FLUCELVAX® QUAD

Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures)

INDICATED IN ADULTS AND CHILDREN 6 MONTHS AND OLDER

FLUCELVAX® QUAD is a quadrivalent inactivated vaccine indicated for active immunization of adults and children aged 6 months or older for the prevention of influenza disease caused by influenza virus subtypes A and types B contained in the vaccine.

The National Advisory Committee on Immunization (NACI) provides additional guidance on the use of the influenza vaccine in Canada. Please refer to the published Statement on Seasonal Influenza Vaccine for the current season.

The first influenza vaccine available in Canada made using cell-based manufacturing[1,2†]

FLUCELVAX® QUAD vaccine is made by propagating cell-derived candidate vaccine viruses (CVV) in a continuous line of cells.[1‡§]

† Comparative clinical significance has not been established.
‡ Clinical significance has not been established.
§ FLUCELVAX® QUAD is a subunit influenza vaccine manufactured using CVV that are propagated in Madin Darby Canine Kidney (MDCK) cells, a continuous cell line. These cells were adapted to grow freely in suspension in culture medium. Each of the 4 virus strains is produced and purified separately then pooled to formulate the quadrivalent vaccine.

CSL Seqirus

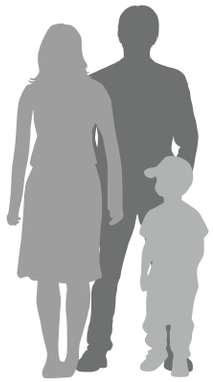
FLUCELVAX® QUAD
Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures)

INFLUENZA HAS IMPACTED THE LIVES OF MANY CANADIANS

INFLUENZA HAS BEEN REPORTED TO HAVE A HIGH BURDEN OF DISEASE†

INFLUENZA-RELATED HOSPITALIZATION AND MORTALITY IN CANADA[3†]
Estimated averages per year

12,200
Hospitalizations
Influenza-related all age groups



3,500
Deaths
Influenza-related all age groups

† FLUCELVAX® QUAD is not indicated to reduce hospitalization, mortality or the burden of influenza.

SEVERAL FACTORS IMPACT SEASONAL INFLUENZA VACCINES

Vaccination rates[4‡]

Age and health of the recipient[5]

Prior influenza exposure and vaccination history[5]

Types and subtypes of circulating influenza viruses[5]

Antigenic mismatch

Through antigenic drift[5,6,7]

Influenza viruses may change genetically from the time the vaccine virus is chosen for the current season to the time when influenza vaccines become widely available.

‡ According to PHAC data (2017-2018), the most common reason for non-vaccination was the perception that the vaccine was not necessary or not needed (22.4%).[4]

STRAIN MISMATCH

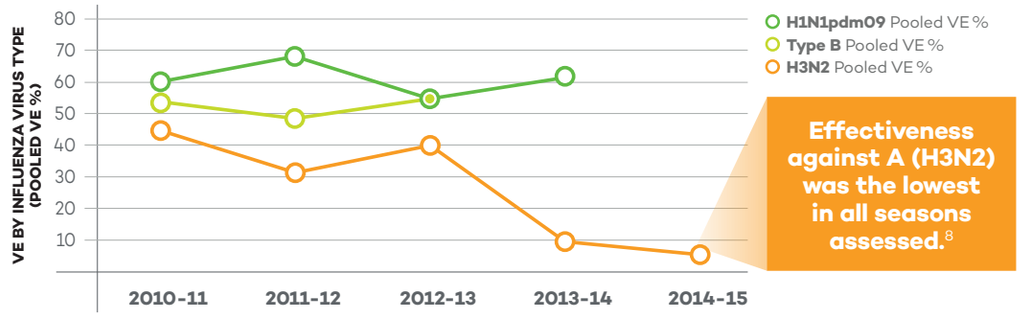
ANTIGENIC DRIFT AND STRAIN MISMATCH[5,7]

- Over time, antigenic variation (antigenic drift) of strains occurs within an influenza A subtype or B lineage.
- The ever-present possibility of antigenic drift requires seasonal influenza vaccines to be reformulated annually.
- Antigenic drift may occur in one or more influenza virus strains and can lead to strain mismatch.

STRAIN MISMATCH IS ONE OF SEVERAL FACTORS THAT HAS IMPACTED VACCINE EFFECTIVENESS

Year-to-year variation of vaccine effectiveness (VE) shown – international meta-analysis[8§]

POOLED VE ESTIMATES BY SEASON

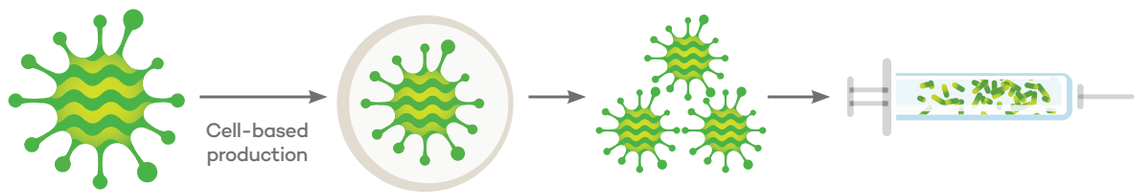


Adapted from Belongia *et al.*[8]

§ Meta-analysis based on search of PubMed and Embase from Jan 1, 2004, to March 31, 2015. 56 studies from Europe, North America (Canada and US), Australia, Asia and Africa were included.

