



Public Health  
England

Protecting and improving the nation's health

# The national influenza immunisation programme 2021 to 2022

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## Document history

Version number	Change details	Date
01.00	New information document	August 2021

# Influenza vaccination programme 2021 to 2022 and control measures to prevent the spread of coronavirus (COVID-19)

This document contains information on the influenza vaccination programme 2021 to 2022, the inactivated influenza vaccine and the Live Attenuated Influenza Vaccine (LAIV). It may be updated throughout the year with any new information that becomes available as the flu vaccination season progresses. The final section of this document provides additional information and advice on common issues that may be encountered whilst delivering the flu immunisation programme.

JCVI have published [interim advice on COVID-19 booster vaccination](#). As booster doses of COVID-19 vaccine are currently being considered trials are taking place to ascertain whether co-administration of COVID-19 vaccine and influenza vaccine will be permissible, subject to the advice of JCVI.

It is recommended that you read the letters and resources available on the [PHE Annual flu programme webpage](#) and that you also read the information and resources available on the [PHE COVID-19 vaccination programme webpage](#) during the flu vaccination period. These webpages should be regularly checked as any further information that becomes available about the flu vaccination programme or the COVID-19 vaccination programme will be published there.

Further programme updates may also be reported in Vaccine Update so please subscribe using the link for [New subscribers](#) if you are not currently a subscriber.

As COVID-19 is likely to continue to co-circulate with flu this winter, 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, including recommendations around the use of personal protective equipment (PPE) in keeping with the current advice from the Government.

# Background and 2021 to 2022 programme summary

In the situation where social mixing and social contact return towards pre-pandemic norms, it is expected that winter 2021 to 2022 will be the first winter in the UK when seasonal influenza virus (and other respiratory viruses) will co-circulate alongside COVID-19. Seasonal influenza and COVID-19 viruses have the potential to add substantially to the winter pressures usually faced by the NHS, particularly if infection waves from both viruses coincide. The timing and magnitude of potential influenza and COVID-19 infection waves for winter 2021 to 2022 are currently unknown, but the [JCVI interim advice](#) stated that mathematical modelling indicates the 2021 to 2022 influenza season in the UK could be up to 50% larger than typically seen and it is also possible that the 2021 to 2022 influenza season will begin earlier than usual.

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), pregnant women (in 2010), those with a body mass index (BMI) of 40 or more (2016) and children (2013).

During 2020 to 2021 an expanded offer was made which enabled those aged 50 to 64 years to receive the flu vaccine as part of an NHS funded programme. This offer will continue for this age group, as a temporary measure, for the 2021 to 2022 programme.

Studies commissioned by JCVI [\(1\)](#) suggested that, despite the high cost, extending the flu vaccination programme to all children is highly likely to be cost-effective and well below the established cost-effectiveness threshold when indirect protection to the whole population is considered, particularly over the longer term. This is because offering influenza vaccine to healthy children not only provides individual protection to the child, it also reduces transmission across all age groups to lessen levels of flu activity overall and reduces the burden of flu across the population. Pebody and others [\(2\)](#) reported reductions in GP consultations for influenza-like illness, swab positivity in primary care, laboratory confirmed hospitalisations and percentage of respiratory emergency department attendances.

The programme for children was recommended in 2012 by JCVI [\(3\)](#) and has been phased in over a number of years beginning in 2013 with additional age groups being added each year. This year, the childhood flu vaccination programme has been extended to include, as a temporary measure, all children from Year 7 to Year 11 in secondary schools (all children between 2 and 15 years old (but not 16 years or older)

on 31 August 2021). Some school aged children might be outside of the age ranges (for example, if a child has been accelerated or held back a year). It is acceptable to offer and deliver immunisations to these children with their class peers. Children from 6 months of age in clinical risk groups should continue to be offered flu vaccine.

A comprehensive list of the groups included in the national immunisation programme for the 2021 to 2022 flu season are described in Appendix A of the [National flu immunisation programme plan](#).

They include:

- all children aged 2 to 15 (but not 16 years or older) on 31 August 2021
- those aged 6 months to under 50 years in clinical risk groups
- pregnant women
- those aged 50 years and over
- those in long-stay residential care homes
- carers
- close contacts of immunocompromised individuals

All frontline health and social care workers are expected to have influenza vaccination to protect those they care for. Providers should use the current definition of healthcare workers as set out in [chapter 12 of the green book](#).

## Key documentation

Statement of amendments to the annual flu letter can be found on the [PHE Annual flu programme webpage](#).

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

1. The [National flu immunisation programme plan](#) provides detailed information to support the successful implementation of the programme
2. The general practice specification for seasonal influenza immunisation will be published on the [NHS GP contract web page](#). This document 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 2 and 3 on 31 August 2021). It includes eligible frontline health and care workers working in residential care and nursing homes, domiciliary care providers, the

voluntary managed hospice sector and those employed through Direct Payment (personal budgets) and/or Personal Health Budgets, such as Personal Assistants.

3. The Enhanced Service (ES) specification for the childhood seasonal influenza vaccination programme will be published on the [NHS GP Contract web page](#). This document describes the services to be provided by GP practices for children aged 2 and 3 but not 4 years on 31 August 2021.
4. Community pharmacies will be offering a flu vaccination service. Details of this service will be published on the [Community Pharmacy Seasonal Influenza Vaccine Service](#) webpage.
5. Green Book [Influenza chapter](#) provides information on influenza disease, epidemiology, the vaccines and the vaccination programme.

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.

## Influenza

Detailed information on influenza infection, epidemiology and the vaccination programme is included in the Green Book [Influenza chapter](#) and on [NHS.UK](#).

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.

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 6 months, pregnant women, those aged over 65 years and those with underlying health conditions. These groups are at higher risk of developing severe complications such as bronchitis, secondary bacterial pneumonia, or otitis media in children.

## 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 6 months should benefit from passive protection if their mother received the vaccine during pregnancy.

Vaccination of eligible individuals should commence as soon as stock of the recommended vaccine is available and should be given in sufficient time to ensure patients are protected before flu starts circulating in their community.

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 2022.

The specific vaccines recommended in the NHSEI letters should be used in order for providers to receive payment for administration and reimbursement.

## 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](#) and a [Patient Group Direction \(PGD\) template for Live attenuated influenza vaccine \(LAIV\)](#) to support the administration of influenza vaccines each year. The PGDs are not legally valid until they have had the relevant organisational authorisation from an appropriate authorising person in Section 2 of the PGD.

### 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 the administration of injectable inactivated influenza vaccines.



## Written Instruction

The PHE PGD covers NHS commissioned services. It does not cover the provision of occupational health schemes or peer-to-peer influenza immunisation. For this reason, a written instruction template for Occupational Health vaccination of health and social care staff (2021 to 2022 season) will be available in due course and will be published on the [NHS Specialist Pharmacy Service website](#). This template can be adopted by organisations, to provide an appropriate written instruction for the offer of seasonal flu vaccinations to employees, for administration of vaccine in accordance with an appropriate legal framework.

## Vaccine eligibility

Detailed descriptions of those eligible to receive the NHS-funded flu vaccine can be found in [Chapter 19 of the Green Book](#), Appendix A of the [Annual flu letter for 2021 to 2022](#) and within the inclusion criteria for the appropriate vaccine [Patient group direction \(PGD\)](#).

## Summary of eligible groups

A summary of eligible groups include:

- all children aged 2 to 15 (but not 16 years or older) on 31 August 2021
- those aged 6 months to under 50 years in clinical risk groups
- pregnant women
- those aged 50 years and over
- those in long-stay residential care homes
- carers
- close contacts of immunocompromised individuals
- frontline health and social care workers (HSCWs) should receive a vaccination provider by their employer – HSCWs include those employed by a registered residential or care home, a registered domiciliary care provider, a voluntary managed hospice provider or by those receiving direct payment (personal budgets) and/or personal health budgets such as personal assistants

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

Some patients may have been eligible to receive an NHS funded influenza 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, 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 medical condition.

