Immunisation Advisory Centre

VERSION 6

Cell-based influenza vaccines

Most inactivated influenza vaccines are produced by growing the virus in eggs. This factsheet provides information on an alternative vaccine which involves growing the influenza virus in cultured mammalian cells.

2026 Available influenza vaccines

Trade name	Age group
Inactivated influenza vaccine, Surface antigen, Egg-based	
INFLUVAC TETRA	6 months and over
Inactivated influenza vaccine, Split virion, Egg-based	
FLUZONE	6 months and over
Inactivated influenza vaccine, Surface antigen, Adjuvanted, Egg-based	
FLUAD	50 years and over
Inactivated influenza vaccine, Surface antigen, Cell-based	
FLUCELVAX	6 months and over

'Drift' and 'shift'

In nature, influenza viruses continuously mutate and can change in two different ways – antigenic 'drift' and 'shift'. These genetic mutations impact the way an influenza virus can transmit in populations and can impact the effectiveness of seasonal influenza vaccines.

Antigenic shift is a major change in influenza A virus. This can occur when two or more strains of the virus combine into a new subtype.

Antigenic drift consists of small mutations in the influenza virus genes over time. These mutations cause changes in the surface proteins of the virus, HA (haemagglutinin) and NA (neuraminidase). Antigenic drift is responsible for annual outbreaks and epidemics of influenza.

Vaccine mismatches

As the influenza virus continues to mutate over time, vaccine production must take this into account and adjust the virus strains for the following influenza season. However, predicting and matching the exact influenza strains is an imperfect science, and vaccines that are developed are not always a perfect match for the circulating virus, sometimes resulting in a reduction in vaccine effectiveness.

An 'antigenic mismatch' is thought to contribute to lower effectiveness, particularly during years when A/H3N2 is the dominant influenza strain.

Egg-based manufacture

Egg-based influenza vaccine manufacture is a well-established process, with chicken eggs being the preferred medium to grow viruses since the 1950s.

Virus mutations occur not only in nature but can also occur during the replication process in egg-based influenza vaccine manufacture.

Additionally, influenza strains often do not replicate well in chicken eggs and selective pressure can lead to binding site mutations – this process is referred to as 'egg adaptation'.[1] This adaptation may reduce vaccine effectiveness by as much as 16%.[2]

Cell-based manufacture

To manufacture cell-based influenza vaccines, the vaccine viruses are grown in mammalian cell-line cultures. This eliminates the requirement for chicken eggs and can be advantageous in scenarios where egg-based production faces challenges, such as poor antigenic match due to mutations in the circulating seasonal influenza virus, or egg adaptation.

Benefits of cell-based vaccines

An advantage of cell-based vaccine production is that large quantities of virus can be produced more rapidly and less resource intensively than for egg manufacture. This is beneficial for potential future influenza pandemics.

As cell-based vaccine production avoids the risk of egg adaptation, this may lead to improved vaccine effectiveness due to the vaccines matching the circulating influenza virus more accurately.

Benefits of influenza vaccines vary from season to season and by age group and other factors, such as co-morbidities. It is estimated that small improvements in influenza vaccine effectiveness can lead to significant reductions in the burden of disease.

Efficacy and effectiveness

No randomised controlled trials have directly compared the efficacy of egg-based and cell-based vaccines, but a number of other types of trials have been performed.

Some studies have shown that cell-based vaccines, such as Flucelvax, have been more effective at preventing illness or inducing an immune response in comparison to standard egg-based vaccines during certain seasons. Of these comparative studies, cell-based advantage is more pronounced during seasons when there are substantial variations between the egg- based vaccine strains and the influenza strains circulating in the population.

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The effectiveness of cell-based influenza vaccine is equivalent to or moderately superior to egg-based vaccines in children and adults aged 4 to 64 years.

A recent review evaluating the effectiveness of seasonal cell-based quadrivalent influenza vaccine (QIVc) compared to quadrivalent and trivalent egg-based influenza vaccines found an overall pooled relative vaccine effectiveness (rVE) of 8.4% (95% CI, 6.5–10.2).[3]

A retrospective analysis (conducted by Seqirus) of 106,779 individuals during the 2023/2024 influenza season in the US found that the overall vaccine effectiveness QIVc was approximately 20% higher than that of QIVe against symptomatic, test-confirmed influenza in individuals aged 6 months to 64 years.[4] With this improved effectiveness, QIVc could avert more symptomatic illness and hospitalisation than egg-based IIV. Notably, the study provided evidence of improved effectiveness for QIVc in the paediatric population from 6 months of age.

Studies examining cell-based effectiveness in preventing influenza-related medical encounters found that cell-based influenza vaccines often had a higher rVE in age groups from 4 years to 64 years.[5-9] However, the range of effectiveness fluctuated depending on the dominant circulating virus strains and levels of drift or egg-adaptation. In two studies, rVE estimates favoured egg-based vaccines over cell-based vaccines for those aged over 65 years.

Another study found no significant difference in effectiveness between cell or egg-based influenza vaccines against influenza-related medical encounters or PCR-confirmed influenza hospitalisations in adults aged over 65 years during the 2022/23 season.[10] Both egg-based and cell-based influenza vaccines effectively prevent severe disease and hospitalisations. Although certain studies indicate modest improvements for cell-based vaccines, the margin of efficacy against egg-based vaccines fluctuates across seasons.

Who may be interested in cell-based vaccines?

Individuals with ethical concerns, particularly those sensitive to environmental impact, may opt for cell-based influenza vaccines over egg-based alternatives.

A traditional egg-based influenza vaccine manufacturing facility is capable of processing up to 600,000 eggs per day.[12]

Who cannot receive the influenza cell-based vaccine, Flucelvax?

Flucelvax is contraindicated for individuals who have had documented anaphylaxis to any ingredient in the vaccine or a to a previous dose of any influenza vaccine.

Cell-based influenza vaccines have a similar safety profile to standard influenza vaccines.

Injection-site reactions and systemic reactions occurred slightly more frequently in children aged 4-17 years after cell-based vaccine compared with standard vaccine (53% vs 43% and 37% vs 30%, respectively).[13] These were typically mild to moderate, with <1% reported as severe.

In adults aged 18-60 years, the rate of local and systemic reactions (reported by ~25% of recipients) were similar for both vaccine types.[14]

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