

11

Influenza

Non-live trivalent vaccine introduced in 1988

Non-live quadrivalent vaccine introduced in 2019

Live attenuated influenza vaccine introduced in 2020

Adjuvanted vaccine introduced in 2021

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the product Summary of Product Characteristics (SmPC). When this occurs, NIAC advises that the recommendations in these guidelines, which are based on current expert advice from NIAC, are followed.

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11.1. Introduction

Influenza is an acute illness of the respiratory tract with systemic symptoms. It affects all age groups and is characterised by the abrupt onset of fever, headache, myalgia, cough, sore throat and malaise. It is usually self-limited, with recovery in 2-7 days, but it can be severe.

Influenza is caused by a highly infectious RNA virus that spreads rapidly, especially in institutions. There are three types of influenza virus, A, B and C. Types A and B cause most influenza illness.

Influenza outbreaks occur most years with the extent and severity varying widely. In some outbreaks, influenza A and B viruses circulate simultaneously. Pandemics provide the most dramatic evidence of the impact of influenza, although outbreaks that occur between pandemics account for greater mortality and morbidity, albeit over a longer period of time. Since 2009, influenza A (H1N1 2009), influenza A (H3N2) and influenza B have been in circulation.

Influenza A viruses infect a wide range of animal and avian species, particularly waterfowl. They have two surface antigens- haemagglutinin (H) and neuraminidase (N). The viruses are divided into subtypes, based on their H and N content. Only H1, H2, H3, N1 and N2 have been implicated in widespread human infection. Periodic mutations of the surface antigens occur. Minor changes (antigenic drift) are seen from season to season and are the reason why the vaccine composition changes each year. Major changes (antigenic shift) occur periodically and result in an immunologically distinct virus, facilitating pandemic spread with the potential for severe morbidity and high mortality. The most recent pandemic was in 2009/2010, caused by H1N1 (2009) virus. Most seasonal influenza is caused by Type A.

Influenza B viruses only infect humans and seals. This limited host range is likely to be the reason for the lack of Influenza B virus caused pandemics. Mutations rarely occur in influenza B. Type B causes outbreaks every few years. The illness is generally less severe than that caused by Type A.

Influenza C is a common cause of mild upper respiratory tract illness. It infects humans and pigs. Lower respiratory tract complications and systemic illness are uncommon and occur mainly in children. Most people have acquired immunity by adulthood.

Influenza epidemics begin abruptly, reach a peak over a 2-3 week period, generally last for 2-3 months and often subside as rapidly as they began. Epidemics in temperate climates begin almost exclusively during late autumn.

During the COVID-19 pandemic, influenza activity globally remained at low levels.

The COVID-19 pandemic influenced health seeking behaviours, surveillance and reporting in sentinel sites. Public hygiene and social measures implemented to reduce SARS-CoV-2 virus transmission likely played a role in reducing influenza virus transmission.

11.2. Transmission

Influenza is spread from person to person by aerosol, droplets or by contact with materials recently contaminated by respiratory secretions. It is highly infectious, especially in close contact environments such as homes for the elderly. It is contagious from 1-2 days before to 4-5 days after symptom onset. Shedding can be more prolonged in young children and in the immunocompromised. Asymptomatic carriers may shed the virus.

11.3. Effects of influenza

Although infection may be asymptomatic in up to 75% of cases, influenza outbreaks result in significant morbidity. The incubation period is 1-4 days. Onset is sudden, with fever, rhinitis, cough, myalgia and headache. Pneumonia, either primary viral or secondary bacterial, can occur.

Symptoms generally last for 3-5 days, and recovery is usually rapid.

The illness is more severe in the elderly, in those with chronic heart or lung disease, in children aged <4 years or with cerebral palsy and in pregnant women.

Eighty to 90% of reported deaths from influenza occur in the elderly, mainly from secondary bacterial pneumonia, but also from exacerbations of underlying disease e.g. chronic obstructive pulmonary disease or cardiac disease.

