



Public Health  
England

Protecting and improving the nation's health

# The national influenza immunisation programme 2020 to 2021

## Inactivated influenza vaccine information for healthcare practitioners

Withdrawn August 2021

# About Public Health England

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# Influenza vaccination programme 2020 to 2021 and control measures to prevent the spread of the SARs-CoV-2

The flu vaccination programme for the 2020 to 2021 flu season has been extended, with more groups eligible to receive flu vaccine than in previous years. As Coronavirus Disease 2019 (COVID-19) is likely to be co-circulating with flu, protecting those at high risk of flu, who are also those most vulnerable to hospitalisation as a result of COVID-19, is vitally important.

Control measures to prevent the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) such as shielding and social distancing will mean that delivering the flu vaccine this year will be more challenging as flu vaccines are likely to be delivered in a very different way than in previous years. Flu immunisers will need to wear the recommended personal protective equipment (PPE) in keeping with the current advice from the government when delivering the flu vaccine.

This information document will focus specifically on the national flu programme recommendations for the 2020 to 2021 flu season (a separate information document is available for the childhood flu programme). However, those involved in delivering this year's flu vaccine programme should ensure that they are aware of the specific guidance that they should follow in order to safely and effectively deliver flu vaccines during the ongoing COVID-19 pandemic. This includes, but is not limited to, guidance on PPE and infection prevention and control measures.

Please ensure that you read the [national flu immunisation programme 2020 to 2021](#) letters available on the [PHE Annual flu programme webpage](#) ([www.gov.uk/government/collections/annual-flu-programme](http://www.gov.uk/government/collections/annual-flu-programme))

In addition to providing key information about this year's flu programme, these letters also contain links to the relevant coronavirus-related guidance. **It is recommended that you regularly check the [PHE Annual flu programme webpage](#) during the flu vaccination period as any further information that becomes available about the flu vaccination programme will be published there.** Any further programme updates will also be reported in Vaccine Update so please ensure that you subscribe using this link: [New subscribers](#).

## Background and 2020 to 2021 programme summary

The seasonal influenza vaccination programme was introduced in England during the late 1960s to protect those in clinical risk groups. These groups were found to be at higher risk of influenza associated morbidity and mortality. Since then, the programme has been extended to include all those aged 65 years and over (in the year 2000) and pregnant women (in 2010). In 2013, a phased programme commenced to offer influenza vaccine to all children from 2 years of age.

All those who were eligible for the NHS-funded flu vaccination programme during 2019/20 remain eligible during 2020/21. However, in light of the risk of flu and COVID-19 co-circulating this winter, the following groups are also eligible to receive NHS-funded flu vaccine during the 2020/21 flu season:

- household contacts of those on the NHS shielded patient list ([Coronavirus \(COVID-19\): Shielded patients list - NHS Digital](#))
- children of school year 7 age in secondary schools (aged 11 on 31 August 2020)
- health and social care workers employed through direct payment and /or personal health budgets to deliver domiciliary care to patients and service users

Following prioritisation of eligible risk groups (as above) during the first three months of the flu vaccination programme (Sep. - Nov 2020) and procurement of additional flu vaccine supplies, the offer of inactivated influenza vaccine is being extended to all adults aged 50-64 years old from 1 December 2020.

The vaccine recommendations for the 2020 to 2021 flu season were first described in the [National flu immunisation programme 2020 to 2021 letter: update \(August 2020\)](#). These recommendations have been updated in November 2020 and will be published in the Statement of amendments to the annual flu letter on the [PHE Annual flu programme webpage](#). These are summarised below:

- **at risk children aged 6 months to 2 years:** offer egg grown quadrivalent influenza vaccine (QIVe)
- **at risk children aged 2 years up to 18<sup>th</sup> birthday:** offer live attenuated influenza vaccine (LAIV) unless contraindicated\*
- **aged 2 and 3 years on 31 August 2020, all primary school aged children and those in year 7 (ages 4 to 11 on 31 August 2020):** offer LAIV unless contraindicated\* \*\*

- **at risk adults aged 18 to 64 year olds, including pregnant women, HCWs and carers:** offer the QIVc or QIVr (Flublok Quadrivalent)<sup>\*\*\*</sup> or if these are not available at the point of vaccine delivery, one of the QIVe vaccines
- **'Healthy' adults aged 50 to 64 years (not in at risk groups, from 1<sup>st</sup> December 2020):** QIVc, or QIVr (Flublok Quadrivalent)<sup>\*\*\*</sup> or if these are not available at the point of vaccine delivery, one of the QIVe vaccines
- **aged 65 years and over (including those who become 65 before 31 March 2021):** offer adjuvanted trivalent influenza vaccine (aTIV) or QIVc if aTIV is unavailable

\* Where a recommended vaccine is contraindicated, immunisers should follow the recommendations in the summary table of Appendix B in the **second (update) letter** detailing the national flu immunisation programme.

\*\* A supply of inactivated influenza vaccine for children whose parents object to the porcine gelatine content of Fluenz Tetra (LAIV) is now available to order by General Practice and school aged immunisation teams via ImmForm. The vaccine is Fluarix<sup>®</sup> Tetra, manufactured by GlaxoSmithKline. This vaccine is also available to order for children in clinical risk groups. See **Statement on the childhood flu programme: the alternative offer to live attenuated Influenza vaccine (LAIV)**

\*\*\* The MHRA have provided a statement on Flublok Quadrivalent vaccine: **Flublok vaccine given authorisation for temporary supply in the UK to meet public health need**. This is published on their website as is **The Public Assessment Report (PAR) and the Patient Information Leaflet (PIL)** for the vaccine. See page 14 for more information about this vaccine.

The requirements of the influenza vaccination programme are set out in the following key documents:

1. The **annual flu letter 2020 to 2021<sup>1</sup>** and the **National flu immunisation programme 2020 to 2021 letter: update** provides detailed information to support the successful implementation of the programme
2. **Directed Enhanced Service Specification Seasonal influenza and pneumococcal polysaccharide vaccination programme 2020/21<sup>2</sup>** (updated November 2020) describes the services to be provided by GP practices delivering the programme in England. It sets out all eligible groups for vaccination (apart from those aged two and three on 31 August

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<sup>1</sup>Department of Health, Public Health England, NHS England. The national flu immunisation programme 2020/21. 14 May 2020. Available at: [www.gov.uk/government/publications/national-flu-immunisation-programme-plan](http://www.gov.uk/government/publications/national-flu-immunisation-programme-plan)

<sup>2</sup> NHS England. Directed Enhanced Service Specification - Seasonal influenza and pneumococcal polysaccharide vaccination programme 2020/21. Available at: [www.england.nhs.uk/publication/directed-enhanced-service-specification-seasonal-influenza-and-pneumococcal-polysaccharide-vaccination-programme-2020-21/](http://www.england.nhs.uk/publication/directed-enhanced-service-specification-seasonal-influenza-and-pneumococcal-polysaccharide-vaccination-programme-2020-21/)

2020). It includes eligible frontline health and care workers working in residential care and nursing homes, domiciliary care providers and the voluntary managed hospice sector.

3. **Enhanced Service Specification: Childhood seasonal influenza vaccination programme 2020/21**<sup>3</sup> describes the services to be provided by GP practices for children aged 2 and 3 but not 4 years on 31 August 2020.
4. **Community Pharmacy Seasonal Influenza Vaccination Advanced service specification for 2020/21**. Community pharmacies offering a flu vaccination service for adults are required to offer this service in accordance with the service specification.
5. Green Book **Influenza chapter** provides information on influenza disease, epidemiology, the vaccines and the vaccination programme. This chapter was updated on 29 October 2020 to include details on QIVr (Flublok Quadrivalent vaccine).

Additional resources to support the implementation of the programme include template letters, leaflets, posters, a training slide set and an e-learning programme, all of which can be found on the **Annual flu programme** page of the GOV.UK website. This will be updated to include a leaflet for the expansion to 50 to 64 year olds.

Any updates to the flu programme are also published in the monthly PHE publication **Vaccine Update**.

The information in this document focuses on the inactivated influenza vaccine. A separate document containing information for healthcare practitioners on the childhood programme (**The national childhood flu immunisation programme 2020 to 2021: information for healthcare practitioners**) is also available.

## Influenza

Influenza is a highly infectious, acute viral respiratory tract infection which has a usual incubation period of 1 to 3 days. Patients can experience sudden onset of symptoms such as dry cough, headache, fever and extreme fatigue.