## Timing of vaccination

Influenza vaccine should be given in sufficient time to ensure protection 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 and can continue as long as they have unexpired vaccine in stock and unvaccinated patients in their practice (up until 31 March 2022).

If an eligible individual presents late for vaccination it is generally appropriate to still offer it. Providers should apply clinical judgement, considering the level of flu-like illness in their community and the fact that the immune response following flu vaccination takes about 2 weeks to develop fully.

As the immunisation teams have to go into a considerable number of schools in a short space of time, some children may be offered immunisation later in the season. Parents of any child at risk from flu because of an underlying medical condition can choose to receive flu vaccination in general practice, especially if the parent would prefer this, the child missed the session at school or they do not want their child to have to wait for the school vaccination session. GP practices should invite these children for vaccination, making it clear to their parents that they have the option to have their child vaccinated in general practice (and that if they receive it in general practice, they will not then require a dose in school).

## Pregnancy and breastfeeding

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. The vaccines recommended for use in pregnancy are QIVc or QIVr. If either of these vaccines are not available, QIVe can be used.

Influenza infection during pregnancy may be associated with perinatal mortality, prematurity, lower birth weight and smaller neonatal size in the infant (4, 5, 6) and an increased risk of complications in the pregnant woman (7, 8).

Studies have demonstrated that pregnant women can safely receive inactivated 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 (9).

There is limited data on the use of live attenuated flu vaccine in pregnancy. While there is no evidence of risk with LAIV, inactivated flu vaccines are preferred for those who are pregnant. There is no need to specifically test eligible girls for pregnancy or to advise avoidance of pregnancy in those who have been recently vaccinated. There are no specific precautions regarding pregnant women who are exposed to children who have been vaccinated with LAIV as the likelihood of onward transmission is considered very low.

Pregnant women can access the influenza vaccine from their GP or community pharmacy. In addition, a national service specification has been commissioned by NHSEI to enable maternity service providers to vaccinate pregnant women.

## 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 2 to 3 months of flu transmission. Although it takes around 2 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, on the 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 or 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.

## Influenza vaccine and its components

A table of the influenza vaccines available for 2021 to 2022 has been published on the [Annual flu page](#).

Changes to the portfolio of influenza vaccines recommended for use during 2021 include:

- replacement of trivalent vaccines (aTIV) for quadrivalent vaccines (aQIV) for the adjuvanted formulation
- addition of recombinant quadrivalent vaccine Supemtek (QIVr)
- change to the age indications on the Influvac (QIVe) licence from 3 years to 6 months
- cell based quadrivalent vaccine (QIVc) is now licensed for use in those aged 2 years and older

## 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.

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.

For the 2021 to 2022 flu season (northern hemisphere winter) WHO have recommended (10) that quadrivalent vaccines contain the following:

- Egg-based Vaccines
  - an A/Victoria/2570/2019 (H1N1)pdm09-like virus
  - an A/Cambodia/e0826360/2020 (H3N2)-like virus
  - a B/Washington/02/2019 (B/Victoria lineage)-like virus
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus
  
- Cell- or recombinant-based Vaccines
  - an A/Wisconsin/588/2019 (H1N1)pdm09-like virus
  - an A/Cambodia/e0826360/2020 (H3N2)-like virus
  - a B/Washington/02/2019 (B/Victoria lineage)-like virus
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

This vaccine composition differs from the 2020 to 2021 vaccine composition as both influenza A virus strains have been replaced.

The [Vaccine Knowledge Project Inactivated Flu Vaccine webpage](#) contains comprehensive information about the constituents of flu vaccines.

## Egg allergy and ovalbumin content of influenza vaccines

There are 2 egg free vaccines available for the 2021 to 2022 flu season. Flucelvax tetra (QIVc) (indicated from 2 years of age) and Supemtek (QIVr) (indicated from 18 years of age).

The other inactivated influenza vaccines (QIVe and aQIV) contain traces of egg such as the egg protein ovalbumin. The ovalbumin content of the flu vaccines for the 2021 to 2022 season is available in [Influenza vaccine: ovalbumin content](#) on the [Annual flu programme](#) webpage.

JCVI have previously advised (11) that children aged 2 years and over with an egg allergy, including those with previous anaphylaxis to egg, can be safely vaccinated with LAIV in any setting (including primary care and schools). The only exception is for children who have required admission to intensive care for a previous severe anaphylaxis to egg, for whom no data are available; such children are best given LAIV in the hospital setting. LAIV remains the preferred vaccine for this group and the intranasal route is less likely to cause systemic reactions.

Children with egg allergy but who also have another condition which contraindicates LAIV (for example, immunosuppression) should be offered either an age appropriate egg free inactivated influenza vaccine or one with a very low ovalbumin content (less than 0.12 micrograms/ml). Inactivated vaccines with ovalbumin content more than 0.12 micrograms/ml (equivalent to 0.06 micrograms/ml for 0.5ml dose) or where content is not stated should not be used in egg-allergic children. If these children are aged under 9 years and have not previously been vaccinated against influenza, they will require a second dose of vaccine 4 weeks after the first.

Egg-allergic children with asthma can receive LAIV if their asthma is well controlled (please see the advice on asthma in the Precautions section).

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 age appropriate 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 an age appropriate egg-free quadrivalent influenza vaccine.

## Vaccine adjuvant in aQIV

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.

The aQIV vaccine contains an adjuvant called MF59C.1 which improves the immune system's response to vaccination and helps it to produce more antibodies against the influenza virus strains in the vaccine. MF59C.1 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. In humans, it is made in the liver and circulates in the bloodstream. 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 aQIV 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 (12).

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 aQIV vaccine is obtained from the spiny dog fish and shark liver oil forms around 80% of the squalene for MF59C.1 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 (13). Patients who report hypersensitivity to fish should be assessed as to the nature and severity of their allergy before the vaccine is given.

## Latex

The influenza vaccines for 2021 to 2022 are not contraindicated in latex allergic individuals. The vaccine components that are in contact with the injection solution or suspension are latex-free.

Some vaccines may be supplied with needle shields that are not latex-free. Summary of Product Characteristics (SPC/SmPC) 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 such as kanamycin and neomycin sulphate. Patients with a severe or anaphylactic allergy to any vaccine components, including antibiotic residues, should be offered an alternative vaccine.



The flu vaccine Flucelvax Tetra (QIVc) does not contain any antibiotics as this vaccine is made in cells, not eggs and means that there is no need to use antibiotics during the manufacturing process.

## Recommendations for the use of inactivated influenza vaccine

For the 2021 to 2022 flu season, the Joint Committee on Vaccination and Immunisation (JCVI) have made the following recommendations (14). Details on the reimbursement of these vaccines as part of the NHS seasonal influenza immunisation programme 2021 to 22 are included in a [letter describing the achievements and developments during 2020 to 2021 flu season](#).

**Table 1: Recommendations for the use of inactivated influenza vaccines**

<ul style="list-style-type: none"> <li>Those aged 65 years and over**</li> </ul>	<ul style="list-style-type: none"> <li>aQIV*</li> <li>if aQIV is not available, use QIVc or QIVr</li> </ul>
<ul style="list-style-type: none"> <li>At risk adults aged 18 to less than 64 years</li> <li>pregnant women</li> <li>All adults aged 50 to 64 years</li> </ul>	<ul style="list-style-type: none"> <li>QIVc or QIVr</li> <li>if QIVc or QIVr are not available, use QIVe</li> </ul>
<ul style="list-style-type: none"> <li>Children aged 2 years and over and contraindicated to receive LAIV</li> </ul>	<ul style="list-style-type: none"> <li>QIVc (if LAIV is contraindicated or otherwise unsuitable)</li> </ul>
<ul style="list-style-type: none"> <li>Infants aged 6 months to 2 years in a clinical risk group</li> </ul>	<ul style="list-style-type: none"> <li>QIVe (LAIV and QIVc are not licensed for use under 2 years of age)</li> </ul>

## Adults 65 years of age and over and those who will become 65 before 31 March 2022

For vaccination of those aged 65 years and over in the 2021 to 2022 flu season, and those aged 64 years who will become 65 before 31 March 2022, JCVI advises the use of the following inactivated vaccines:



- adjuvanted quadrivalent influenza vaccine (aQIV)\*
- or, if aQIV is not available, cell-based quadrivalent influenza vaccine (QIVc) or recombinant quadrivalent influenza vaccine (QIVr)

\*off-label use for those who become 65 before 31 March 2022

The current available evidence indicates additional benefit from aQIV in those aged 65 years and over, compared with standard dose egg-cultured inactivated trivalent and quadrivalent vaccines (TIVe/QIVe).

