on the HPSC website and area available at [www.hpsc.ie](http://www.hpsc.ie).

### **Bibliography**

CDC (2007). Prevention and control of influenza. Recommendations of the advisory committee on immunization practices (ACIP) 2007. MMWR;56: 1-40.

CDC. Vaccine storage and handling toolkit. (Available at [http://www2a.cdc.gov/vaccines/ed/shtoolkit/pages/prep\\_disposal.htm](http://www2a.cdc.gov/vaccines/ed/shtoolkit/pages/prep_disposal.htm) last accessed 03/11/2009).

Department of Health UK (2006). Immunisation against infectious disease (the Green Book). 3rd ed. London: The Stationery Office. (Available at [http://www.dh.gov.uk/en/PublicHealth/HealthProtection/Immunisation/Greenbook/dh\\_4097254](http://www.dh.gov.uk/en/PublicHealth/HealthProtection/Immunisation/Greenbook/dh_4097254) ).

EMA (2009). Pandemic influenza A(H1N1)v vaccines authorised via the core dossier procedure- Explanatory note on scientific considerations regarding the licensing of pandemic A(H1N1)v vaccines. London, (Available at <http://www.emea.europa.eu/pdfs/human/pandemicinfluenza/60825909en.pdf>).

Fukuda K, Levandowski RA, Bridges CB, Cox NJ (2004). Inactivated influenza vaccines (In Plotkin S and Orenstein W (Eds) Vaccines, 4<sup>th</sup> Edition, Saunders, pp 339-70.

HPSC (2009). Anti-viral medicines. (Available at <http://www.hpsc.ie/hpsc/A-Z/EmergencyPlanning/AvianPandemicInfluenza/SwineInfluenza/AdviceforHealthProfessionals/AntiviralMedicines/>).

IMB (2009). Anti-Viral Medication. IMB update (Available at <http://www.imb.ie/EN/Medicines/Pandemic-H1N1-2009/Antiviral-Medication.aspx>).

Mak TK, Mangtani P, Leese J, Watson JM, Pfeifer D (2008). Influenza vaccination in pregnancy: current evidence and selected national policies. *Lancet Infect Dis*;8(1):44-52.

National Immunisation Office (2009). Adjuvants and the Pandemic Vaccine. (Available at [http://www.immunisation.ie/en/Downloads/PDFFile\\_16248\\_en.pdf](http://www.immunisation.ie/en/Downloads/PDFFile_16248_en.pdf) ).

National Immunisation Office (2009). Thiomersal and the Pandemic Vaccine. (Available at [http://www.immunisation.ie/en/Downloads/PDFFile\\_16249\\_en.pdf](http://www.immunisation.ie/en/Downloads/PDFFile_16249_en.pdf) ).

Stowe J, Andrews N, Wise L, Miller E (2009). Investigation of the temporal association of Guillain-Barré Syndrome with influenza vaccine and influenza like illness using the United Kingdom General Practice Research Database. *American Journal of Epidemiology* 169(3):382-388; doi:10.1093/aje/kwn310.

Whitley RJ, Monto AS, Bartlett J, Hayden FG, Tapper M and Pavia A(2006). Seasonal and pandemic influenza: at the crossroads, a global opportunity, *JID*; S65-161.

WHO (2009) Experts advise WHO on pandemic vaccine policies and strategies. Pandemic (H1N1) 2009 briefing note 14. (Available at: [http://www.who.int/csr/disease/swineflu/notes/briefing\\_20091030/en/index.html](http://www.who.int/csr/disease/swineflu/notes/briefing_20091030/en/index.html) ).

WHO (2009) Safety of pandemic (H1N1) 2009 vaccines WHO statement. 30<sup>th</sup> October 2009. (Available at [http://www.who.int/csr/disease/swineflu/frequently\\_asked\\_questions/vaccine\\_preparedness/safety\\_approval/en/index.html](http://www.who.int/csr/disease/swineflu/frequently_asked_questions/vaccine_preparedness/safety_approval/en/index.html)).

WHO (2008) Squalene-based adjuvants in vaccines. (Available at [http://www.who.int/vaccine\\_safety/topics/adjuvants/squalene/questions\\_and\\_answers/en/index.html](http://www.who.int/vaccine_safety/topics/adjuvants/squalene/questions_and_answers/en/index.html) ).