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<sup>3</sup> NHS England. Enhanced Service Specification – Childhood seasonal influenza vaccination programme 2020/21 Available at: [www.england.nhs.uk/wp-content/uploads/2020/03/20-21-VI003-Childhood-Flu-Final-Version.pdf](http://www.england.nhs.uk/wp-content/uploads/2020/03/20-21-VI003-Childhood-Flu-Final-Version.pdf)



There are 3 types of influenza virus which affect humans: types A, B and C. Types A and B are responsible for most disease. Influenza is spread by droplets, aerosol or through direct contact with the respiratory secretions of someone with the infection. For otherwise healthy individuals, it is an unpleasant but usually self-limiting disease with recovery occurring within 2 to 7 days. However, more serious illness may occur in children under six months, pregnant women, those aged over 65 years and those with underlying health conditions. These groups are at higher risk of developing severe disease or complications such as bronchitis or secondary bacterial pneumonia, or otitis media in children.

Further information on influenza infection is included in the Green Book [Influenza chapter](#) and on [NHS.UK](#).

## Influenza vaccination programme

The purpose of the influenza vaccination programme is to protect those most at risk of developing severe disease or complications or from dying if they develop the infection.

Individuals not eligible for vaccination will benefit from reduced circulation in the community gained through the childhood flu vaccination programme and infants under the age of six months will benefit from passive protection if their mother received the vaccine during pregnancy<sup>4</sup>.

Vaccination of eligible individuals should commence as soon as stock of the recommended vaccine is available and given in sufficient time to ensure patients are protected before flu starts circulating. However, eligible patients can be offered influenza vaccine at any point in the flu season and the [enhanced service specification for flu](#) includes payment for vaccines given up until 31 March 2021.

## Vaccine eligibility

In 2020/21, flu vaccination will be offered under the NHS flu vaccination programme to the following groups:

- all children aged 2 to 11 (but not twelve years or older) on 31 August 2020
- people aged 65 years or over (including those who become 65 by 31 March 2021)

- all those in aged from 6 months to less than 65 years of age in a clinical risk group such as those with:
  - chronic (long-term) respiratory disease, such as severe asthma, chronic obstructive pulmonary disease (COPD) or bronchitis
  - chronic heart disease, such as heart failure
  - chronic kidney disease at stage 3, 4 or 5
  - chronic liver disease
  - chronic neurological disease, such as Parkinson's disease or motor neurone disease
  - learning disability
  - diabetes
  - splenic dysfunction or asplenia
  - a weakened immune system due to disease (such as HIV/AIDS) or treatment (such as cancer treatment)
  - morbid obesity<sup>3</sup> (defined as BMI of 40 and above)
- all pregnant women, including those who become pregnant during the delivery of the influenza programme
- household contacts of those on the **NHS shielded patients list** or of immunocompromised patients
- people living in long-stay residential care homes or other long-stay care facilities
- those in receipt of carers allowance or who are the main carer of an older or disabled person
- health and social care staff employed by a registered residential care/nursing home or registered domiciliary care provider who are directly involved in the care of vulnerable patients/clients who are at increased risk from exposure to influenza
- health and social care staff, employed by a voluntary managed hospice provider, who are directly involved in the care of vulnerable patients/clients who are at increased risk of exposure to influenza
- health and social care workers employed through direct payments (personal budgets) and/or Personal Health Budgets, such as Personal Assistants, to deliver domiciliary care to patients and service users

In the 2020 to 2021 flu vaccine programme, flu vaccination will also be offered to all those aged between 50 and 64 years from 1 December 2020, following the prioritisation of other eligible groups.

Further details of those eligible to receive the NHS-funded flu vaccine can be found in **Chapter 19 of the Green Book** **Error! Bookmark not defined.** and in the **Annual flu letter for 2020/21**<sup>1</sup>.

# Inactivated influenza vaccine recommendations

For the 2020 to 2021 flu season, in response to evidence about the currently available influenza vaccines, the Joint Committee on Vaccination and Immunisation (JCVI) have made the following recommendations<sup>4</sup> for the different patient groups:

## Adults 65 years of age and over

For vaccination of those aged 65 years and over in the 2020/21 flu season, JCVI advises the use of the following inactivated vaccines:

- adjuvanted trivalent influenza vaccine (aTIV)
- cell-based quadrivalent influenza vaccine (QIVc) if aTIV is not available

aTIV should be offered 'off label' to those aged 64 years who will become 65 before 31 March 2021.

The current available evidence indicates additional benefit from aTIV in those aged 65 years and over, compared with standard dose egg-cultured inactivated trivalent and quadrivalent vaccines (TIVe/QIVe), and to outweigh the potential additional benefits of a second B strain in a quadrivalent egg-culture vaccine. The quadrivalent influenza cell-culture vaccine (QIVc) however, is considered suitable for use in this age group if aTIV is not available.

## At risk adults (including pregnant women) aged under 65 years

At risk adults aged up to 65 years should be offered:

- cell-based quadrivalent influenza vaccine (QIVc)
- recombinant quadrivalent influenza vaccine (QIVr) as an alternative to QIVc
- egg-grown quadrivalent influenza vaccine (QIVe) if QIVc or QIVr are not available at the point of delivery

Evidence from recent flu seasons indicates a clear additional benefit from the use of quadrivalent flu vaccines in those under 65 years of age in a clinical risk group

<sup>4</sup> Joint Committee on Vaccination and Immunisation. Advice on influenza vaccines for 2020/21. Published September 2019. Available at: [www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#influenza-vaccines-jcvi-advice](http://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#influenza-vaccines-jcvi-advice)

compared with trivalent flu vaccines. Limited evidence also shows there is a potential advantage to using cell-cultured flu vaccines compared with egg-cultured flu vaccines, due to the possible impact of 'egg-adaption' on vaccine effectiveness, particularly against A(H3N2) strains. However, quadrivalent egg-culture inactivated vaccine (QIVe) can also be given to this age group.

## Children in clinical risk groups for whom live flu vaccine (LAIV) is contraindicated

Children aged from 2 years to less than 18 years are recommended to receive the quadrivalent live attenuated influenza vaccine (LAIV) unless contraindicated.

As LAIV is not licenced for use in those aged 6 months to 2 years, eligible at-risk children are recommended to receive an age appropriate inactivated quadrivalent influenza vaccine (injected). QIVe will be centrally supplied for these children and for children in risk groups for whom LAIV is contraindicated or otherwise unsuitable.

If LAIV is contraindicated or otherwise unsuitable, the following alternatives should be offered:

- children less than 9 years of age should be given Quadrivalent influenza egg-culture vaccine (QIVe)
- children aged 9 years and over should be given Quadrivalent influenza cell-culture vaccine (QIVc). If QIVc is unavailable, QIVe should be offered. (QIVe can be offered to the small number of children aged 9 years and over who are contraindicated to receive LAIV and who are scheduled to be vaccinated in the school setting).

Children aged 9 years and over who access flu vaccine through general practice should ideally be offered the QIVc from the practice's locally procured vaccine stocks. GP practices offering QIVc to these children will be reimbursed by NHS England and NHS Improvement (NHSEI). Where QIVc vaccine is unavailable, practices can either offer QIVe ordered through ImmForm from centrally purchased supplies (not reimbursed), or their own locally procured QIVe which will be reimbursed by NHSE/I.

## Quadrivalent influenza vaccines

Quadrivalent influenza vaccines (QIV) contain two influenza A strains and the two main influenza B strains. By including both B strains, they should provide better protection in seasons when the circulating influenza B strain is not well matched to the single B strain contained in the previously used non-adjuvanted, standard-dose trivalent vaccines (TIV).

As influenza B is relatively more common in children than older age groups, the main clinical advantage of quadrivalent vaccines is in childhood. The use of the quadrivalent LAIV in children should not only protect the age group where flu infection is most common but additionally, by preventing transmission from children to others, it also reduces circulation of influenza B across the whole population and thus indirectly protects them.

However, modelling suggests that, even with a fully established flu programme in children of primary school age, there is still benefit from using QIV in adults under 65 years of age in clinical risk groups, pregnant women and healthcare workers.

Quadrivalent flu vaccines may be either egg-grown or cell-based.

### Egg-grown quadrivalent influenza vaccine (QIVe)

The egg-grown quadrivalent influenza vaccine (QIVe) protects against four strains of flu: two A types and both B types. Because it contains both B types, it is recommended for people aged under 65 years in clinical risk groups since circulating flu B strain(s) are more likely to affect this younger patient group compared to older people.

### Cell-based quadrivalent influenza vaccine (QIVc)

The cell-based quadrivalent influenza vaccine (QIVc), Flucelvax Tetra, was first used in the UK for the 2019 to 2020 flu season. Previously, virtually all flu vaccines had been cultured in fertilised chicken eggs but when flu vaccine viruses are grown this way, the viruses adapt to live in the egg. This can lead to changes in the viruses during the manufacturing process which means the egg-derived virus used in the vaccine is then not a complete antigenic match to the original wild-type strain recommended by the WHO. This means the vaccine virus may not match the circulating flu strain as closely and the vaccines produced may therefore not be as effective. Although this 'egg adaptation' has been known about for a long time, it has become more of a problem in the last decade, particularly for the A(H3N2) virus which appears to be more affected by egg adaptation than the other flu A and B viruses.