11.4. Influenza vaccines

Annual revaccination is recommended because immunity declines during the year after vaccination and circulating strains of influenza virus change from year to year.

Vaccines recommended by WHO are prepared each year, using virus strains similar to those considered most likely to circulate in the forthcoming season. The WHO has recently concluded that B/Yamagata lineages are no longer circulating (last detected March 2020) and are unlikely to cause future epidemics. Therefore, inclusion of a B/Yamagata antigen component of influenza vaccine is no longer warranted. Manufacturers will move from quadrivalent to trivalent influenza vaccine formulations and are currently prioritising supply of trivalent live attenuated vaccines for the 2024/2025 season. The trivalent live vaccine will offer the same level of protection against the 2A and 1B flu virus strains in it as the quadrivalent live vaccine.

Live trivalent attenuated influenza vaccine (LAIV) will be available in Ireland in 2024/2025. It is likely that non-live trivalent influenza vaccines will become available for future flu seasons.

All licensed influenza vaccines comply with the WHO (Northern hemisphere) recommendations for the 2024/2025 season.

Two types of influenza vaccine are licensed and available in Ireland: non-live influenza vaccines and live attenuated influenza vaccines (LAIV).

- *Non-live quadrivalent influenza vaccines (QIV)* contain antigens from two type A and two type B virus strains, cultured in fertilised hens' eggs or cell lines.

All parenteral influenza vaccines are supplied in a prefilled syringe for IM injection.

- *Live attenuated trivalent influenza vaccine (LAIV)* is a reassortant influenza virus vaccine containing antigens from two type A and one type B virus strains, produced in Vero cells and cultured in hens' eggs. The vaccine complies with WHO (Northern hemisphere) recommendation for the 2024/2025 season.

The vaccine is provided as a nasal spray suspension.

Influenza vaccines provide seasonally variable protection of 40-90% against influenza. Protective efficacy is lower in the elderly and the

immunocompromised. However, influenza associated morbidity and mortality are significantly reduced in older people who have been vaccinated. Protection lasts about one year.

An up-to-date list of licensed vaccines can be accessed on the HPRA website www.hpra.ie

A list of the currently available vaccines from the National Cold Chain Service can be found at www.immunisation.ie

Influenza vaccines should be stored at +2°C to +8°C.

If a vaccine has been frozen, it should not be used.

Licensed indications

Non-live quadrivalent influenza vaccine (QIV): active immunisation of adults and children for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine.

Non-live adjuvanted quadrivalent inactivated influenza vaccine (aQIV): active immunisation against influenza in the elderly (65 years of age and over), especially those with an increased risk of associated complications.

Non-live quadrivalent influenza vaccine high dose (QIV-HD): active immunisation in adults 60 years and older for the prevention of influenza disease.

Non-live quadrivalent influenza vaccine recombinant (QIVr): active immunisation for the prevention of influenza disease in adults.

Non-live quadrivalent influenza vaccine cell based (QIVc): active immunisation for the prevention of influenza in adults and children from two years of age.

Live attenuated trivalent influenza vaccine (LAIV): prophylaxis of influenza in children and adolescents from 24 months to less than 18 years of age caused by the two influenza A virus subtypes and the one influenza B virus types contained in the vaccine.

LAIV should not be used below 24 months of age because of safety concerns regarding increased rates of hospitalisation (for any cause) and wheezing in this population.

LAIV is more effective in children than non-live influenza vaccines. In addition, LAIV may offer some protection against strains not contained in the vaccine, as well as strains that have undergone antigenic drift.

Since LAIV contains live attenuated viruses, it mimics natural infection, which induces more durable immune memory (thereby offering better long-term protection to children than non-live influenza vaccines).

As the vaccine viruses are cold adapted, they cannot replicate efficiently at body temperature. Millions of doses of LAIV have been administered in the US for over 10 years and serious illness amongst immunocompromised contacts inadvertently exposed to vaccine virus has never been observed.