If aQIV is not available, JCVI consider QIVc and QIVr to be acceptable alternative influenza vaccines for use in this age group and are preferable to standard egg culture influenza vaccines.

Although JCVI recommended the use of QIV-HD in those aged 65 and over, this vaccine is not available in the UK market during 2021 to 2022.

## At-risk adults aged under 65 years, adults aged 50 to 64 years and pregnant women

All adults aged 18 to less than 65 years old should be offered:

- cell-based quadrivalent influenza vaccine (QIVc) or Recombinant quadrivalent influenza vaccine (QIVr)
- if QIVc or QIVr are not available, egg-grown quadrivalent influenza vaccine (QIVe) can be considered for use.

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 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.

JCVI also consider that there is good evidence that QIVr is more effective than QIVe in adults under 65 years of age and is also not affected by egg adaption.

However, quadrivalent egg-culture inactivated vaccine (QIVe) can also be given to this age group if QIVc or QIVr are not available.

## Health and social care workers aged 65 years old and over

All frontline health and social care workers are expected to have flu vaccine to protect those they care for and should be offered it at the earliest opportunity.

Most health and social care workers are likely to be under 65 years of age and relatively healthy and should therefore derive benefit from the QIV whether it is cell-based or a recombinant vaccine. Immunisers should make it clear to staff aged 65 years and over that they can get aQIV 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 aQIV.

## 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 QIVc or QIVr 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.

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

As LAIV and QIVc are not licensed for use in those aged **6 months to less than 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 should be ordered through **ImmForm**.

If LAIV is contraindicated or otherwise unsuitable for children aged from **2 years old to less than 18 years**, QIVc or QIVe (in that order of preference and with QIVe as a second option) should be offered as an alternative. QIVc will be centrally supplied for these children and should be ordered through **ImmForm**. PHE has not procured QIVe for this purpose.

Children who are household contacts of very severely immunocompromised people should also be offered inactivated rather than live flu vaccine.

## Children whose parents decline LAIV

If the parent of an eligible child refuses LAIV because of its porcine gelatine content (and they understand that it is the most effective product in the programme), they can request an alternative injectable vaccine. QIVc will also be centrally supplied for these children and should be ordered through [ImmForm](#).

## Inactivated vaccines available during 2021 to 2022

Some inactivated flu vaccines are restricted to use in particular age groups or are not suitable for those with an egg allergy. Those administering flu vaccines must be familiar with and refer to the manufacturer's SPC for individual brands when administering inactivated flu vaccines.

## Quadrivalent influenza vaccines

Quadrivalent influenza vaccines (QIV) contain 2 influenza A strains and the 2 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). All the vaccines recommended for use in 2021 to 2022 are quadrivalent.

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

## Adjuvanted quadrivalent influenza vaccines (aQIV)

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.

Published data indicated that an adjuvanted trivalent influenza vaccine (aTIV) had higher immunogenicity and effectiveness than non-adjuvanted vaccines in older people and in 2017, aTIV was licensed for use in those aged 65 years and older in the UK and was widely used for 3 flu seasons.

For 2021 to 2022 the trivalent formulation in the adjuvanted vaccine has been replaced by a quadrivalent one. This is expected to provide greater protection for those aged 65 years and older as it contains 2 B strains rather than the 1 strain that was present in the trivalent vaccine.

## 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 and contains whole inactivated virus. 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 (QIVc), 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 (15). 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)

Supemtek (QIVr) 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 3 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 Supemtek are similar to those seen following vaccination with other flu vaccines (injection site tenderness, headache, fatigue, muscle ache and joint pain).

Non-egg grown vaccines (such as Flucelvax Tetra (QIVc) and Supemtek Quadrivalent (QIVr)) are widely used in the US and in multiple European countries. Flucelvax was first approved for use in the US in 2012. In the UK, QIVr was approved in 2013 and was known as Flublok. This year, it is licensed as Supemtek. 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 gelatine.

Further information on how cell-based and recombinant flu vaccines are made is available from the [Centres for Disease Control and Prevention](#).

## Egg-grown quadrivalent influenza vaccine (QIVe)

The egg-grown quadrivalent influenza vaccine (QIVe) protects against 4 strains of flu: 2 A types and both B types. This vaccine can be considered for use in at risk adults and pregnant women aged less than 65 years if the recommended vaccines are not available as any impact of egg adaptation is likely to be limited to influenza seasons dominated by well-matched H3N2 strains. However, JCVI supports a preference for QIVc and QIVr over QIVe for these groups. QIVe is the recommended vaccine for children aged 6 months to 2 years in clinical risk groups.

## High dose quadrivalent influenza vaccines

High dose quadrivalent influenza vaccine is not available in the UK market during 2021 to 2022.

## Trivalent influenza vaccines

As there is increasing evidence of the limited effectiveness of non-adjuvanted, standard-dose trivalent egg-based influenza vaccines in older people, they are not recommended to be used in any age or clinical risk group for the 2021 to 2022 influenza season.

## Recommendations for the use of Live attenuated influenza vaccine (LAIV)

Live attenuated intranasal vaccine (LAIV) should be offered to eligible children aged 2 to less than 18 years unless contraindicated. LAIV contains an attenuated (weakened) vaccine virus that is cold adapted so it cannot cause clinical flu in immunocompetent children.

Influenza vaccines for children are centrally procured by PHE and should be ordered through ImmForm. As the vaccines are supplied free of charge via ImmForm they will not be reimbursed as part of the NHS annual influenza programme.

Table 2 shows the recommended vaccines for children.

**Table 2: Recommended vaccines for children**

At risk children aged 2 to under 18 years*	Offer LAIV.  If LAIV is contraindicated (or it is otherwise unsuitable) offer: <ul style="list-style-type: none"><li>• QIVc</li></ul>
Aged 2 and 3 years on 31 August 2021 Primary school aged children and those in Year 7 to 11 in secondary school (aged 4 to 15 on 31 August 2021)*	Offer LAIV  If LAIV is contraindicated (or it is otherwise unsuitable) offer: <ul style="list-style-type: none"><li>• QIVc*</li></ul>

\* QIVe is suitable to offer to these children but as a second option. QIVe has not been procured by PHE and should not be ordered from ImmForm for this age group.

LAIV is manufactured by AstraZeneca/MedImmune, was first approved by use in 2003 (16) and has been sold in many countries since. Only one LAIV vaccine is available,

marketed as Fluenz Tetra for the UK and EU market, and FluMist Quadrivalent for the US market. Fluenz Tetra and FluMist Quadrivalent are the same product in different packaging.

LAIV may not be suitable for all children who are eligible for the flu vaccine (please refer to contraindications section). For those children in whom LAIV is contraindicated, a suitable, age appropriate injectable inactivated influenza vaccine should be offered instead.

In England, LAIV should be offered to all children who are aged from 2 years on 31 August 2021 to those aged 15 years on 31 August 2021 and to those in clinical risk groups aged 2 to less than 18 years, unless contraindicated (please refer to contraindications section).