The cell-based vaccine manufacturing process used to make the quadrivalent cell-based flu vaccine Flucelvax, uses the Madin-Darby Canine Kidney (MDCK) cell line to grow the influenza virus. The original cells in this cell line were taken by Madin and Darby from the kidney tubule of an adult dog in 1958. This is the cell line that is still used today so the cell-based manufacturing process does not require any new cells to be taken. The MDCK cell line is used because the influenza virus grows well in it, it is able to produce high volumes of flu virus for use in vaccines and the influenza virus isolated following culture in these cells retains the antigenic properties of the original

strain. This method of vaccine virus production should result in the vaccine virus being a closer match to the wild-type circulating flu viruses. After the vaccine viruses are grown, they are highly purified in a purification process that removes the cell culture materials. This means that it is unlikely that any cell culture material remains in the vaccine.

## Recombinant quadrivalent influenza vaccine (QIVr)

Flublok Quadrivalent is a quadrivalent flu vaccine made using recombinant DNA technology. It does not require the use of, or growth of flu virus during the manufacturing process which means that the antigen in the vaccine cannot adapt or mutate and should therefore be an exact match to the flu A and B strains contained in the vaccine. It also contains three times the amount of flu virus antigen contained in the other flu vaccines currently used in the UK in order to enhance the immune response made to it.

To make recombinant vaccine, the manufacturers take the DNA (genetic instructions) for making the surface protein, haemagglutinin, found on flu viruses. The haemagglutinin DNA is then combined with a baculovirus (a virus that infects invertebrates). This results in a "recombinant" virus. The role of the baculovirus is to help transport the DNA instructions for making the haemagglutinin antigen into a host cell. Once the recombinant virus enters the host cell line (an insect cell line in which the baculovirus grows well), it instructs the cells to rapidly produce the haemagglutinin antigen. This antigen is grown in bulk, collected, purified, and then packaged as recombinant flu vaccine. When the vaccine is injected, the haemagglutinin antigen in it triggers the immune system to create antibodies that specifically target the flu virus.

The type and rates of local and systemic reactions following vaccination with Flublok Quadrivalent are similar to those seen following vaccination with other flu vaccines (injection site tenderness, headache, fatigue, muscle ache and joint pain). Flublok Quadrivalent can be given to people aged 18 years and above but for the 2020/21 flu season in the UK, it is recommended that it should be specifically offered to people aged under 65 years old.

Flucelvax Tetra and Flublok Quadrivalent are widely used in the US and in multiple European countries. Flucelvax was first approved for use in the US in 2012 and Flublok was approved in 2013. Since eggs are not required to grow the flu virus, cell-based flu vaccines contain no egg and they also do not contain any live virus, antibiotics or gelatin.

Further information on how cell-based and recombinant flu vaccines are made is available at: [www.cdc.gov/flu/prevent/how-fluvaccine-made.htm](http://www.cdc.gov/flu/prevent/how-fluvaccine-made.htm)

## Trivalent influenza vaccines

As there is increasing evidence of the limited effectiveness of non-adjuvanted, standard-dose egg-based influenza vaccines in older people, they are not recommended to be used in any age or clinical risk group for the 2020/21 influenza season.

## High dose trivalent influenza vaccines

A high dose trivalent influenza vaccine containing four times the amount of antigen contained in standard-dose inactivated flu vaccines is available but due to the higher cost of this vaccine, it is not commissioned by NHSE/I and will not be reimbursed by NHSE/I in 2020/21.

## Adjuvanted trivalent influenza vaccines

Adjuvanted vaccines are vaccines that have a substance added to them to enhance the immune response made. More information can be found in the section on [Influenza vaccine components](#) below.

An adjuvanted trivalent inactivated influenza vaccine (aTIV), was licensed for use in those aged 65 years and older in the UK in 2017 and has been widely used in the past two flu seasons. The aTIV has been licensed in some countries in Europe since 1997 and in the USA since 2015. It has been used for 20 years and is used in over 20 countries.

Published data indicates that aTIV has higher immunogenicity and effectiveness than non-adjuvanted vaccines in older people.

At the present time, an adjuvanted quadrivalent flu vaccine is not available for use in the NHS-funded flu vaccine programme.

Based on the existing evidence, JCVI have said that the adjuvanted vaccine should be offered to 65 year olds and over even though it is trivalent. Although quadrivalent vaccine offers the potential to provide broader direct protection against influenza B, this strain is relatively less common in the elderly than in children and young adults. The successful childhood programme which uses quadrivalent LAIV is likely to offer indirect protection by reducing transmission of the additional B strain contained in the quadrivalent vaccine.

## Flu vaccination for health and social care workers aged 65 years old and over

All frontline health and social care workers are eligible to receive flu vaccine and should be offered it at the earliest opportunity. Vaccine providers should use the current definition of healthcare worker as set out in [chapter 12](#) (Immunisation of healthcare and laboratory staff) of the Green Book and should also refer to appendix A of the [second flu letter](#) (dated 5 August 2020).

The **Specialist Pharmacy Service written instruction for the administration of seasonal influenza vaccine for 2020 to 2021** states 'Staff from 65 years of age may be immunised with QIVe as part of an occupational health scheme. Where a vaccine recommended for the over 65's is not provided by the organisation's occupational health scheme and the individual is unlikely to access another provider for an alternative recommended vaccine the available vaccine should be offered'.<sup>5</sup>

Most health and social care workers are likely to be under 75 years of age and relatively healthy and should therefore derive benefit from the QIV whether it is cell-based or egg-grown. Immunisers should make it clear to staff aged 65 years and over that they can get aTIV from their GP or a pharmacy should they wish.

Health and social care workers aged 65 years and over with underlying medical conditions that make them less likely to respond to standard vaccines should be encouraged to go to their GP or pharmacy to get aTIV or QIVc instead.

### **Flu vaccination for health and social care workers aged under 18 years old**

Most health and social care workers are aged 18 years and over. For the small number of employees under 18 years of age, it is acceptable to offer QIVe or QIVc to ensure high coverage.

Employees under 18 years of age in an at-risk group, who are not contraindicated to receive the live attenuated influenza vaccine (LAIV), should be advised to attend their GP surgery to be immunised with LAIV although the effectiveness of LAIV and QIV for 16 and 17 year olds is likely to be equivalent.

## **Pregnancy**

All pregnant women, including those who become pregnant during the flu season, should be offered an inactivated quadrivalent influenza vaccine, regardless of their stage of pregnancy. Influenza infection during pregnancy may be associated with perinatal mortality, prematurity, lower birth weight and smaller neonatal size. Studies have demonstrated that pregnant women can safely receive influenza vaccine during pregnancy and that infants also receive some protection from maternal antibodies as a result of their mother having the vaccination whilst pregnant.

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<sup>5</sup> Specialist Pharmacy Service (SPS) Written instruction template for the administration of seasonal 'flu vaccination 2020/21  
Available at: [www.sps.nhs.uk/articles/written-instruction-for-the-administration-of-seasonal-flu-vaccination/](http://www.sps.nhs.uk/articles/written-instruction-for-the-administration-of-seasonal-flu-vaccination/)



The **second flu letter** (dated 5 August 2020) states that although hospital trusts will be asked to offer influenza vaccine to pregnant women attending maternity appointments for the 2020 to 2021 season. However, pregnant women can choose to receive flu vaccine from their GP practice or a community pharmacy instead if they prefer.

### Vaccination of women who become pregnant late in the flu season

Women who become pregnant during the flu season should be offered flu vaccine as soon as possible. The timing of the flu season varies each year but usually commences later in December or in the New Year, followed by two to three months of flu transmission. Although it takes around two weeks to make a response to the flu vaccine, pregnant women and their unborn babies are at higher risk of influenza associated morbidity and mortality and should still benefit from vaccination throughout the remaining season.

### Administering influenza vaccine at the same time as whooping cough (pertussis) containing vaccine and/or anti-D immunoglobulin

Pregnant women should be offered the flu vaccine as soon as the vaccine becomes available, regardless of their stage of pregnancy. Influenza vaccine should not be deferred in order to give it at the same appointment as the pertussis containing vaccine for pregnant women.

Pertussis containing vaccine is recommended for all pregnant women from 16 weeks of pregnancy but is generally offered at around 20 weeks. It is not recommended that pregnant women wait until they reach 16 weeks of pregnancy before having their flu vaccine as this would leave them, and their unborn baby, at risk of potentially severe illness if they develop flu.

The injected influenza and pertussis containing vaccines are both inactivated vaccines and so can be administered at the same time, same day or with any interval between them and both should be given at the recommended stage of pregnancy (from 16 weeks for pertussis containing vaccine and at any stage of pregnancy for influenza vaccine).

Anti-D immunoglobulin, where required, can also be given at the same time as, or at any interval before/after the flu and pertussis containing vaccines.