Note: After LAIV administration, a positive influenza PCR result can be obtained from upper respiratory samples for up to 7 days and rarely longer.

Dose and route of administration

QIV (for those aged 6 months to 64 years)

The dose is 0.5ml given by intramuscular injection into the anterolateral thigh or deltoid.

Children under nine years of age and those in specific at risk groups require two doses of vaccine separated by four weeks if receiving influenza vaccine for the first time or if their vaccination history is unknown.

All others and children aged six months to <9 years who have received influenza vaccine before, require one dose of vaccine ([Table 11.1](#)).

Table 11.1 Schedule for QIV

Group	Number of doses
Children aged 6 months to < 9 years ¹	Two doses 4 weeks apart, if <ul style="list-style-type: none"> receiving influenza vaccine for the first time or vaccination history is unknown
Post haematopoietic stem cell transplant or post solid organ transplant	Two doses 4 weeks apart, if <ul style="list-style-type: none"> receiving influenza vaccine for the first time post-transplant
Cancer patients who receive the vaccine while on chemotherapy and who complete their treatment in the same season ²	Two doses <ul style="list-style-type: none"> second dose at least 4 weeks after completion of treatment and at least 4 weeks after 1st dose (regardless of influenza vaccination in previous seasons)
All others	One dose

- Note that children aged 2-17 years will be offered LAIV; only for those for whom LAIV is contraindicated should receive QIV.
- If the lymphocyte count is $> 1.0 \times 10^9/L$.

aQIV (for those aged 65 years and older)

The dose is 0.5ml given by intramuscular injection into the deltoid.

- All those aged 65 years and older require one dose of aQIV (QIV is recommended if aQIV is not available).

LAIV (for those aged 2 to 17 years)

The dose is 0.1 ml into each nostril.

LAIV must **only** be given intranasally.

Post marketing effectiveness studies have shown that a second dose of LAIV is of little added benefit to healthy children. For this and for logistical reasons, healthy children should receive a single dose of LAIV.

Children aged two to <9 years in a clinically at risk group should receive two doses of LAIV, at least four weeks apart, if receiving influenza vaccine for the first time or if their vaccination history is unknown (Table 11.2).

Table 11.2 Schedule for live attenuated influenza vaccine (LAIV)

Age Group	Dose
Children aged 2 to <18 years	One dose
Children aged 2 to <9 years in a clinically at-risk group (section 11.5.2.iii) ¹	Two doses ² four weeks apart, if: <ul style="list-style-type: none"> • receiving influenza vaccine for the first time or • influenza vaccination history is unknown

¹LAIV is contraindicated in children:

- on long-term aspirin therapy
- with severe immunocompromise due to disease or treatment (e.g. acute/chronic leukaemia, lymphoma, HIV positive not on highly active antiretroviral therapy, cellular immune deficiency, high dose steroids $\geq 0.5\text{mg/kg/day}$ in children <40kgs or other immunosuppressing drugs).

²QIV can be given for the second dose if LAIV is unavailable

If the child sneezes or blows their nose after LAIV administration, neither dose needs to be repeated.

Influenza antibodies take from 10-14 days to reach protective levels following vaccination.

11.5. Recommendations

The ideal time for vaccination is before the influenza season, i.e., from September to October, but the vaccine may be given until the end of April.

Note: if travelling to the Southern hemisphere refer to [Chapter 5](#).

11.5.1 LAIV is recommended for all children aged 2 to 17 years.

11.5.2 aQIV is recommended for those aged ≥ 65 years. QIV is recommended if aQIV is unavailable.