Some school aged children might be outside of the age ranges (for example, if a child has been accelerated or held back a year). In these circumstances it is acceptable to offer and deliver immunisations to these children with their class peers.

For further information about the childhood flu immunisation programme 2021 to 2022, please refer to Appendix F of the annual flu letter which can be found on the [Annual flu programme](#) webpage.

## Live attenuated influenza vaccine (LAIV)

### Presentation of LAIV

LAIV is supplied in a box containing 10 single-use, prefilled nasal applicators. Each applicator contains 0.2ml nasal suspension. The nasal applicator is ready to use and the vaccine does not require reconstitution or dilution. The nasal suspension is colourless to pale yellow, clear to opalescent though small white particles may be present.

### LAIV applicator components

The LAIV is supplied in a single use nasal applicator (type 1 glass) with nozzle (polypropylene with polyethylene transfer valve), nozzle tip-protector (synthetic rubber), plunger rod, plunger stopper (butyl rubber) and dose divider clip, none of which should affect latex sensitive individuals.



## LAIV efficacy

LAIV provides good overall protection for children against influenza virus and is expected to provide some cross-protection against mismatched strains. Using a live attenuated vaccine provides more antigenic stimuli; more elements of the immune system are involved resulting in the production of IgA antibody (important in mucosal immunity), and cell mediated immunity including T-cell responses. Vaccine effectiveness varies from season to season depending upon the circulating strains and the vaccine composition. The overall adjusted vaccine effectiveness for 2019 to 2020 for 2 to 17 year olds receiving LAIV was 45.4% but as 2020 to 2021 had extremely low levels of circulating flu, it has not been possible to calculate vaccine effectiveness for 2020 to 2021.

## Cold adapted influenza virus

The live viruses in LAIV are cold adapted so that they cannot replicate efficiently at body temperature (37°C). This means that the vaccine viruses will not replicate in the lungs but will reproduce at the cooler temperatures found in the nose (nasal mucosa). This allows the child to produce localised antibodies in the lining of the airways which then protect against infection if they encounter flu virus (which enters the body via the nose and mouth).

These localised antibodies are not produced in response to the inactivated flu vaccine. In addition to localised antibodies in the nose, antibodies are also produced in the blood (systemic antibodies).

## Transmission of vaccine virus in LAIV

There is a theoretical potential risk of transmission of the live attenuated flu virus in LAIV to very severely immunosuppressed contacts (for example bone marrow transplant patients requiring isolation) for 1 to 2 weeks following vaccination. In the USA, where there has been extensive use of LAIV, there have been no reported instances of illness or infections from the vaccine virus among immunocompromised patients inadvertently exposed. Where close contact with very severely immunosuppressed contacts (for example household members) is likely or unavoidable however, consideration should be given to using an appropriate inactivated flu vaccine instead.

Healthcare workers and school staff may be asked questions in relation to the safety of the LAIV being given in schools. Specific information on potential exposure during administration, and from recently vaccinated children, is outlined below.



The nasal influenza vaccine uses a live attenuated (weakened) influenza virus which helps protect against influenza infection in those who receive it. LAIV does not cause clinical influenza in those immunised and is offered to children because it provides good overall protection for children against influenza virus and is expected to provide some cross-protection against mismatched strains. It has a good safety record and is easier to administer than injected vaccines. Millions of doses of LAIV have been given in the USA and in Canada. This vaccine is also given to children in Finland. In the UK, millions of doses of LAIV have been given to young children and to school age children during the last 8 flu seasons. A small number of respiratory illnesses (including wheeze) were reported in the contacts of vaccinated children. Most of these events were self-limiting and some of them are likely to have been coincidental.

LAIV has a good safety record and unvaccinated contacts are not at risk of becoming seriously ill with the flu vaccine virus, either through being in the same room where flu vaccine has been given or by being in contact with a recently vaccinated individual. Excluding children from school during the period when LAIV is being offered or in the following weeks is therefore not considered necessary. The only exception to this would be the tiny number of children who are extremely immunocompromised (for example, those who have just had a bone marrow transplant). These children are normally advised not to attend school anyway because of the definite and much higher risk of being in contact with other infections, including 'wild' influenza, that spread in schools.

## Exposure to vaccine virus during administration

Administration of the vaccine is via a nasal applicator which delivers 0.1ml (around one-fiftieth of a teaspoon) of fluid into each nostril. There is not a 'mist' of vaccine virus in the air when children are being vaccinated and therefore others in the room should not be at risk of "catching" the vaccine virus. The room or school in which administration of nasal influenza vaccine has taken place does not require any special cleaning afterwards.

Images of the vaccine being squirted into the air (which are widely available on the internet) and the USA name of the vaccine (FluMist Quadrivalent) may give a false impression that a vaccine mist fills the room. These images are intended to show how gently the vaccine comes out when inserted into the nose, but the vaccine does not create an external mist – almost all the fluid is immediately absorbed into the child's nose where it has been sprayed.

Healthcare workers administering LAIV may, theoretically, be exposed to the vaccine virus if it is accidentally released outside of the child's nose. In the USA, where there has been extensive use of the vaccine over many years, transmission of the vaccine virus to healthcare workers has not been reported to date. Healthcare workers who are immunocompromised and those who are pregnant can safely administer the vaccine. As

a precautionary measure, however, very severely immunocompromised healthcare workers should not administer LAIV.

## Shedding of vaccine virus

Although vaccinated children are known to shed virus a few days after vaccination, it is less able to spread from person-to-person than the natural infection. The amount of virus shed is normally below the levels needed to pass on infection to others and the virus does not survive for long outside of the body. This is in contrast to natural flu infection, which spreads easily during the flu season. In schools where LAIV is administered therefore, the overall risk of contact with influenza viruses is massively reduced by having a large number of children vaccinated, thus reducing their risk of wild flu infection.

In the USA, where there has been extensive use of LAIV for many years, serious illness amongst immunocompromised contacts who are inadvertently exposed to vaccine virus has never been observed. Expert doctors at Great Ormond Street Hospital, who deal with many children with very serious immune problems, do not recommend keeping such children off school purely because of LAIV vaccination.

## Number of influenza vaccine doses required (inactivated and LAIV vaccines)

Healthcare professionals are reminded that in some circumstances, the recommendations regarding vaccines given in the Green Book chapters may differ from those in the SmPC for a particular vaccine. When this occurs, the recommendations in the Green Book are based on current expert advice received from the JCVI and this advice should be followed. The Green Book recommendations and/or further advice from the Department of Health and Social Care and Public Health England should be reflected in PGDs.

Children who have received 1 or more doses of any flu vaccine before should be considered as previously vaccinated. 2 doses are only required for children under 9 years of age and in an at risk group during the first year the child receives any flu vaccine. In subsequent years, they can be given a single dose as their immune system will already have been primed.

The marketing authorisation holder's [Summary of Product Characteristics \(SmPC\)](#) states that, for children who have not previously been vaccinated against seasonal flu, a second dose should be given after an interval of at least 4 weeks. The JCVI has

considered this issue and has recommended that as a second dose of the vaccine provides only modest additional protection, children who are not in a clinical risk group should be offered a single dose of LAIV.

## Age 0 to 6 months

Flu vaccine is not licenced for use in infants less than 6 months old although they may develop some protection through the transfer of maternal antibodies if their mother is vaccinated during pregnancy.

## Age 6 months to 2 years and not in a clinical risk group

Infants and children aged 6 months to 2 years who are not in a clinical risk group are not eligible to receive influenza vaccine as part of an NHS funded vaccination programme.

## Age 6 months to 2 years and in a clinical risk group

Influenza vaccine is recommended for infants and children aged 6 months to 2 years who are in a clinical risk group. However, LAIV is not licenced for use in this age group.

Children aged 6 months – 2 years in a clinical risk group who have never received influenza vaccine in previous flu seasons should receive 2 doses (0.5ml) of inactivated vaccine with a 4 week interval between doses.