## Administering influenza vaccine to breastfeeding women

Breast-feeding is not a clinical indication for influenza vaccination. However, inactivated flu vaccine can be given to breast-feeding women if they are pregnant or in a clinical risk group.

## Medical conditions

For the 2020 to 2021 influenza season, all hospital trusts will be asked to offer influenza vaccine to those clinically at risk attending in- and out-patient appointments.

### Immunosuppression

The inactivated influenza vaccine can be safely given to immunosuppressed individuals though they may make a suboptimal response to the vaccine.

Individuals may be immunosuppressed because of a medical condition or because of medical therapy that they are taking/receiving. As these patients are at risk of increased morbidity and mortality if they develop influenza, they should be offered the vaccine as soon as stock is available. Immunosuppression may continue for several months following completion of treatment. If there is any uncertainty regarding an individual's level of immunosuppression, further advice should be taken from their consultant.

Household contacts of immunocompromised individuals are also eligible to receive the NHS-funded influenza vaccine.

### Patients taking steroid medication

Patients taking steroids can be safely vaccinated with inactivated flu vaccine. As systemic steroids at a dose equivalent to prednisolone 20mg or more per day are considered to be immunosuppressive, patients taking steroids are at risk of serious illness if they develop flu and so should be vaccinated. Patients who are receiving high-dose steroids may be immunosuppressed for at least 3 months after cessation of treatment. Also refer to section above headed Immunosuppression.

### Patients having chemotherapy

Patients receiving chemotherapy should receive their flu vaccine at the earliest opportunity. For individuals due to commence immunosuppressive treatments, inactivated vaccines should ideally be administered at least two weeks before commencement. In some cases this will not be possible and therefore vaccination may

be carried out at any time. Also refer to section above headed 'Immunosuppression'. Further advice regarding vaccination of immunosuppressed individuals can be found in [Chapter 7 of the Green Book](#)

## Patients taking checkpoint inhibitors

There is no evidence of an association between the squalene adjuvant used in aTIV and autoimmune disease, or of any potential risk of enhanced risk of autoimmune disease in those who are given checkpoint inhibitors who receive the adjuvanted flu vaccine (aTIV). The national policy therefore remains in place for use of the recommended inactivated flu vaccinations. Alternative recommended vaccines without adjuvant are available. These vaccines should be used if there is clinician decision to use an alternative to an adjuvanted vaccine in those on checkpoint inhibitors. In 2020/21 for those over 65 years, this includes QIVc.

## The NHS Shielded patient list and household contacts

All household contacts of those on the [Coronavirus \(COVID-19\): Shielded patients list](#) are eligible to receive NHS-funded influenza vaccine. This specifically includes those who expect to share living accommodation with a shielded person on most days over the winter and those with unavoidable continuing close contact.

## Vaccine ordering and national supply of additional adult vaccine

A list of vaccines available for the 2020 to 2021 flu programme is available [here on the GOV.UK website \(www.gov.uk/government/publications/influenza-vaccine-ovalbumin-content\)](#). General Practices and Community Pharmacists are responsible for ordering inactivated influenza vaccine for all eligible patients aged 18 years and over directly from the manufacturer and will already have done so for the 2020/21 flu season.

However, as the flu programme has been expanded for the 2020 to 2021 season and there is expected to be an increased demand for flu vaccine across all flu cohorts, Additional supplies of adult vaccine have been centrally procured. Guidance on how and when this additional stock can be accessed is available for [GP practices](#), [community pharmacies](#) and [NHS Trusts](#).

As some influenza vaccines may be restricted for use in particular age groups, the Summary of Product Characteristics (SPCs) for individual products should always be

referred to when ordering vaccines to ensure that they can be given appropriately to particular patients or patient age groups.

For the 2020/21 flu season, two types of influenza vaccine are available to order by providers of the children's flu programme via Public Health England's ordering platform **ImmForm**:

1. LAIV for all children aged from 2 years old to those in school year 7 and children in clinical risk groups aged from 2 years to less than 18 years, and
2. An inactivated vaccine (QIVe) for children aged 6 months to less than 9 years in clinical risk groups for whom LAIV is medically contraindicated or otherwise unsuitable.

Vaccine arrangements for children in clinical risk groups aged 9 years and over for whom LAIV is unsuitable are:

- Those vaccinated in general practice should be offered locally procured QIVc where available. Where QIVc is unavailable, GPs can offer QIVe, either from locally procured stock or centrally supplied stock available via ImmForm.
- School aged providers should offer centrally supplied QIVe.

QIVe can now also be ordered by General Practice and school aged immunisation teams via **ImmForm** for children whose parents refused LAIV due to the porcine gelatine content, subject to vaccine availability. See **Statement on the childhood flu programme: the alternative offer to live attenuated Influenza vaccine (LAIV)**.

## Vaccine storage and handling

### Storage of inactivated influenza vaccine

Inactivated influenza vaccines should be stored between 2°C and 8°C and should be stored in the original packaging to protect the vaccine from light. Vaccine should not be removed from the cold chain until it is required for use.

### Vaccine storage incidents

Should vaccines be inadvertently stored outside the recommended temperature range of 2°C to 8°C, the vaccine should be quarantined, and risk assessed for suitability of continued off-label use or appropriate disposal. Refer to the **Vaccine Incident Guidance document**<sup>6</sup> and seek further advice on vaccine stability and cold chain storage incidents

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<sup>6</sup> Public Health England. Vaccine Incident Guidance. Responding to errors in vaccine storage, handling and administration. August 2019. Available at: [www.gov.uk/government/publications/vaccine-incident-guidance-responding-to-vaccine-errors](http://www.gov.uk/government/publications/vaccine-incident-guidance-responding-to-vaccine-errors)

from the vaccine manufacturer and your local NHS England Screening and Immunisation team.

## Influenza vaccine components

### Vaccine antigens

Each year, the World Health Organisation (WHO) monitors the epidemiology of influenza across the world and makes recommendations to vaccine manufacturers regarding the strains of influenza to include in the vaccine<sup>7</sup>.

As egg-based and cell-based vaccine production systems differ, different viruses with similar properties are used to facilitate timely vaccine production. For cell-based vaccines, cell-isolated vaccine viruses would be recommended<sup>8</sup>.

For the 2020/21 flu season (northern hemisphere winter), it is recommended that quadrivalent vaccines contain the following:

#### Egg-based vaccines

- A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus
- A/Hong Kong/2671/2019 (H3N2)-like virus
- B/Washington/02/2019 (B/Victoria lineage)-like virus
- B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

#### Cell- or recombinant-based vaccines

- A/Hawaii/70/2019 (H1N1)pdm09-like virus
- A/Hong Kong/45/2019 (H3N2)-like virus
- B/Washington/02/2019 (B/Victoria lineage)-like virus
- B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

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<sup>7</sup> World Health Organization. Recommended composition of influenza virus vaccines for use in the 2020 - 2021 northern hemisphere influenza season. 28 February 2020. Available at: [www.who.int/influenza/vaccines/virus/recommendations/2020-21\\_north/en/](https://www.who.int/influenza/vaccines/virus/recommendations/2020-21_north/en/)

<sup>8</sup> World Health Organisation. Recommended composition of influenza virus vaccines for use in the northern hemisphere 2020-2021 influenza season and development of candidate vaccine viruses for pandemic preparedness, questions and answers. 28 February 2020. Available at: [https://www.who.int/influenza/vaccines/virus/recommendations/202002\\_qanda\\_recommendation.pdf?ua=1](https://www.who.int/influenza/vaccines/virus/recommendations/202002_qanda_recommendation.pdf?ua=1)

This vaccine composition differs from the 2019/20 vaccine composition as both influenza A virus strains and one of the B virus strains have been replaced.

The influenza B component in the 2020 to 2021 trivalent vaccines will be the B/Washington/02/2019 (B/Victoria lineage)-like virus<sup>9</sup>.

## Egg (ovalbumin) content

Some of the inactivated influenza vaccines (QIVe) may contain traces of egg such as the egg protein ovalbumin. A table stating the ovalbumin content of the flu vaccines for the 2020/21 season is available in the [National flu immunisation programme 2020 to 2021 letter](#)<sup>1</sup> and is also available as a separate document: [Influenza vaccines: 2020 to 2021 flu season](#) on the [PHE Annual flu programme](#) webpage.

With the exception of those individuals with a severe anaphylaxis to egg which has previously required intensive care, patients with less severe egg allergy can be immunised in any setting using an inactivated influenza vaccine with an ovalbumin content less than 0.12 micrograms/ml (equivalent to 0.06 micrograms in a 0.5 ml dose) or using the egg-free cell-based quadrivalent influenza vaccine (QIVc), Flucelvax Tetra (licensed from 9 years of age).

The aTIV vaccine contains more than the recommended ovalbumin content for patients with egg allergy (each 0.5ml dose contains less than or equal to 0.2 micrograms ovalbumin). Patients aged 65 years and over with an egg allergy should therefore be given the egg-free cell-based quadrivalent influenza vaccine (QIVc).