11.5.3 QIV is recommended for

- i. Those aged 2 to 17 years for whom LAIV is contraindicated
- ii. Those aged 50 to 64 years
- iii. Those aged 6 months to < 2 years and those aged 18 to 49 years at

increased risk of influenza- related complications:

- Those with chronic illness, e.g. chronic heart disease (including acute coronary syndrome), chronic liver disease, chronic neurological disease (where the neurological condition compromises clearance of respiratory secretions), serious mental health conditions, chronic renal failure, chronic respiratory disease (including chronic obstructive pulmonary disease, cystic fibrosis, moderate or severe asthma, and bronchopulmonary dysplasia), diabetes mellitus and other metabolic disorders, or haemoglobinopathies
- Those with immunosuppression due to disease or treatment, including asplenia or hyposplenism, and all cancer patients
- Those with any condition that can compromise respiratory function (e.g., spinal cord injury, seizure disorder, or other neuromuscular disorder,) especially those attending special schools/ day centres
- Children and adults with Down syndrome
- Children with moderate to severe neurodevelopmental disorders such as cerebral palsy and intellectual disability
- Children on long-term aspirin therapy (because of the risk of Reye syndrome)
- Those with morbid obesity (Body mass index >40)
- Residents of nursing homes, old people's homes, and other long stay facilities where rapid spread is likely to follow introduction of infection

iv. Those likely to transmit influenza to a person at high risk for influenza complications (section iii)

- Health Care Workers (HCWs), for their own protection and to protect patients who may have a suboptimal response to influenza vaccinations (Chapters 3 and 4)
- Household contacts of at-risk persons¹
- Out-of-home care givers² to at-risk persons¹.

v. Pregnant women at any stage of pregnancy

Pregnancy increases the risk of complications from influenza because of alterations in heart rate, lung capacity, and immunological function.

Because non-live influenza virus vaccine is not a live vaccine it is very safe in pregnancy.

vi. People who have close, regular contact with pigs, poultry or water fowl.

¹ Persons with an underlying chronic health condition or Down syndrome

² A carer is someone who provides ongoing significant level of care to a person who is in need of care in the home due to illness or disability or frailty (HSE)

Anyone who wishes to reduce their own or their child's risk of infection may choose the influenza vaccine for themselves and/or their child.

Contraindications

All influenza vaccines

- Anaphylaxis following a previous dose of influenza vaccine or any of its constituents (*other than ovalbumin – see precautions*)
- Those with severe neutropenia (absolute neutrophil count $<0.5 \times 10^9/L$) should not receive any vaccines, to avoid an acute vaccine related febrile episode. This does not apply to those with primary autoimmune neutropenia who can receive influenza vaccine unless contraindicated.

LAIV

- Asthma
 - Those experiencing an acute exacerbation of asthma, including those who have had increased wheezing and/or needed additional bronchodilator treatment in the previous 72 hours
- Children who live with severely immunocompromised persons requiring isolation (e.g. post haematopoietic stem cell transplant)
- Concomitant use of aspirin/salicylates, because of the association of Reye syndrome with salicylates and wild-type influenza infection
- Influenza antiviral medication within the previous 48 hours
- Pregnancy
- Significant immunocompromise due to disease or treatment (see [Chapter 3](#))
- Those post cochlear implant until the risk of a CSF leak has resolved - consult with the relevant specialist
- Those with a cranial CSF leak.

QIV is recommended if LAIV is contraindicated.

LAIV is not contraindicated for use in those with asymptomatic HIV infection, those who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids or those receiving corticosteroids as replacement therapy, e.g. for adrenal insufficiency.

Precautions

All influenza vaccines

- Acute severe febrile illness, defer until recovery
- Egg allergy: Those with confirmed egg anaphylaxis or egg allergy can be given influenza vaccine in a primary care or school setting *with the exception of those who have required admission to ICU for a previous severe anaphylaxis to egg.*

LAIV has an ovalbumin content of ≤ 0.024 micrograms per dose and QIV vaccines have an ovalbumin content of ≤ 0.06 micrograms per dose. Adjuvanted QIV vaccine has an ovalbumin content equal to or less than 1 microgram per dose.

LAIV is the preferred vaccine for children who have required admission to ICU for a previous severe anaphylaxis to egg as the intranasal route is less likely to cause systemic reactions; it should be given in hospital.