Children in a clinical risk group who have received 1 or more doses of influenza vaccine in previous flu seasons should be considered as previously vaccinated and only require a single dose (0.5ml) of influenza vaccine each season.

Those age 6 months to less than 2 years with egg allergy should be offered inactivated flu vaccine with a very low ovalbumin content (less than 0.12micrograms/ml).

## Age 2 years to less than 9 years and in a clinical risk group or is a household contact of an immunosuppressed individual

Children aged 2 to 9 years who are in a clinical risk group or are household contacts of an immunosuppressed individual and have never previously received any influenza vaccine should be offered 2 doses of LAIV with a minimum of a 4 week interval between

them. Those children who have received a dose of flu vaccine in a previous flu season only require a single dose in subsequent years.

If LAIV is contraindicated or is otherwise unsuitable, 2 doses of a suitable age appropriate inactivated vaccine should be given with a 4 week interval between doses. The inactivated flu vaccines are interchangeable so the second dose does not have to be the same vaccine as given for the first dose.

## Age 2 years to less than 9 years and not in a clinical risk group

Children NOT in clinical risk groups only require 1 dose of LAIV. A single dose is 0.2ml (administered as 0.1ml per nostril).

## Age 9 years to less than 16 years and not in a clinical risk group

Children age 9 years to less than 16 years require 1 dose of LAIV. A single dose is 0.2ml (administered as 0.1ml per nostril).

## Age 9 years to less than 18 years and in a clinical risk group

Children age 9 years to less than 18 years require 1 dose of LAIV. A single dose is 0.2ml (administered as 0.1ml per nostril).

## 18 years and over (including pregnant women)

A single 0.5ml dose of an inactivated influenza vaccine is recommended for eligible adults aged 18 years of age or older each year that they are eligible. This includes pregnant women, health and social care workers and those aged 65 years and over.

## Contraindications and precautions

There are very few individuals who cannot receive any flu vaccine. When there is doubt, appropriate advice should be sought promptly from the local NHS England Screening and Immunisation team, local Health Protection team or a consultant paediatrician to minimise the period the individual is left unvaccinated

## Inactivated influenza vaccine and LAIV

Inactivated influenza vaccine and LAIV are contraindicated for all patients who have had:

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

## Additional contraindications for LAIV

LAIV should not be given to a child or adolescent who:

- is under 24 months or 18 years or older
- is clinically severely immunodeficient due to conditions or immunosuppressive therapy. This includes acute and chronic leukaemias; lymphoma; HIV infection not on highly active antiretroviral therapy (HAART); cellular immune deficiencies;
- Taking high dose corticosteroids (prednisolone at least 2mg per kg per day for a week, or 1mg per kg per day for a month or equivalent)
- is receiving salicylate therapy
- is pregnant

LAIV is not contraindicated for use in children or adolescents with stable HIV infection receiving antiretroviral therapy; those receiving topical steroids, standard dose inhaled corticosteroids, low-dose systemic corticosteroids or those receiving corticosteroids as replacement therapy, for example for adrenal insufficiency.

## Risk of anaphylaxis following administration of inactivated influenza vaccine or LAIV

As with all vaccines, there is a very rare possibility of any influenza vaccine causing a severe allergic reaction (anaphylaxis). All healthcare professionals who administer vaccines should be trained to recognise and treat anaphylaxis.

The [Green Book chapter on 'contraindications and special considerations' \(chapter 6\)](#) gives further advice on the use of live vaccines in individuals who are severely immunosuppressed. Where LAIV is contraindicated, consideration should be given to the use of inactivated flu vaccine instead.

For a full list of influenza vaccine components, please see the manufacturer's Summary of Product Characteristics (SmPC/SPC) available on the [Electronic Medicines Compendium](#) website. The SmPC 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).

Where a recommended vaccine is contraindicated, immunisers should follow the recommendations in the summary table of Appendix C in the annual flu letter detailing the national flu immunisation programme.

## Acute exacerbation of Asthma symptoms

LAIV is not recommended for children and adolescents currently experiencing an acute exacerbation of asthma symptoms including those who have had increased wheezing and/or needed additional bronchodilator treatment in the previous 72 hours. Such children should be offered a suitable inactivated influenza vaccine to avoid a delay in protection.

There are limited safety data in children who require regular oral steroids for maintenance of asthma control or have previously required intensive care for asthma exacerbation – such children should only be given LAIV on the advice of their specialist. As these children may be at higher risk from influenza infection, those who cannot receive LAIV should receive a suitable inactivated influenza vaccine.

## Temporary deferral of immunisation

If a child is acutely unwell or 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. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to any adverse effects of the vaccine. However, minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation.

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.

## Vaccine ordering and national supply of additional adult vaccine

A list of vaccines available for the 2021 to 2022 flu programme is available on the annual flu pages of the GOV. UK website

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 2021 to 2022 flu season.

However, the ambitions for 2021 to 2022 have been set in the expectation that we build on the momentum of last year's successful programme and achieve even higher uptake.

As some influenza vaccines may be restricted for use in particular age groups, the Summary of Product Characteristics (SmPCs) 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.

LAIV and inactivated injectable flu vaccines (QIVc and QIVe) for children can be ordered through the [ImmForm](#) website.

1. LAIV for all children aged from 2 years old to those in school Year 11 and children in clinical risk groups aged from 2 years to less than 18 years, except where contraindicated
2. An inactivated vaccine (QIVc) for children aged 2 years to less than 18 years in clinical risk groups for whom LAIV is medically contraindicated or otherwise unsuitable (for example, parents decline LAIV because of the porcine gelatine content).
3. An inactivated vaccine (QIVe) for children aged 6 months to 2 years

## Ordering controls and excess stock

It is important not to order or hold more than 2 weeks' worth of LAIV as local stockpiling can cause delays in stock being released and increases the risk of significant loss if there are cold chain failures. It also increases the risk of out of date vaccine being used as Fluenz Tetra has a short shelf life.

In previous flu seasons, ordering controls using allocations based on previous years uptake were introduced on centrally supplied flu vaccines. These were put in place to reduce the amount of excess vaccine, in particular LAIV, ordered by providers but not administered to children. Ordering controls will also be in place in 2021 to 2022. Further



information on ordering controls and other ordering advice for LAIV will be available in [Vaccine Update](#) and on the ImmForm news item both prior to, and during, the flu vaccination period.

## Vaccine storage

### Storage of inactivated influenza vaccine

Inactivated influenza vaccines must be stored in accordance with the manufacturer's instructions between +2°C and +8°C, in their original packaging and protected from light. These vaccines must not be frozen and should not be exposed to heat as this can lead to a decline in potency and subsequent reduced shelf life

### Storing LAIV

LAIV must be stored in accordance with the manufacturer's instructions between +2°C and +8°C, in its original packaging and protected from light. These vaccines must not be frozen and should not be exposed to heat as this can lead to a decline in potency and subsequent reduced shelf life

Before use, LAIV may be out of the refrigerator for a maximum period of 12 hours at a temperature not above 25°C as indicated in the [Summary of Product Characteristics](#) (SPC/SmPC). If the vaccine has not been used after this 12 hour period, it should be disposed of. If LAIV is involved in cold chain failure incident, **do not** immediately dispose of the vaccine. Label and isolate the vaccine involved, keep it between +2 to +8°C, and seek further advice from the local Screening and Immunisation team and the vaccine manufacturer.

### Shelf life of LAIV

LAIV has an expiry date 18 weeks after manufacture. This is much shorter than inactivated injectable flu vaccines. Expiry dates should be checked regularly, and all efforts should be made to use the vaccine as soon as possible.

### Expired doses of any influenza vaccine

Inactivated influenza vaccines or LAIV from previous years' programmes should be discarded before stock for the current year is received.



