Immunisation Advisory Centre

VERSION 4

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.

2024 Available Influenza Vaccines

Tradename	Age Group
Inactivated Influenza Vaccine, Surface Antigen, Egg-Based	
INFLUVAC TETRA	6 months and over
Inactivated Influenza Vaccine, Split Virion, Egg-Based	
FLUQUADRI	6 months and over
AFLURIA QUAD	3 years and over
Inactivated Influenza Vaccine, Surface Antigen, Adjuvanted, Egg-Based	
FLUAD QUAD	65 years and over
Inactivated Influenza Vaccine, Surface Antigen, Cell-Based	
FLUCELVAX QUAD	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 an influenza A virus. This occurs 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 (hemagglutinin) and NA (neuraminidase). Antigenic drift is responsible for annual outbreaks and epidemics of influenza.

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

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.

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 the years when A/H3N2 was the dominant influenza strain.

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

A cell-based influenza vaccine does not require chicken eggs during manufacture, as the vaccine viruses are grown using mammalian cell cultures.

Replication via cell-line 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.

Efficacy and effectiveness

There are no randomised trials comparing 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.

A recent review evaluating the effectiveness of seasonal cell-based quadrivalent influenza vaccine 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]

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,[4-8] 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.

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.

Currently, there is limited data using test-confirmed influenza outcomes. Further studies on cell-based vaccine effectiveness are expected to be released in 2024.

Benefits of cell-based vaccines

The accelerated production speed of cell-based vaccines and higher yield of end-product can lead to faster manufacture times. This may be beneficial for future potential flu 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 comorbidities. It is estimated that small improvements in influenza vaccine effectiveness can lead to significant reductions in the burden of disease.

Mathematical modelling in the US has estimated that a 5% absolute increase in vaccine effectiveness would prevent more than 1,000,000 influenza cases and 25,000 hospitalisations in those aged above 65 years, and 785,000 influenza cases and 11,000 fewer hospitalisations in adults aged 18–64 years.[12]

The benefit of improved vaccine effectiveness is greatest in those aged ≥65 years, while improvements in coverage have a greater impact in age groups ≤65 years.

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.[9]

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

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

Cell-based influenza vaccine safety

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

In one study among children aged 4–17 years, injection site reactions were reported in 53% of cell-based vaccine recipients compared to 43% standard influenza vaccine recipients. Systemic reactions were reported by 37% and 30% respectively.[10] Both injection site and systemic responses were typically mild to moderate, with < 1% reported as severe.

In adults aged 18–60 years, injection site reactions were reported in 29% cell-based vaccine recipients and 25% of standard vaccine recipients.[11] Systemic reactions were reported by 25% and 23%, respectively. No severe systemic reactions were reported for this age group in this study.