Those requiring non-live influenza vaccine who have had a previous ICU admission for a severe anaphylaxis to egg should be referred for specialist assessment with regard to vaccine administration in hospital.

- Receiving combination checkpoint inhibitors (e.g. ipilimumab plus nivolumab), because of a potential association with immune related adverse reactions.

LAIV

Salicylates should not be used for four weeks after vaccination unless medically indicated, as Reye syndrome has been reported following the use of salicylates during wild-type influenza infection.

Seek specialist advice for those who require regular oral steroids or who have previously required ICU care for asthma.

Note: There have been no reported cases of live vaccine virus transmission among health care workers. Health care workers, including those who are pregnant, should ensure they are appropriately vaccinated against influenza.

QIV

If influenza vaccine is given to children aged 12-23 months of age, it should be separated from PCV vaccine by at least one week. This is because of a slightly

increased risk of febrile convulsions if the vaccines are given at the same time in this age group.

Co-administration

All influenza vaccines and other vaccines* (including COVID-19 vaccines) may be administered at the same time or at any interval.

Co-administered vaccines should be given in different limbs if possible. If administration in separate limbs is not feasible or desired, administration in the same limb, separated by at least 2.5 cm, is appropriate.

In keeping with international recommendations, seasonal influenza and COVID-19 vaccines should be co-administered where practicable to maximise uptake. A UK study revealed no unexpected safety concerns with co-administration.

Vaccinees should be informed there may be a slight increase in short term mild adverse events after co-administration with a COVID-19 vaccine. These include pain at the site of injection, fatigue, headache and myalgia.

*except PCV for children aged 12-23 months (see Precautions above)

Adverse reactions

QIV

- Local:* Injection site pain and swelling are very common.
- General:* Fever, fatigue, myalgia, and irritability in young children are very common. Drowsiness, sweating and arthralgia are common.
- Very rare:* Immediate allergic reactions.

Very rare reports of Guillain-Barré syndrome (GBS) have been observed in the post-marketing setting following influenza vaccination. The incidence cannot be estimated from known data. The risk of GBS following influenza infection is several times greater than that following influenza vaccination.

aQIV

- Local:* Injection site pain is very common. Injection site bruising, erythema and redness are common.
- General:* Fatigue and headache are very common. Arthralgia, chills, diarrhoea, influenza like illness, loss of appetite, myalgia and nausea are common. Fever and vomiting are uncommon. A higher incidence of mild post-immunisation reactions has been reported with adjuvanted compared to non-adjuvanted influenza vaccines.
- Very rare:* Immediate allergic reactions.

Very rare reports of Guillain-Barré syndrome (GBS) have been observed in the post-marketing setting following influenza vaccination. The incidence cannot be estimated from known data. The risk of GBS following influenza infection is several times greater than that following influenza vaccination.

Injectable influenza vaccines are non-live and cannot cause influenza.

LAIV:

- Local:* Nasal congestion is very common.
- General:* Malaise is very common. Decreased appetite, headache, myalgia and fever are common. Fever is no more frequent than that following other recommended childhood vaccines, is generally mild and resolves in a few days.
- Very rare:* Immediate allergic reactions. Very rare reports of Guillain-Barré syndrome (GBS) have been observed in the post-marketing setting following influenza vaccination. The incidence cannot be estimated from known data. The risk of GBS following influenza infection is several times greater than that following influenza vaccination.

LAIV viruses cannot cause influenza as they are cold adapted and cannot replicate efficiently at body temperature.

11.6. Use of antiviral medication to prevent or treat influenza

Antivirals such as neuraminidase inhibitors can be used for treatment and prophylaxis of influenza during influenza outbreaks. If considering using antiviral medication check the HPSC website to ascertain if influenza is circulating and only use antivirals if this is confirmed.