## 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](#) and seek further advice on vaccine stability and cold chain storage incidents from the vaccine manufacturer and your local NHS England Screening and Immunisation team.

## Influenza vaccine preparation

### Preparation of inactivated influenza vaccines

Inactivated flu vaccines are presented as prefilled syringes for intramuscular injection. The preferred site for injection is the anterolateral aspect of the thigh for infants 6 months to under 1 year. Children over 1 year of age and adults can receive the vaccine in the deltoid region of the upper arm.

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 SmPC/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 (17).

### Preparation of LAIV

Each LAIV is supplied in a pre-filled applicator for intranasal administration. The applicator contains 0.2ml of LAIV and a dose divider clip enables the vaccine to be administered as a half dose of 0.1ml into each nostril. The dose divider clip should not be removed until the first half dose has been administered.

## Vaccine administration

### Administering inactivated influenza vaccines

The inactivated influenza vaccine should be administered as an intramuscular injection. For infants aged 6 months to 1 year, the anterolateral aspect of the thigh should be used. For those aged 1 year and over, the deltoid muscle in the upper arm is the preferred muscle.

Due to the presence of the adjuvant (MF59C.1), aQIV should be administered intramuscularly using a 25mm needle to enable the vaccine to be delivered into the muscle.

### 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 aQIV this vaccine 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.

### Administering an inactivated influenza vaccine after a first dose of LAIV

In the event that all LAIV stock expires before children scheduled to receive a second dose are able to do so, a suitable inactivated injectable flu vaccine should be offered as an alternative, allowing a 4-week minimum interval period between the 2 doses.

### Administering LAIV

LAIV is administered by the intranasal route and is supplied in an applicator that allows 0.1ml to be administered into each nostril (total dose of 0.2ml). Clear diagrams showing administration are provided in the [SPC](#) and NHS Education for Scotland has made a [video for health professionals on how to administer the vaccine](#).

## Administration of LAIV by healthcare staff in clinical risk groups

In theory, healthcare workers may have low level exposure to live attenuated influenza vaccine viruses during administration of the vaccine and/or from recently vaccinated patients. The vaccine viruses are cold-adapted and attenuated and are unlikely to cause symptomatic influenza. In the USA, where there has been extensive use of LAIV, no transmission of vaccine virus in healthcare settings has ever been reported and there have been no reported instances of illness or infections from the vaccine virus among healthcare professionals inadvertently exposed. The [US Centres for Disease Control and Prevention \(CDSC\)](#) has considered that the risk of acquiring vaccine viruses from the environment is unknown but is probably low (18). As a precaution, however, very severely immunosuppressed individuals should not administer LAIV. Other healthcare workers who have less severe immunosuppression or are pregnant, should take reasonable precautions to avoid inhaling the vaccine and ensure that they themselves are appropriately vaccinated.

## Administering LAIV when the patient has a blocked or runny nose

There are no data on the effectiveness of LAIV when given to children with a heavily blocked or runny nose (rhinitis) caused by infection or allergy. As heavy nasal congestion might impede delivery of the vaccine to the nasopharyngeal mucosa, deferral of administration until resolution of the nasal congestion or use of an appropriate alternative intramuscularly administered inactivated flu vaccine should be considered.

## Administration both half doses in the same nostril

It is recommended that LAIV be administered as 2 divided sprays (0.1ml into each nostril) to maximise the vaccine's contact surface area of epithelial cells within the nasopharynx. No clinical trials have been conducted using a single-nostril administration. However, there is no need to repeat immunisation as each half dose (0.1ml) contains enough viral particles to induce an immune response.

## Administering LAIV with other vaccines

LAIV can be given at the same time as, or at any interval before or after other currently used vaccines, including live vaccines. Although it was previously recommended that, where vaccines cannot be administered simultaneously, a 4-week interval should be observed between live viral vaccines, JCVI has now advised that no specific intervals need to be observed between the live attenuated intranasal flu vaccine and other live

vaccines. See ‘Intervals between vaccines’ section in [Green Book Chapter 11](#) for more information. If any new vaccines are introduced during the flu vaccination season, please ensure you follow the specific guidance given about concomitant administration for these.

## Administering LAIV with antiviral agents against flu

There is a potential for flu antiviral agents to lower the effectiveness of LAIV. Therefore, flu antiviral agents and LAIV should not be administered concomitantly. LAIV should be delayed for at least 48 hours after cessation of treatment with flu antiviral agents. Administration of flu antiviral agents within 2 weeks of administration of LAIV may adversely affect the effectiveness of the vaccine and an additional dose of vaccine may be required.

## Adverse reactions

As with all vaccines and other medicines, healthcare professionals and patients are encouraged to report suspected adverse reactions to flu vaccines using the [yellow card reporting scheme](#). The black triangle symbol (▼) is used as a reminder to healthcare professionals and the public to report all suspected side-effects to the Medicines and Healthcare Products Regulatory Agency (MHRA) using the Yellow Card scheme. 4 of the 7 vaccines available during 2021 to 2022 have a black triangle symbol.

## 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 and injection site reactions such as redness, swelling and tenderness are also commonly reported symptoms following flu vaccination. These symptoms usually disappear within 1 to 2 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.

## Fever following LAIV

The nasal spray flu vaccine may cause a runny or blocked nose, reduced appetite, feeling generally unwell and headache. These symptoms usually disappear within 1 to 2 days without treatment, but paracetamol can be given if necessary. It is not necessary for children to stay off school or self-isolate when presenting with these symptoms unless there are reasons to suspect COVID-19. Studies have found that the likelihood of children presenting with a fever after receiving the flu nasal spray is similar to that in the general population, that is, children of the same age who have not received LAIV are just as likely to present with a fever. On this basis, if a child does present with fever after LAIV administration, then COVID-19 guidance should be followed.

## Adverse 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.

The vaccine manufacturer reports in the product Summary of Product Characteristics (SmPC) that in clinical trials, the incidence of both mild local and systemic reactions following immunisation with an adjuvanted influenza vaccine was found to be higher than the incidence of reactions following unadjuvanted TIV vaccines (19). Both Flucelvax Tetra (QIVc) and Supemtek Quadrivalent (QIVr) 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.

## Adverse reactions following administration of LAIV

Nasal congestion and/or runny nose (rhinorrhoea), reduced appetite, fever, malaise and headache are common adverse reactions following administration of LAIV.

Hypersensitivity reactions such as urticaria, facial oedema, bronchospasm and anaphylaxis can occur rarely.

## Common issues

Common issues relating to influenza vaccination are described in the following pages. Please click on the bold CI number to be taken to the bookmarked section of this document.

- CI1** Patients who are acutely unwell when presenting for vaccination
- CI2** Vaccination of individuals recently diagnosed with influenza infection
- CI3** Vaccination of patients recently diagnosed with COVID-19 infection
- CI4** Vaccination of individuals experiencing prolonged COVID-19 symptoms ('Long COVID')
- CI5** Uncertainty regarding previously administered dose of influenza vaccine
- CI6** Patients who have already received an influenza vaccine during early 2021
- CI7** Individuals who have inadvertently been given a flu vaccine that is not the 1 recommended for their age group
- CI8** Patients under 65 years of age at time of vaccination but who will be 65 years old by 31st March 2022
- CI9** Administering an incomplete dose of inactivated influenza vaccine or LAIV
- CI10** Inadvertent administration of an extra dose of influenza vaccine
- CI11** Inadvertent administration of expired doses of vaccine
- CI12** Inadvertent administration of LAIV to a child who is aged less than 24 months
- CI13** Immunosuppression
- CI14** Inadvertent administration of LAIV to a child who is immunosuppressed
- CI15** Patients taking steroids
- CI16** Patients having chemotherapy
- CI17** Patients taking checkpoint inhibitors
- CI18** Sneezing, nose blowing and nasal dripping following administration
- CI19** LAIV mist in the eye
- CI20** Patients with a previous severe anaphylactic reaction to egg
- CI21** Vaccination of patients taking anticoagulants or with a bleeding disorder
- CI22** Guillain-Barré Syndrome (GBS) and influenza vaccine
- CI23** Porcine gelatine
- CI24** Alternative vaccine Statement on the childhood flu programme: the alternative offer to live attenuated Influenza vaccine (LAIV).