## Patients with a previous severe anaphylactic reaction to egg

Patients with severe anaphylaxis to egg who have previously required intensive care should be referred to specialists for immunisation in hospital or, if 9 years of age or over, should be given the egg-free cell-based quadrivalent influenza vaccine (QIVc). If there is any uncertainty about the cause of an anaphylactic reaction, the patient should be advised to consult with an immunologist.

Further information about egg allergy and influenza vaccine can be found in the [Influenza chapter 19 of the Green Book](#)<sup>Error! Bookmark not defined.</sup>.

## Vaccine adjuvant in aTIV

Vaccine adjuvants can reduce the amount of virus required for the production of a vaccine but they are primarily added to vaccines to enhance and lengthen the duration of the immune response.

This is particularly important for those aged 65 years and older as the ageing immune system may result in a suboptimal response to influenza vaccine and there is evidence of limited effectiveness of standard trivalent vaccines in those aged 65 years and over<sup>Error! Bookmark not defined.</sup>.

The aTIV vaccine contains an adjuvant called MF59 which improves the immune system's response to vaccination and helps it to produce more antibodies against the influenza virus strains in the vaccine. MF59 is an oil-in-water emulsion of squalene oil, polysorbate 80, sorbitan trioleate, sodium citrate, citric acid and water for injections. Squalene is a naturally occurring substance that is found in humans, animals and plants<sup>9</sup>. In humans, it is made in the liver and circulates in the bloodstream<sup>10</sup>. Squalene is also found in a variety of foods, cosmetics, over-the-counter medications and health supplements. The squalene used in pharmaceutical products and vaccines is commercially extracted from fish oil and is then highly purified during the manufacturing process.

A single dose of aTIV contains less than 10mg of squalene. To put this in context, over 1000mg of squalene is made in the liver every day, and humans ingest around 50mg to 200mg of squalene every day in a normal diet<sup>11</sup>.

Polysorbate 80, sorbitan trioleate and sodium citrate are emulsifiers which stop the squalene oil from separating out of the water in the vaccine. These, along with citric acid (also contained in the adjuvant) are all commonly used in foods and drinks.

The squalene in the aTIV vaccine is obtained from the spiny dog fish and shark liver oil forms around 80% of the squalene for MF59. aTIV is not tested for residual fish protein and there is no data available as to whether or not residual fish protein remains in the vaccine following the purification process<sup>12</sup>. Patients who report hypersensitivity to fish should be assessed as to the nature and severity of their allergy before the vaccine is given.

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<sup>9</sup> Centers for Disease Control and Prevention. FLUAD™ Flu Vaccine With Adjuvant. Available at: [www.cdc.gov/flu/protect/vaccine/adjuvant.htm](http://www.cdc.gov/flu/protect/vaccine/adjuvant.htm)

<sup>10</sup>World Health Organization. Squalene-based adjuvants in vaccines. Available at: [www.who.int/vaccine\\_safety/committee/topics/adjuvants/squalene/questions\\_and\\_answers/en/](http://www.who.int/vaccine_safety/committee/topics/adjuvants/squalene/questions_and_answers/en/)

<sup>11</sup> Personal communication from Seqirus. 8 June 2018

<sup>12</sup> Personal communication from Seqirus October 2019

## Latex

The influenza vaccines for 2020/21 are not contraindicated in latex allergic individuals. The vaccine components that are in contact with the injection solution/suspension are latex-free.

Some vaccines may be supplied with needle shields that are not latex-free. Summary of Product Characteristics are not required to provide warnings where the needle shield may contain latex and the risk of contamination from latex proteins from the needle sheath into the vaccine is considered negligible by experts. Individuals, including those with a latex allergy, are therefore recommended to receive an influenza vaccine recommended for them in accordance with their age.

As with all vaccines, immunisers must be trained in the management of anaphylaxis and an anaphylaxis pack must always be available whenever vaccines are given.

## Antibiotics

Some egg-grown inactivated flu vaccines may contain residues of antibiotics which are used during the vaccine manufacturing process. For example, aTIV may contain residues of the antibiotics kanamycin and neomycin sulphate so patients with a severe / anaphylactic kanamycin or neomycin sulphate allergy should be offered an alternative vaccine.

The flu vaccines Flucelvax Tetra and Flublok Quadrivalent do not contain any antibiotics. The way in which they are made (in cells, not eggs) means that there is no need to use antibiotics during the manufacturing process.

## Other additives

The [Vaccine Knowledge Project Inactivated Flu Vaccine webpage](#)<sup>13</sup> contains comprehensive information about the constituents of inactivated flu vaccines.

## Suitability of QIVc for vegetarians and vegans

The original cells used in the Madin-Darby Canine Kidney (MDCK) cell line in which the flu vaccine viruses used in QIVc are grown were taken by Madin and Darby from the

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<sup>13</sup> Oxford Vaccine Group. Vaccine Knowledge Project. Inactivated Flu Vaccine webpage: [vk.ovg.ox.ac.uk/inactivated-flu-vaccine](http://vk.ovg.ox.ac.uk/inactivated-flu-vaccine)



kidney tubule of an adult dog in 1958. This is the cell line that is still used today. It is a continuous cell line where the cells have adapted to grow and divide continually with unlimited availability so the cell-based manufacturing process does not require any new cells to be taken<sup>14</sup>.

After the vaccine viruses are grown, they are highly purified and this purification process removes the cell culture materials. It is extremely unlikely that any cell culture material remains in the vaccine (the risk of a dose of the final vaccine product containing an intact MDCK cell is calculated to be less than 1 per 10<sup>34</sup> doses<sup>15</sup>).

The MDCK cell line is used because the influenza virus grows well in it, it is able to produce high volumes of flu virus for use in vaccines and the influenza virus isolated following culture in these cells retains the antigenic properties of the original strain. So this method of vaccine virus production should result in the vaccine virus being a closer match to the wild-type circulating flu viruses.

### Suitability of QIVc for those with a history of allergy to canine allergens

A history of hypersensitivity to canine allergens is not listed as a contraindication or precaution to immunisation with QIVc. MDCK cells do not express known major canine allergens associated with hypersensitivity reactions, however minor canine allergens may be present, posing a hypothetical concern about the possibility of hypersensitivity reactions. In clinical trials (totaling over 16,000 participants), none of the participants who reported a dog allergy reported any hypersensitivity reactions following administration of QIVc. There was no indication of any increased incidence in immediate local or systemic reactions in those who received QIVc compared to those who received an egg-grown influenza vaccine or who were in the placebo groups<sup>15</sup>. If there is significant concern, patients can be given an egg-grown vaccine instead.

### Vaccine dose

Inactivated influenza vaccines contain 0.5ml of vaccine. JCVI has advised that where alternative doses are given in the manufacturer's Summary of Product Characteristics (SPC), the 0.5ml dose of intramuscular inactivated influenza vaccine should be given to infants and young children aged six months and older because there is evidence that this dose is effective in young children.

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<sup>14</sup> Personal communication from Seqirus. 7 May 2019

<sup>15</sup> Gregersen JP, Schmitt HJ, Trusheim H et al. Safety of MDCK cell culture-based influenza vaccines. *Future Microbiol.* 2011 Feb;6(2):143-52

Children in a clinical risk group who have received one or more doses of influenza vaccine in previous flu seasons should be considered as previously vaccinated and only require a single dose of influenza vaccine each season.

Children under nine years of age who are in a clinical risk group or who are household contacts of those on **the NHS shielded patients list** or of immunocompromised patients who have never previously received any influenza vaccine should be offered two doses of influenza vaccine with a minimum of a four week interval between them.

All others eligible to receive an influenza vaccine, including children aged 2 to 9 years and not in a clinical risk group, pregnant women and those aged 65 years and over, should receive a single 0.5ml dose each season they are eligible.

## Contraindications and precautions

The inactivated influenza vaccine is contraindicated for all patients who have had:

- an anaphylactic reaction to a previous dose of the vaccine
- an anaphylactic reaction to any of the vaccine components (see section on **egg content** above for those with egg allergy)

For a full list of influenza vaccine components, please see the manufacturer's Summary of Product Characteristics (SPC) available on the **Electronic Medicines Compendium** website. The SPC for individual products should be referred to when assessing the suitability of the vaccine for the patient (for example if they have an egg or antibiotic allergy). As Flublok Quadrivalent vaccine is not currently licensed in the UK, there is no SPC available but the Package Insert for this vaccine is provided on the US Food and Drug Administration (FDA) website at [www.fda.gov/media/123144/download](http://www.fda.gov/media/123144/download)

### Temporary deferral of immunisation

If there is evidence of current neurological deterioration, temporary deferral of vaccination may be considered to avoid incorrect attribution of any change in the underlying condition. The risk of deferring the vaccine should be balanced against the risk of flu and vaccination should be promptly given once the diagnosis and/or the expected course of the condition becomes clear.