Indications for prophylaxis include:

- Non-immunised persons in at risk groups, including health-care workers, for two weeks while the vaccine takes effect.
- Control of influenza outbreaks in a closed setting such as institutions with high-risk individuals.
- Protection of immunocompromised children who may not respond to vaccine.

Note: Use of antiviral medication within two weeks after LAIV administration may adversely affect the effectiveness of the vaccine.

11.7. Influenza surveillance

The Health Protection Surveillance Centre, the Irish College of General Practitioners (ICGP) and the National Virus Reference Laboratory (NVRL) have established a network of 60 sentinel practices who report on a weekly basis the number of patients seen with influenza-like illness. Virological confirmation by the NVRL is required to identify that influenza is the causative virus, with classification of type and sub-type.

Throughout the inter-season period weekly reports on clinical data, fortnightly reports on virological data and weekly or fortnightly surveillance reports are produced. Reports of worldwide influenza activity are also provided as part of the overall monitoring of influenza activity.

Bibliography

Ambrose CS, Levin MJ, Belshe RB (2011). The relative efficacy of trivalent live attenuated and inactivated vaccines in children and adults. *Influenza And Other Respiratory Viruses*;5:67-75

Australian Immunisation Handbook (2020). <https://immunisationhandbook.health.gov.au/vaccination-for-special-risk-groups/vaccination-for-people-who-are-immunocompromised>

Blanton L, Peacock G, Cox C et al (2012). Neurological Disorders among pediatric deaths associated with the 2009 pandemic influenza. *Pediatrics*; 130:390-396

Centers for Disease Control and Prevention (2021). Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) https://www.cdc.gov/mmwr/volumes/70/rr/rr7005a1.htm?s_cid=rr7005a1_w

Department of Health UK (2020). Chapter 19, Influenza. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/931139/Green_book_chapter_19_influenza_V7_OCT_2020.pdf

Caini S, Meijer A, Nunes MC et al (2024). Probable extinction of influenza B/Yamagata and its public health implications: a systematic literature review and assessment of global surveillance databases. *Lancet Microbe* doi: 10.1016/S2666-5247(24)00066-1. Epub 2024 May 7. PMID: 38729197.

Domnich A, Arata L, Amicizia D et al. (2017). Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly: A systematic review and meta-analysis. *Vaccine* 35. 513–520

ECDC (2020). Systematic review of the efficacy, effectiveness and safety of newer and enhanced seasonal influenza vaccines <https://www.ecdc.europa.eu/en/publications-data/seasonal-influenza-systematic-review-efficacy-vaccines>

Gagnon R, Primeau MN, Des Roches A et al. (2010) Safe vaccination of patients with egg allergy with an adjuvanted pandemic H1N1 vaccine. *J. Allergy Clin Immunol.* 126: 317-23.

Grohskopf LA, Alyanak E, Broder KR, Walter EB, Fry AM, Jernigan DB. (2019). Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices – United States, 2019–20 Influenza Season. *MMWR Recomm Rep*; 68(No. RR-3):1–21. DOI: <http://dx.doi.org/10.15585/mmwr.rr6803a1>

Kwong J, Vasa P, Campitelli, M et al (2013). Risk of Guillain-Barré syndrome after seasonal influenza vaccination and influenza health-care encounters: a self-controlled study. *Lancet Inf Dis* Published *Online* June 28, 2013
[http://dx.doi.org/10.1016/S1473-3099\(13\)70104-X](http://dx.doi.org/10.1016/S1473-3099(13)70104-X)

Pérez-Padilla R, Fernández R, García-Sancho C, et al. (2010). Pandemic (H1N1) 2009 virus and Down syndrome patients. *Emerging Infectious Diseases*;16:1312-4.

Turner P et al (2015), Safety of live attenuated influenza vaccine in atopic children with egg allergy. *Jour Allergy Clin Immunology* Feb 1. pii: S0091-6749(15)00005

Vellozzi C, Iqbal S, Broder K.(2014). Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence. *Clin Infect Dis.* 58(8):1149-55.