**CI25** History of allergy to canine allergens

**CI26** Patients requesting live intranasal influenza vaccine (LAIV) instead of an inactivated injected vaccine due to needle phobia

## 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 follow the latest Government guidance (20).

## 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 patients recently diagnosed with COVID-19 infection

Patients 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](#) to ensure recommendations that are current at the time of vaccination are followed.

If the child has an acute severe febrile illness, LAIV administration should be deferred until recovered. Minor illnesses without fever or systemic upset are not valid reasons to postpone vaccination.



## 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-19 symptoms with flu symptoms

## 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 1 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 and/or pain at the injection site and malaise.

## Patients who have already received an influenza vaccine during early 2021

If a patient received the vaccine produced for the 2020 to 2021 season in the first few months of 2021, then they will still need a dose of the vaccine produced for the 2021 to 2022 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 1 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 2021 formulated for the Southern hemisphere (for example because they were in Australia or New Zealand during the flu season there), and they will be in the UK (Northern hemisphere) over winter 2021 to 2022, they should receive another dose of flu vaccine in the UK as the vaccines formulated for the northern hemisphere for the 2021 to 2022 flu season have a slightly different composition to the vaccines given in the southern hemisphere in 2021. The recommendations in the summary table of Appendix C in the annual flu should be followed.



Further information on the composition of Influenza vaccines is published on the WHO global influenza programme webpage.

## 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. 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 (aQIV, QIVc or QIVr).

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 2022

Patients who will become 65 years of age by 31<sup>st</sup> March 2022 but who are 64 years at the time of vaccination can receive aQIV off-label in accordance with the recommendations for the national influenza immunisation programme for 2021 to 2022. This off-label use is covered in the PHE [national template PGD for inactivated influenza vaccine](#).

## Administering an incomplete dose of inactivated influenza vaccine or LAIV

If it is thought that the patient did not receive a full dose of injected flu 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.

An incomplete dose of LAIV does not need to be repeated as long as at least 0.1ml of the vaccine has been given intranasally as each half dose (0.1ml) contains enough viral particles to induce an immune response (21).

## Inadvertent administration of an extra 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 and/or pain at the injection site, malaise, and so on. The patient should be advised of this and offered reassurance that children in clinical risk groups under the age of 9 years who have never received influenza vaccine in previous years are specifically recommended to have 2 doses 4 weeks apart. Local systems should be reviewed to prevent this happening again.

## Inadvertent administration of expired doses of vaccine

Inadvertently administering an expired dose of inactivated influenza vaccine or LAIV is unlikely to cause harm other than that the expired dose may not offer adequate protection. Healthcare practitioners should inform the patient, parent or carer of the error, provide reassurance where necessary and discount the expired dose. An additional dose of an age appropriate influenza vaccine that is in date should be offered as soon as possible (on the same day as the expired vaccine was given or as soon as the error is discovered), to ensure satisfactory protection. There is no minimum interval between an expired and a valid dose of influenza vaccine as it is the same product being administered. In the event that a repeat dose of LAIV is required and 'in date' LAIV is not available, a suitable inactivated flu vaccine should be offered as an alternative.

Inadvertently administering an expired dose of inactivated influenza vaccine/LAIV is a clinical incident that should be reported via the local governance system(s), so that appropriate action can be taken.

## Inadvertent administration of LAIV to a child who is aged less than 24 months

LAIV is contraindicated in children aged less than 24 months due to an increase in adverse events in this age group. An increase in wheezing and hospitalisation was observed in clinical trials that included children aged from 6 to 23 months of age. The decision not to license the vaccine for use in children aged less than 24 months was based on these observations rather than vaccine efficacy in this age group.

Children who have received LAIV at less than 24 months of age do not require a replacement dose. The inadvertently administered vaccine should count as a valid dose as LAIV will provide protection in this age group. However, the child's parents or carers should be informed of the possible adverse events in the short term and advised to seek medical care if adverse events occur. They should be reassured that no long-term effects from receiving LAIV are anticipated.

Children from 6 months of age in clinical risk groups who have not received a flu vaccine previously should count the inadvertently administered LAIV as the first dose. The child should also be offered the inactivated flu vaccine 4 weeks later to complete the 2 dose schedule (in line with the recommendation that children in clinical risk groups aged 6 months to under 9 years who have not received inactivated flu vaccine previously should be offered a second dose at least 4 weeks after the first dose). If the child reaches their second birthday in the 4 weeks between the dose of LAIV and when a second dose of flu vaccine would be due, a further dose of LAIV can be given (if not contraindicated).

Healthcare professionals should report the administration error via their local governance system(s) so that lessons can be learnt and the risk of future errors minimised.

## Immunosuppression and inactivated influenza vaccine

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 or 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.

## Inadvertent administration of LAIV to a child who is immunosuppressed

If an immunocompromised individual receives LAIV then the degree of immunosuppression should be assessed. If the individual is severely immunocompromised, antiviral prophylaxis should be considered. Otherwise they should be advised to seek medical advice if they develop flu-like symptoms in the 4 days (the usual incubation period) following administration of the vaccine. If antivirals are used for prophylaxis or treatment, then in order to maximise their protection in the forthcoming flu season, the patient should also be offered inactivated influenza vaccine. This can be given straight away.

Healthcare professionals should report the administration error via their local governance system(s) so that the appropriate action can be taken, lessons can be learned and the risk of future errors minimised.

## 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 2 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 to 2021 for those over 65 years, this includes QIVc.

## Sneezing, nose blowing and nasal dripping following administration

If the child sneezes, blows their nose or has nasal dripping following administration of LAIV, the vaccine dose does not need to be repeated. Binding of the virus to epithelial cells occurs very rapidly and there are more virus particles in the vaccine than are needed to establish immunity. Therefore, sneezing or blowing the nose immediately after immunisation with LAIV will not affect immunity (21) and reassurance should be given that the vaccine will still be effective if any of these occur.

There is no evidence that crying or screaming is aerosol generating and coughing and sneezing, which may occur following administration of live attenuated influenza vaccine (LAIV), are not included as high-risk aerosol generating procedures.

Immunisers should follow the recommendations for PPE which are current at the time of delivering the flu vaccines.

## LAIV mist contact with the eye

If the vaccine is accidentally squirted into the child's eye, it may cause some slight irritation to the eye and eyewash or normal saline should be used to wash out the eye. The child or parent should be advised to seek medical advice if any irritation occurs and persists beyond what might reasonably be expected.

## 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 2 years of age or over, should be given the egg-free cell-based quadrivalent influenza vaccine (QIVc).

The Quadrivalent influenza cell-culture vaccine (QIVc) is egg free and egg allergic individuals can be safely vaccinated in any setting with this vaccine, including those who have required admission to intensive care for a previous severe anaphylaxis to egg.

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](#).

## 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 (international normalised ratio, this is a measure of the time it takes for blood to clot) 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 or treatment to reduce bleeding, for example treatment for haemophilia, intramuscular vaccination can be scheduled shortly after such medication or 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, (22) and the individual, parent, carer should be informed about the risk of haematoma from the injection.

Flucelvax Tetra (QIVc), Supemtek Quadrivalent (QIVr) and Adjuvanted Quadrivalent Influenza Vaccines 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.

## 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. [Stowe and others](#) reported that a causal relationship between immunisation with influenza vaccine and GBS has not been established (23).

## Porcine gelatine

LAIV contains a highly processed form of gelatine (derived from pigs) as one of its additives. Gelatine is commonly used in a range of pharmaceutical products, including many capsules and some vaccines. The gelatine in LAIV is used as a stabiliser to protect the live viruses from the effects of temperature.