This precaution does not apply to individuals with a chronic neurological condition who should be offered vaccine once vaccine stock becomes available.

## Patients who are acutely unwell when presenting for vaccination

Vaccination may be postponed in those who are acutely unwell until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Those displaying symptoms of COVID-19, other infections, or who are self-isolating because they are contacts of suspected or confirmed COVID-19 cases, should not attend.<sup>16</sup>

## Guillain-Barré Syndrome (GBS) and influenza vaccine

Previous GBS is not a contraindication to influenza vaccination. A UK study found that there was no association between GBS and influenza vaccines although there was a strong association between GBS and influenza-like illness. A causal relationship between immunisation with influenza vaccine and GBS has not been established<sup>17</sup>.

## Authorisation of Flublok Quadrivalent vaccine

Although not currently licensed in the UK, Flublok Quadrivalent (QIVr) vaccine has been authorised for temporary supply in the UK for the 2020/21 flu season in order to enable flu vaccine to be offered to many more people during the COVID-19 pandemic. Flublok Quadrivalent (QIVr) is licensed in the United States by the Food and Drug Administration (FDA) where it has been used for several years and has been proven to be safe and effective.

In response to certain public health threats, such as the current pandemic, the UK Medicines and Healthcare products Regulatory Agency (MHRA) can temporarily authorise the supply of an unlicensed medicine or vaccine for use, under regulation 174 of The Human Medicines Regulations 2012, when it is satisfied that there is robust evidence to show the safety, quality and effectiveness of the medicine/vaccine.

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<sup>16</sup> PHE Clinical guidance for healthcare professionals on maintaining immunisation programmes during COVID-19 Available at: [www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/06/clinical-guidance-for-hcps-on-imms-for-covid-19.pdf](http://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/06/clinical-guidance-for-hcps-on-imms-for-covid-19.pdf)

<sup>17</sup> Stowe J, Andrews N, et al. Investigation of the temporal association of Guillain-Barre syndrome with influenza vaccine and influenza like illness using the United Kingdom General Practice Research Database. Am J Epidemiol. 2009 Feb 1;169(3):382-8. Abstract at: [www.ncbi.nlm.nih.gov/pubmed/19033158](http://www.ncbi.nlm.nih.gov/pubmed/19033158)

The MHRA assessed the available scientific evidence for Flublok Quadrivalent (QIVr) and sought advice from the government's independent expert scientific advisory body – the Commission on Human Medicines (CHM). The CHM recommended that as the evidence shows that Flublok Quadrivalent protects against flu and meets high standards of safety and quality, based on the data and the public health need, Flublok Quadrivalent (QIVr) could be temporarily authorised for use under regulation 174.

The use of Flublok Quadrivalent (QIVr) will be closely monitored and batches of the vaccine will be independently evaluated prior to use in the UK. Temporary authorisation under regulation 174 does not affect standards of quality, safety and efficacy which will be as tightly maintained as they are for all flu vaccines.

As part of the consent process, vaccinators should inform the individual patient that this vaccine does not have a UK marketing authorisation but has been authorised for temporary supply in the UK by the MHRA, that it has been licensed and used in the US since 2013 and that it is being offered in accordance with national guidance.

For more information, see the following news story on the MHRA website "[Flublok vaccine given authorisation for temporary supply in the UK to meet public health need](#)".

## Legal issues affecting the administration of Flublok Quadrivalent vaccine

In October 2020, new legislation was passed to allow medicines which have been temporarily authorised using regulation 174 to be administered using a Patient Group Direction (PGD). Prior to this, PGDs could not be used for unlicensed medicines. The change to legislation will enable those registered healthcare professionals who are allowed to work to a PGD to supply and administer temporarily authorised vaccines such as Flublok Quadrivalent without the patient having to be seen by a prescriber. This will allow flu immunisation services to continue to operate under a PGD if appropriate, including for the administration of Flublok Quadrivalent. All immunisers must be trained, assessed as competent and continue to seek informed consent as they would for all flu vaccines.

The changes in relation to the PGDs are specifically to make it possible for professionals who already use PGDs to be able to use them for temporarily authorised products – the workforce that can administer under PGDs has not changed.

# Legal frameworks to supply and/or administer flu vaccines

## Patient Group Direction

PHE develop and publish a **Patient Group Direction (PGD) template for inactivated flu vaccine** to support the administration of inactivated influenza vaccine each year. The PGD is not legally valid until it has had the relevant organisational authorisation from an appropriate authorising person in Section 2 of the PGD. The inactivated influenza PGD V08.00 may now be used to administer vaccine to the extended cohorts defined in the PGD inclusion criteria. Confirmation of the extension of eligible cohorts is published at: [www.gov.uk/government/publications/intramuscular-inactivated-influenza-vaccine-patient-group-direction-pgd-template](http://www.gov.uk/government/publications/intramuscular-inactivated-influenza-vaccine-patient-group-direction-pgd-template).

The inactivated influenza PGD V08.00 does not cover the administration of recombinant quadrivalent influenza vaccine (QIVr) (Flublok Quadrivalent). A separate Flublok Quadrivalent PGD has been developed by PHE and is available at: [www.gov.uk/government/collections/immunisation-patient-group-direction-pgd](http://www.gov.uk/government/collections/immunisation-patient-group-direction-pgd). Immunisers need to ensure they use the correct PGD for the vaccine they are administering and that they do not use this PGD template until it has been authorised in Section 2.

## Patient Specific Direction

As Flublok Quadrivalent has been provided temporary authorisation under regulation 174 for supply and administration in England (see next section), a prescriber may provide a Patient Specific Direction (PSD) for the supply or administration of this product.

This means that Healthcare Support Workers (HCSWs) may administer Flublok Quadrivalent vaccine under a PSD. In delegating the immunisation of the patient to the HCSW, the prescriber should ensure that the appropriate prescribing mechanisms, governance arrangements and a medicines policy to support the use of PSDs by healthcare support staff are in place. See **National minimum standards and core curriculum for immunisation training of healthcare support workers** for further information regarding the use of PSDs for administration of vaccines by HCSWs.

## National Protocol

New legislation, regulation 247A, also allows for a national protocol authorised by ministers to be used for the supply and administration of influenza vaccines. If such a protocol is approved by ministers, this may also provide authority for HCPs and HCSWs to administer injectable influenza vaccines, including Flublok Quadrivalent. More information will be added to this document if a protocol is made available for flu vaccine.

## Written Instruction

The PHE PGD template covers NHS commissioned services. It does not cover the provision of occupational health schemes or peer-to-peer influenza immunisation. So that organisations can offer employee seasonal flu vaccinations within the legislation, a written instruction for seasonal influenza vaccination has been produced. This is available on the NHS Specialist Pharmacy Service website: [Written instruction for the administration of seasonal 'flu vaccination](#).

## Preparing flu vaccine

Vaccines in prefilled syringes may contain an air bubble. This should not be expelled unless it is specifically stated to do so in the vaccine SPC. To try to expel it risks accidentally expelling some of the vaccine and therefore not giving the patient the full dose. Once injected, the air bubble forms an airlock preventing the vaccine seeping out along the needle track into subcutaneous tissue and onto the skin. The small bolus of air injected following administration of the vaccine clears the needle and prevents a localised reaction to the vaccination<sup>18</sup>.

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<sup>18</sup> Crisp, J. & Taylor, C. Potter and Perry's Fundamentals of Nursing. 2005 (2nd ed.). Australia: Elsevier. Cited in Floyd S. Administering the influenza vaccine: what is best practice for administering the influenza vaccine? Some techniques are safer than others. Available at: [www.thefreelibrary.com/Administering+the+influenza+vaccine%3A+what+is+best+practice+for...-a0227796751](http://www.thefreelibrary.com/Administering+the+influenza+vaccine%3A+what+is+best+practice+for...-a0227796751)

## Vaccine administration

Influenza vaccine should ideally be offered before influenza viruses start to circulate so the ideal time for immunisation is between late September and end of November. However, as peak influenza activity generally occurs in January or February or sometimes later, providers should continue vaccinating patients throughout the influenza season, as long as they have unexpired vaccine in stock and unvaccinated patients in their practice. Providers should apply clinical judgement, taking into account the level of flu-like illness in their community and the fact that the immune response following flu vaccination takes about two weeks to develop fully.

The inactivated influenza vaccine should be administered as an intramuscular injection. For infants aged six months to one year, the anterolateral aspect of the thigh should be used. For those aged one year and over, the deltoid muscle in the upper arm is the preferred muscle.

Due to the presence of the adjuvant (MF59), aTIV should be administered intramuscularly using a 25mm needle to enable the vaccine to be delivered into the muscle.

