

Types of Flu Vaccine

There are two main types of vaccine available:

- Inactivated – given by injection
- live attenuated – given by nasal application

These can be:

- Trivalent: flu vaccines contain two subtypes of Influenza A and one type B virus
- Quadrivalent: vaccines contain two subtypes of Influenza A and both B virus types
- **None** of the flu vaccines can cause clinical influenza in those that can be vaccinated
- As quadrivalent vaccines contain both lineages of B viruses and therefore may provide better protection against the circulating B strain(s) than trivalent flu vaccines, **the live intranasal vaccine offered to children aged 2 years and over is a quadrivalent vaccine**
- Quadrivalent vaccines are now recommended for pregnant women and individuals in risk groups aged 6 months to under 65 years

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Inactivated flu vaccines given by intramuscular injection have been used in the UK for many years. The live intranasal influenza vaccine (LAIV) was introduced into the UK schedule in 2013. However, a live intranasal flu vaccine called FluMist (same vaccine as Fluenz, different trade name) was introduced in the US schedule in 2003 so although the live vaccine is newer, there is well over a decade's experience of widespread use of the vaccine in the US.

In previous years, most inactivated flu vaccines were trivalent, containing two subtypes of influenza A and one B virus. However, quadrivalent vaccines, containing two subtypes of influenza A and both B virus types have been developed and are now recommended for pregnant women and those in an at risk group under 65 years of age. The live intranasal vaccine is a quadrivalent vaccine (hence the 'Tetra' part of the name Fluenz Tetra®). An inactivated quadrivalent vaccine was made available for the first time in 2013 and is the preferred vaccine for children who are contraindicated to receive the LAIV .

NB The Fluenz vaccine used in the 2013/14 flu season was a trivalent live vaccine. Fluenz Tetra® was first used in the 2014/15 flu season and has been used since.

Slide courtesy of PHE

Types of Vaccine

Live attenuated influenza vaccine (LAIV)

- A live attenuated intranasal spray is the recommended vaccine for the childhood flu programme (from 2yrs and up to 18yrs)
- The live attenuated influenza vaccine (LAIV) has been shown to be more effective in children compared with inactivated influenza vaccines
- It may offer some protection against strains not contained in the vaccine as well as to those that are and has the potential to offer better protection against virus strains that have undergone antigenic drift
- Since this vaccine is comprised of weakened whole live virus, it replicates natural infection which induces better immune memory (thereby offering better long-term protection to children than from the inactivated vaccines)
- in addition to being attenuated (weakened), the live viruses in LAIV have been adapted to cold so that they cannot replicate efficiently at body temperature
- LAIV has a good safety profile in children aged two years and older

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The quadrivalent live attenuated intranasal influenza vaccine used in the UK is called Fluenz Tetra. The majority of published literature is about Fluenz (a trivalent vaccine used prior to the addition of the other B strain) but most of this will apply to Fluenz Tetra

LAIV has been shown to be more effective in children compared with inactivated flu vaccines¹⁻³ and it may offer some protection against strains not contained in the vaccine as well as to those that are and has potential to offer better protection against strains that have undergone antigenic drift compared to the original virus strains in the vaccine⁴

Since this vaccine is comprised of weakened whole live virus, it replicates natural infection which induces better immune memory. This should mean it also offers better long-term protection to children than they may get from the inactivated vaccines.

LAIV contains live viruses that have been attenuated (weakened) and adapted to cold so that they cannot replicate efficiently at body temperature. The vaccine viruses replicate in the cooler nasal mucosa but not at body temperature in the lungs. This means they cannot cause clinical flu in immunocompetent children.

The live intranasal vaccine has a good safety profile in children aged two years and

older and has been used for over a decade in the United States. The vaccine was extensively tested prior to its launch in the United States market. Since then there has been extensive post launch surveillance in the USA, involving millions of doses in children with no evidence found of any safety concerns. It has also been used in the past four flu seasons in the UK where hundreds of thousands of children have been safely vaccinated. As with all vaccines and medicines, MHRA closely and continuously monitors the safety of LAIV.

Slide courtesy of PHE

References:

- 1 - Belshe RB, Edwards KM, Vesikari T et al. (2007) Live attenuated versus inactivated influenza vaccine in infants and young children. *New England Journal of Medicine* 356(7): 685-96. <http://www.ncbi.nlm.nih.gov/sites/entrez/17301299>
- 2 - Ashkenazi S, Vertruyen A, Aristegui J et al. (2006) Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections. *The Pediatric Infectious Disease Journal* 25(10): 870-9. <http://www.ncbi.nlm.nih.gov/sites/entrez/17006279>
- 3 - Fleming DM, Crovari P, Wahn U et al. (2006) Comparison of the efficacy and safety of live attenuated cold-adapted influenza vaccine, trivalent, with trivalent inactivated influenza virus vaccine in children and adolescents with asthma. *The Pediatric Infectious Disease Journal* 25(10): 860-9. <http://www.ncbi.nlm.nih.gov/sites/entrez/17006278>
- 4 - Immunisation against infectious disease ('the Green Book') Chapter 19 'Influenza'. Available at: <https://www.gov.uk/government/organisations/public-health-england/series/immunisation-against-infectious-disease-the-green-book>

Inactivated flu vaccines

- a number of different manufacturers produce flu vaccines. Those available for 2018/19 season are listed in Scottish [CMO letter](#)
- inactivated influenza vaccines are administered by intramuscular injection
- all currently available flu vaccines are prepared from viruses grown in embryonated hens' eggs, low egg/albumin content vaccine is available
- Some flu vaccines are restricted for use in particular age groups
- **The SPC for individual products should always be referred to when ordering vaccines for particular patients**

All but one of the flu vaccines available in the UK are inactivated, do not contain live viruses and cannot cause clinical influenza in those that can be vaccinated. Inactivated vaccines are administered by intramuscular injection. The currently available flu vaccines are prepared from viruses grown in embryonated hens eggs. The flu vaccines available in the UK for the 2018/19 flu season are listed in the Scottish CMO letter 2018/19.

Adjuvanted influenza vaccine (aTIV)

- during 2018/19, an adjuvanted trivalent influenza vaccine (aTIV) is recommended for use in those aged 75 years and over
- this recommendation was made following a PHE analysis which showed that the non-adjuvanted inactivated vaccine showed no significant effectiveness in this age group over recent seasons
- a sub optimal response to influenza vaccine in those aged 65 years and over is due to their aging immune system
- Adjuvants are added to vaccines to enhance the immune response
- Using an adjuvanted vaccine should improve protection against flu in elderly people
- aTIV (Fluad®) was licenced in the UK in 2017 and has been used for 20 years, is now used in over 20 countries and over 93 million doses have been distributed.
- Fluad® has been proven to be safe and effective
- Due to the MF59 adjuvant, a higher incidence of mild post-immunisation reactions has been reported with Fluad®, compared to non-adjuvanted influenza vaccines

Courtesy of PHE

The adjuvant in aTIV

- Adjuvanted vaccines are vaccines which have had a very small amount of a substance added to them to help create a stronger immune response to that vaccine
- Most inactivated vaccines contain an adjuvant -TIV contains MF59 adjuvant
- MF59 adjuvant is an oil-in-water emulsion of squalene oil which is a naturally occurring substance that is found 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 Fludax[®] contains less than 10mg. 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

Courtesy of PHE