The gelatine used in live vaccines is highly purified and hydrolysed (broken down by water), so it is different from the natural gelatine used in foods. Very sensitive scientific tests have shown that no DNA from pigs can be detected in the LAIV nasal flu vaccine. (Fluenz Tetra). These tests show that the gelatine is broken down so much that the original source cannot be identified.

Some people, including members of Muslim or Jewish religious communities may be concerned about using vaccines that contain gelatine from pigs (porcine gelatine). This statement from representatives of the Jewish community may help some patients, parents or carers to reach a decision about having the vaccine:

Rabbi Abraham Adler from the Kashrus and Medicines Information Service said: “It should be noted that according to Jewish laws, there is no problem with porcine or other animal derived ingredients in non-oral products. This includes vaccines, including those administered via the nose, injections, suppositories, creams and ointments”.

However, it is acknowledged that some groups within the British Muslim community may consider the porcine-containing product to be forbidden. The final decision about whether parents have their child vaccinated is with them. In order to come to an



informed decision, they should be able to consider the evidence about the advantages and disadvantages of the vaccination.

This flu season children whose parents refuse live attenuated influenza vaccine (LAIV) due to the porcine gelatine content can be offered an inactivated influenza vaccine. Vaccine for this cohort is available to order by General Practice and school aged immunisation teams via [ImmForm](#).

## History of allergy to canine allergens

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 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.

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  $10^{34}$  doses (24).

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.

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 10,000 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. If there is significant concern, patients can be given an egg-grown vaccine instead.



## 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 (PHE) procures LAIV and distributes this to general practices, who vaccinate 2 and 3 year olds and children in at risk groups, and to providers responsible for vaccinating children in school (up to and including Year 11). 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. 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.

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 (that is, 'off-label') may be judged by the prescriber to be in the best interest of the patient on the basis of available evidence'<sup>(25)</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.

## Reference list

1. Pitman RJ Nagy LD and Sculpher MJ (2013), [Cost-effectiveness of childhood influenza vaccination in England and Wales: Results from a dynamic transmission model](#). *Vaccine* 31(6) pages 927 to 942 (Viewed on 14 May 2021)
2. Pebody, R. and others. 21 June 2018. [Uptake and impact of vaccinating primary school-age children against influenza: experiences of a live attenuated influenza vaccine programme, England, 2015 to 2016](#). *Eurosurveillance*. Volume 23, Issue 25).
3. Joint committee on Vaccination and Immunisation. [Statement on the annual influenza vaccination programme – extension of the programme to children](#). *JCVI* (2012). 25 July 2012.
4. Pierce M, Kurinczuk JJ, Spark P and others. (2011) [Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study](#). *BMJ*. 342:d3214.
5. McNeil SA, Dodds LA, Fell DB, and others. (2011) [Effect of respiratory hospitalization during pregnancy on infant outcomes](#). *American Journal of Obstetrics and Gynecology*. 204: (6 Suppl 1) S54-7.
6. Omer SB, Goodman D, Steinhoff MC and others. (2011) [Maternal influenza immunization and reduced likelihood of prematurity and small for gestational age births: a retrospective cohort study](#). *PloS Medicine*. 8: (5) e1000441
7. Neuzil KM, Reed GW, Mitchel EF and others. (1998) [Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women](#). *American Journal of Epidemiology*. 148:1094-102
8. Pebody R and others, (2010) [Pandemic influenza A \(H1N1\) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010](#). *Eurosurveillance* 15(20): 19571
9. Tamma PD, Ault KA, del Rio C and others. (2009) [Safety of influenza vaccination during pregnancy](#). *American Journal of Obstetrics and Gynecology*. 201(6): 547-52.
10. [Recommendations for influenza vaccine composition](#). 20th July 2021
11. Joint Committee on Vaccination and Immunisation. [Minutes of the February 2015 meeting](#).
12. Personal communication from Sequirus, 8 June 2018

13. Personal communication from Seqirus October 2019
14. Joint Committee on Vaccination and Immunisation: Advice on influenza vaccines for 2021 to 2022.
15. Personal communication from Seqirus 7 May 2019
16. Approval Letter – Influenza Virus Vaccine Live, Intranasal. US Food and Drug Administration archive. Accessed 30/04/2021.
17. Crisp J Taylor Potter C and others Fundamentals of Nursing. 2005 (2nd edition). 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 (Viewed on 14 May 2021)
18. Centers for Disease Control and Prevention (2013) Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2013–2014. MMWR September 20, 62(RR-07);1- 43. Viewed on 16 July 2021
19. Flud. Summary of Product Characteristics. Date of last revision of text: 07/2018.
20. PHE Clinical guidance for Healthcare professionals on maintaining immunisation programmes during COVID-19. viewed on 16 July 2021
21. Astra Zeneca. FLUMIST® (Influenza Vaccine [Live, attenuated]) – Inadvertent Oral Administration and Inadvertent Eye Exposure [Internet] Message to British Columbia Centre for Disease Control. 2013 July 30. Cited in British Columbia Centre for Disease Control. Live Attenuated Influenza Vaccine Questions and Answers for Health Care Providers 2014-2015. Revised Oct 2014
22. Centers for Disease Control and Prevention. Vaccine recommendations and guidelines of the ACIP. Vaccinating Persons with Increased Bleeding Risk.
23. Stowe J, Andrews N and others 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 February 1;169(3):382-8.
24. Gregersen JP Schmitt HJ Trusheim H and others Safety of MDCK cell culture-based influenza vaccines. Future Microbiology 2011 Feb 6(2) pages 143 to 152

25. Medicines and Healthcare products Regulatory Agency. [Off-label or unlicensed use of medicines: prescribers' responsibilities](#) (Viewed on 14 May 2021)

## Useful links

[Green Book Influenza Chapter](#)

[Letters detailing 2021 to 2022 flu programme and other key documents relating to the flu vaccine programme](#)

[Leaflets, posters, training slides and additional flu resources prepared specifically to support the annual flu programme](#)

[Flu vaccination: easy read resources](#)

[NHS England. Directed Enhanced Service Specification – Seasonal influenza and pneumococcal polysaccharide vaccination programme 2021 to 2022](#)

[Summary of Product Characteristics \(SPC/SmPC\) and patient information leaflet \(PIL\) for flu vaccines](#)

[Flu immunisation PGD templates \(Note: These PGDs require authorisation before use\)](#)

[Written Instruction for the administration of seasonal flu vaccination](#)

[e-learning programme](#)

[Healthcare Workers Flu Immunisation resources \(leaflets, posters, guides and resource packs\)](#)

[ImmForm website for ordering child flu vaccines](#)

[PHE Flu Immunisation Programme home page](#)

[Public information: British Society for Immunology](#)

[Vaccine Knowledge Project. Inactivated Flu Vaccine](#)

[Joint Committee on Vaccination and Immunisation](#)

[NHS England. Primary care frequently asked questions National Seasonal Influenza Immunisation Programme 2020 to 2021: primary care frequently asked questions](#)

## WHO recommendations for influenza vaccine composition

Public Health England. Flu Vaccination Campaign – toolkit (including Questions and Answers)  
(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

For Community Pharmacies

For NHS providers

A video for health professionals on how to administer LAIV produced by NHS Education for Scotland

Toolkit for childhood flu programme

National Institute for Health and Care Excellence (NICE) guidelines on increasing influenza vaccine uptake

NHS England Public Health Commissioning information

NHS England enhanced service specification (For GP providers)

Community Pharmacy Seasonal Influenza Vaccination Advanced Service

Flu vaccine uptake figures

Vaccine Update – PHE monthly newsletter

PHE Campaign Resource Centre – Help Us Help You campaign

# About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-leading science, research, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health and Social Care, and a distinct delivery organisation with operational autonomy. We provide government, local government, the NHS, Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

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