### Vaccination of patients taking anticoagulants or with a bleeding disorder

There is a lack of evidence that the subcutaneous route of vaccination is any safer than the intramuscular route in people taking anticoagulants. The subcutaneous route can itself be associated with an increase in localised reactions.

Individuals on stable anticoagulation therapy, including individuals on warfarin who are up-to-date with their scheduled INR testing and whose latest INR was below the upper threshold of their therapeutic range, can receive intramuscular vaccination. If in any doubt, consult with the clinician responsible for prescribing or monitoring the individual's anticoagulant therapy.

Individuals with bleeding disorders may be vaccinated intramuscularly if, in the opinion of a doctor familiar with the individual's bleeding risk, vaccines or similar small volume intramuscular injections can be administered with reasonable safety by this route. If the individual receives medication/treatment to reduce bleeding, for example treatment for haemophilia, intramuscular vaccination can be scheduled shortly after such medication/treatment is administered.

A fine needle (equal to 23 gauge or finer calibre) should be used for the vaccination of these patient groups, followed by firm pressure applied to the site (without rubbing) for

at least 2 minutes,<sup>19</sup> and the individual/parent/carer should be informed about the risk of haematoma from the injection.

The needle provided with the aTIV vaccine is 25G (gauge) and is therefore suitable for use for patients taking anticoagulants or with a bleeding disorder.

Influenza vaccines licensed for intramuscular or subcutaneous administration may alternatively be administered by the subcutaneous route. However, **Fluarix Tetra (QIVe), Flucelvax Tetra (QIVc), Flublok Quadrivalent (QIVr) and Adjuvanted Trivalent Influenza Vaccine (formerly known as Flud (aTIV)) are not licensed for subcutaneous administration so should only be administered intramuscularly (as per advice above)**. If these vaccines are given subcutaneously in error, they do not need to be repeated but the vaccinated individual should be warned of the increased risk of local reactions at the injection site.

### Reactions following administration of inactivated flu vaccine

Commonly reported reactions following administration of inactivated flu vaccine include: malaise, low grade fever, headache, fatigue, myalgia, arthralgia and redness, swelling and pain at the injection site. Immediate reactions such as urticaria, angio-oedema, bronchospasm and anaphylaxis can occur but are rare.

In clinical trials, the incidence of both mild local and systemic reactions following immunisation with aTIV was found to be higher than the incidence of reactions following unadjuvanted TIV vaccines<sup>20</sup>. Both Flucelvax Tetra and Flublok Quadrivalent are reported to be well tolerated with a similar safety profile to egg-based flu vaccines.

The frequency of injection site pain and systemic reactions may be higher in individuals vaccinated concomitantly with inactivated flu vaccine and pneumococcal polysaccharide vaccine (PPV23) compared to vaccination with influenza vaccine alone and similar to that observed with PPV23 vaccination alone. However, if indicated, flu vaccine and PPV23 can be administered at the same visit in different limbs.

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<sup>19</sup> Centers for Disease Control and Prevention. Vaccine recommendations and guidelines of the ACIP. Vaccinating Persons with Increased Bleeding Risk. Available at: [www.cdc.gov/vaccines/hcp/acip-recs/general-recs/special-situations.html](http://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/special-situations.html)

<sup>20</sup> Flud. Summary of Product Characteristics. Date of last revision of text: 07/2018. Available at: [www.medicines.org.uk/emc/product/9223/smpc](http://www.medicines.org.uk/emc/product/9223/smpc)



## Reporting of adverse reactions

Healthcare professionals and patients/parents/carers are encouraged to report suspected adverse reactions to flu vaccines to the Medicines and Healthcare products Regulatory Agency (MHRA) using the Yellow Card reporting scheme:

[yellowcard.mhra.gov.uk](https://yellowcard.mhra.gov.uk)

Flucelvax Tetra, and most of the quadrivalent egg-grown inactivated influenza vaccines (QIVe) carry a black triangle symbol (▼).

## Patients who have already received an influenza vaccine during early 2020

If a patient received the vaccine produced for the 2019 to 2020 season in the first few months of 2020, then they will still need a dose of the vaccine produced for the 2020 to 2021 season as it contains different viruses to protect against other influenza strains.

In addition, the protection gained from flu vaccine is only thought to last for one season so those eligible to receive the vaccine are recommended to have it every season to ensure on-going protection.

If a patient has received a vaccine in 2020 formulated for the southern hemisphere (eg because they were in Australia, New Zealand etc during the flu season there), and they will be in the UK (northern hemisphere) over winter 2020 to 2021, they should receive another dose of flu vaccine in the UK as the vaccine formulated for the northern hemisphere for the 2020/21 flu season contains different strains than the one given in the southern hemisphere in 2020.

## Individuals who have inadvertently been given a flu vaccine that is not the one recommended for their age group

If an individual has inadvertently received a flu vaccine different to the one recommended for their age group, they should be informed of the error and the potential implications of this error. Although QIVe, QIVc, QIVr and aTIV should provide some protection against flu in all age groups, individuals aged 65 years and over (particularly those more than 75 years of age) may not respond as well to the QIVe as they would to the vaccines recommended for their age group (aTIV, QIVc), and individuals aged under 65 years will not benefit from the opportunity to make protection against an additional B flu strain if they have been given aTIV.

If the individual wishes to receive the vaccine that they should have been given, this can be offered following a discussion of the benefits and risks. The clear benefit is the additional protection that may be offered by the correct vaccine but they should be

alerted to the potential increased risk of a local or systemic reaction. Although there is no data available on the safety and effectiveness of administering a second flu vaccine shortly after the first in adults, this advice is based on general principles of vaccination and experience of flu revaccination following cold chain and administration incidents.

If a decision is made to offer the vaccine the individual should have received, it is recommended that this is done as soon as possible after the first dose was given and ideally within a week. This will enable protection to be made as soon as possible. It can still be given if more than a week has elapsed however.

### Patients under 65 years of age at time of vaccination but who will be 65 years old by 31st March 2021

Although it is stated in the SPC for aTIV that this vaccine is indicated for patients aged 65 years and over, patients who will become 65 years of age by 31<sup>st</sup> March 2021 but who are 64 years at the time of vaccination can receive aTIV off-label in accordance with the recommendations for the national influenza immunisation programme for 2020/21<sup>1</sup>. This off-label use is covered in the PHE national template PGD for inactivated influenza vaccine.

### Uncertainty regarding previously administered dose of influenza vaccine

If there is no documented evidence of an eligible patient having received a flu vaccine during the current flu season then they should be offered a dose. If they have already had one this flu season, an additional dose is unlikely to cause any harm. Any adverse reactions to an extra dose are likely to be similar to those commonly seen after a first dose of flu vaccine such as local redness/pain at the injection site, malaise etc.

### Inadvertent administration of a second dose of influenza vaccine

Any adverse reactions to an extra dose are likely to be similar to those commonly seen after a scheduled first dose of flu vaccine such as local redness/pain at the injection site, malaise etc. The patient should be advised of this and offered reassurance that children in clinical risk groups under the age of nine years who have never received influenza vaccine in previous years are specifically recommended to have two doses four weeks apart. Local systems should be reviewed to prevent this happening again.

### Incomplete dose of vaccine given

If it is thought that the patient did not receive a full dose of vaccine (for example, because some spilt out whilst administering the vaccine), it is recommended that the

dose is repeated. This can be at any interval from the partial dose already given. Giving it the same day or within the next few days will enable protection to be made as soon as possible. The patient should be informed there may be a potential risk of local and systemic reactions from a repeat dose.

### Vaccination of individuals recently diagnosed with influenza infection

Individuals eligible to receive the influenza vaccine should have it even if they have recently had confirmed influenza infection. Having the vaccine will help to protect against other circulating flu strains. Both the inactivated flu vaccine and the LAIV can be given at any time following recovery providing there are no contraindications to vaccination and the patient is not acutely unwell.

### Vaccination of individuals recently diagnosed with COVID-19 infection

Individuals eligible to receive NHS-funded flu vaccine but recently in contact with, or diagnosed with COVID-19 infection can be vaccinated when recovered and self-isolation requirements have been fulfilled. Immunisers should refer to the [GOV.UK Coronavirus pages](https://www.gov.uk/government/coronavirus) to ensure recommendations that are current at the time of vaccination are followed.

### Vaccination of individuals experiencing prolonged COVID-19 symptoms ('Long COVID')

Having prolonged COVID-19 symptoms ('Long COVID') is not a contraindication to receiving flu vaccine, but if there is evidence of current deterioration, deferral of flu vaccination may be considered to avoid incorrect attribution of any change in the person's underlying condition to the flu vaccine.

If their symptoms are stable however and they are eligible to receive flu vaccination, it would be recommended in order to avoid compounding their COVID symptoms with flu symptoms

### Fever following flu vaccination

Vaccinated individuals, parents and carers should be advised that flu vaccines may cause a mild fever which usually resolves within 48 hours. This is a common, expected reaction and isolation is not required unless COVID-19 is suspected.

Feeling generally unwell, shivery, achy and tired are also commonly reported symptoms following flu vaccination. These symptoms usually disappear within one to two days without treatment but paracetamol can be given if necessary to relieve any of these symptoms.

COVID-19 symptoms are: a high temperature, a new, continuous cough, or a loss or change to sense of smell or taste. If someone experiences any of these symptoms, they should get tested.

As has always been recommended, any fever after vaccination should be monitored and if individuals, parents or carers are concerned about their, or their child's health at any time, they should seek advice from their GP or NHS 111.

### Administering inactivated influenza vaccine at the same time as other vaccines or immunoglobulins

The inactivated influenza vaccine can be given at the same time as, or at any interval before or after, any immunoglobulin or other currently used vaccine (whether live or inactivated). The vaccines should be given at separate sites, preferably in different limbs but if given in the same limb, they should be given at least 2.5cm apart and the site of each should be recorded in the patient's record. Because of the increased risk of local reaction following aTIV and TIV-HD, these vaccines should be administered in a separate limb to any other vaccines that need to be given at the same time. If any new vaccines are introduced during the flu vaccination season, please ensure you follow the specific guidance given about concomitant administration for these.

### Inadvertent administration of expired doses of vaccine

Vaccines from previous years' programmes should be discarded before stock for the current year is received.

As new flu vaccine stock is purchased each year, it is unlikely that a patient will receive a dose that has expired. However, in the event that this occurs, an additional dose with a valid expiry date should be offered. This can be given at any interval from the expired dose but should preferably be given the same day or as soon as possible in order not to delay protection.

### Patients previously eligible for influenza vaccine but who are no longer in a risk group

Some patients may have had the vaccine during previous flu seasons whilst in an at risk group but may no longer be in that group. Examples could include women who were pregnant during the last flu season but are not pregnant during this flu season or patients who were taking regular steroids during last flu season but are no longer taking them.

Providing that these patients are not in any other risk group described in the **Green Book** or **annual flu letter**, they would not be eligible for flu vaccination this year. However, the Green Book states that clinicians should exercise professional judgement when assessing a patient and can recommend vaccination for individuals, even if they are not in a listed risk group, if influenza is likely to exacerbate their underlying condition.

### Patients requesting live intranasal influenza vaccine (LAIV) instead of an inactivated injected vaccine due to needle phobia

Patients for whom the inactivated injected vaccine is recommended should be encouraged, where possible, to have the inactivated injected vaccine.

Public Health England procures LAIV and distributes this to general practices, who vaccinate two and three year olds and children in at risk groups and to providers responsible for vaccinating children in primary school. LAIV is licensed for children aged 2 to 17 years of age. It is not licensed in adults because there is some evidence of poorer efficacy in this age group when compared with the inactivated influenza vaccines.

PHE do not supply flu vaccine to occupational health departments, pharmacies or GP practices for adult patients.

However, in exceptional circumstances, individual medical practitioners may choose to use their stocks of LAIV 'off-label' to vaccinate patients with a needle phobia.

It is envisaged that the type of patient who would be offered this might be someone with learning disabilities who becomes seriously distressed about needles. This is part of the requirement that the NHS has to make reasonable adjustments to accommodate the needs of a person with learning disabilities<sup>21</sup>. See **Flu vaccinations: supporting people with learning disabilities** for more information.

Others who might also be offered LAIV include people in a clinical risk group with a serious needle phobia who may otherwise go unimmunised if they refuse to have an injected inactivated vaccine.

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<sup>21</sup> Public Health England. Flu Vaccinations: Supporting people with learning disabilities.  
[www.gov.uk/government/publications/flu-vaccinations-for-people-with-learning-disabilities](http://www.gov.uk/government/publications/flu-vaccinations-for-people-with-learning-disabilities)

The legislation does allow for such situations and the Medicines and Healthcare products Regulatory Agency state that ‘there are clinical situations when the use of medicines outside the terms of the licence (ie, ‘off-label’) may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence’<sup>22</sup>. The responsibility for such use rests with the health professional. In this situation, a Patient Specific Direction (PSD) will be required. In these exceptional circumstances, where it has not proved possible to administer the inactivated vaccine, PHE has agreed that the national LAIV stock can be used for this purpose.

## Useful links

### Letters detailing 2020 to 2021 flu programme

Department of Health and Social Care, Public Health England, NHS England. The national flu immunisation programme 2020/21. Published 14 May 2020 and 5 August 2020. Available at: [www.gov.uk/government/publications/national-flu-immunisation-programme-plan](http://www.gov.uk/government/publications/national-flu-immunisation-programme-plan)

### Immunisation against infectious disease (the Green Book) Influenza chapter 19.

Available at: [www.gov.uk/government/publications/influenza-the-green-book-chapter-19](http://www.gov.uk/government/publications/influenza-the-green-book-chapter-19)

**Leaflets, posters, training slides and additional flu resources** prepared specifically to support the annual flu programme. Available to view at:

[www.gov.uk/government/collections/annual-flu-programme](http://www.gov.uk/government/collections/annual-flu-programme) and to order paper copies at: [www.healthpublications.gov.uk/home.html](http://www.healthpublications.gov.uk/home.html)

### Easy read resources

[www.gov.uk/government/publications/flu-leaflet-for-people-with-learning-disability](http://www.gov.uk/government/publications/flu-leaflet-for-people-with-learning-disability)

**Summary of Product Characteristics (SPC) for flu vaccines** are available at

[www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)

### PGD templates for flu vaccines

[www.gov.uk/government/collections/immunisation-patient-group-direction-pgd](http://www.gov.uk/government/collections/immunisation-patient-group-direction-pgd)

### Written Instruction for the administration of seasonal ‘flu vaccination

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<sup>22</sup> Medicines and Healthcare products Regulatory Agency. Off-label or unlicensed use of medicines: prescribers’ responsibilities. Available on Gov.uk website at: [www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities](http://www.gov.uk/drug-safety-update/off-label-or-unlicensed-use-of-medicines-prescribers-responsibilities)

[www.sps.nhs.uk/articles/written-instruction-for-the-administration-of-seasonal-flu-vaccination/](http://www.sps.nhs.uk/articles/written-instruction-for-the-administration-of-seasonal-flu-vaccination/)

**Links to other key documents relating to the flu vaccine programme** are available on page 5 of “The national flu immunisation programme 2020 to 2021” letter available at [www.gov.uk/government/publications/national-flu-immunisation-programme-plan](http://www.gov.uk/government/publications/national-flu-immunisation-programme-plan)

**Vaccine Knowledge Project. Inactivated Flu Vaccine.** Available at: [vk.ovg.ox.ac.uk/inactivated-flu-vaccine](http://vk.ovg.ox.ac.uk/inactivated-flu-vaccine)

**NHS England. Directed Enhanced Service Specification - Seasonal influenza and pneumococcal polysaccharide vaccination programme 2020/21.** Available at: [www.england.nhs.uk/publication/directed-enhanced-service-specification-seasonal-influenza-and-pneumococcal-polysaccharide-vaccination-programme-2020-21/](http://www.england.nhs.uk/publication/directed-enhanced-service-specification-seasonal-influenza-and-pneumococcal-polysaccharide-vaccination-programme-2020-21/)

**Healthcare Workers Flu Immunisation resources** (leaflets, posters, guides and resource packs). Available at: [campaignresources.phe.gov.uk/resources/campaigns/92-healthcare-workers-flu-immunisation-/resources](http://campaignresources.phe.gov.uk/resources/campaigns/92-healthcare-workers-flu-immunisation-/resources)

**NHS England. Primary care frequently asked questions.** National Seasonal Influenza Immunisation Programme 2020/21: primary care frequently asked questions. Available at: [www.england.nhs.uk/publication/national-seasonal-influenza-immunisation-programme-2020-21-primary-care-frequently-asked-questions/](http://www.england.nhs.uk/publication/national-seasonal-influenza-immunisation-programme-2020-21-primary-care-frequently-asked-questions/)

**Public Health England. Flu Vaccination Campaign – toolkit (including Q&As)**  
[https://digitalcampaignsstorage.blob.core.windows.net/campaign-resource-centre/production/asset/file/5409/Flu\\_marketing\\_campaign\\_toolkit\\_051020.pdf](https://digitalcampaignsstorage.blob.core.windows.net/campaign-resource-centre/production/asset/file/5409/Flu_marketing_campaign_toolkit_051020.pdf) (you will need to register for the campaign resource centre but it is free to do so)

**Guidance on how to access additional centrally procured stock**

For GPs: [www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-gps](http://www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-gps)

For Community Pharmacies: [www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-community-pharmacies](http://www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-community-pharmacies)

For NHS providers: [www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-nhs-providers](http://www.gov.uk/government/publications/accessing-government-secured-flu-vaccines-guidance-for-nhs-providers)