CELL-BASED MANUFACTURING FOR SEASONAL INFLUENZA VACCINES¶

Cell-based manufacturing refers to how the flu vaccine is made. Influenza viruses used in the cell-based vaccine are grown in cultured mammalian cells.[9]



Adapted from the WHO and CDC[9-11]

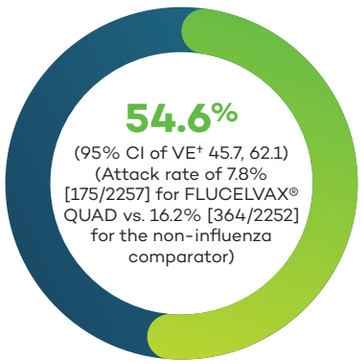
Cell-based technology allows for cell banking which assures an adequate supply of cells is readily available for vaccine production.[9]

¶ Clinical significance has not been established.

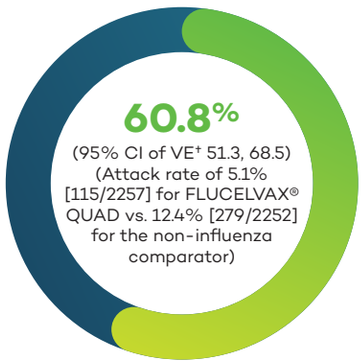
FLUCELVAX® QUAD

A vaccine to help prevent seasonal influenza in children 6 months to <18 years of age

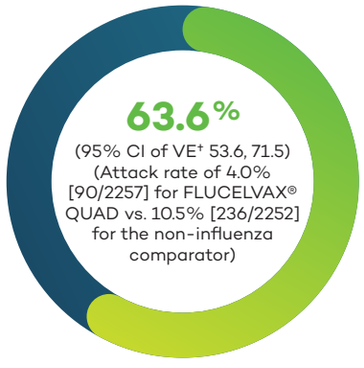
DEMONSTRATED EFFICACY OF FLUCELVAX® QUAD AGAINST FIRST OCCURRENCE OF RT-PCR OR CULTURE-CONFIRMED INFLUENZA[1*]



EFFICACY AGAINST ALL RT-PCR OR CULTURE-CONFIRMED INFLUENZA STRAINS



EFFICACY AGAINST ALL CULTURE-CONFIRMED INFLUENZA STRAINS



EFFICACY AGAINST ALL ANTIGENICALLY MATCHED CULTURE-CONFIRMED INFLUENZA

Adapted from the FLUCELVAX® QUAD Product Monograph[1]

* Comparative clinical significance has not been established.
† CIs for all endpoints have not been adjusted for multiplicity.

VACCINE EFFICACY OF FLUCELVAX® QUAD AGAINST RT-PCR CONFIRMED OR CULTURE-CONFIRMED INFLUENZA BY INFLUENZA VIRAL SUBTYPE IN SUBJECTS 2 YEARS TO LESS THAN 18 YEARS OF AGE.[a†]*

	FLUCELVAX® QUAD (N=2257)		NON-INFLUENZA COMPARATOR (N=2252)		VACCINE EFFICACY[b,c]	
	Attack Rate (%)	Number of Subjects with Influenza	Attack Rate (%)	Number of Subjects with Influenza	VE %	95% Confidence Interval[d]
RT-PCR or Culture Confirmed Influenza						
A/H1N1	0.9	21	4.7	105	80.7	69.2, 87.9
A/H3N2	2.7	60	4.5	102	42.1	20.3, 57.9
Type B	3.6	81	6.7	150	47.6	31.4, 60.0

Adapted from the FLUCELVAX QUAD Product Monograph[1]

a. Number of subjects in the Full-Analysis Set (FAS) – Efficacy, which included all subjects randomized, received a study vaccination and provided efficacy data.
b. Efficacy against influenza was evaluated over three influenza seasons, SH 2017, NH 2017/2018 and NH 2018/2019.
c. The efficacy of FLUCELVAX® QUAD was calculated using a time-to-event methodology based on a Cox proportional hazard model adjusted for age, country, influenza vaccination history, and season. Confidence intervals for all endpoints have not been adjusted for multiplicity.
d. Vaccine efficacy criteria were not pre-specified in the protocol for individual virus subtypes.

* Multinational, randomized, non-influenza vaccine comparator-controlled efficacy, immunogenicity and safety study conducted in 8 countries during the following 3 influenza seasons: Southern Hemisphere 2017, Northern Hemisphere 2017/2018 and Northern Hemisphere 2018/2019. Subjects who received either FLUCELVAX® QUAD (N=2257) or a non-influenza vaccine comparator vaccine (N=2252). Patients received a dose of 0.5 mL IM (previously unvaccinated subjects <9 years of age received a second dose after 4 weeks). FLUCELVAX® QUAD efficacy was assessed by the prevention of confirmed influenza illness caused by any influenza Type A or B strain. Influenza cases were identified by active and passive surveillance of influenza-like illness (ILI) and confirmed by cell culture and/or real-time polymerase chain reaction (RT-PCR). ILI was defined as a fever (oral temperature ≥100.0°F/37.8°C) along with any of the following: cough, sore throat, nasal congestion, or rhinorrhea. Overall vaccine efficacy against all influenza viral subtypes and against individual influenza viral subtypes were calculated.
† The predefined success criterion was defined as the lower limit of the two-sided 95% CI of absolute vaccine efficacy greater than 20%.

CONSIDER THE IMMUNOGENICITY DATA

FLUCELVAX® QUAD (Influenza Vaccine) was demonstrated noninferior to trivalent FLUCELVAX®¶ (Influenza Vaccine) based on data from two studies demonstrating immunogenicity and seroconversion at 3 weeks following vaccination in patients ≥18 years of age (Study 1‡) and in patients 4-<18 years of age (Study 2§).[1]

IMMUNOGENICITY ENDPOINTS

Studies 1 and 2:

The geometric mean antibody titers (GMTs) of HI antibodies response and percentage of subjects who achieved seroconversions.[1]

In both Study 1 and 2:[1,12]

- Seroconversions were defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or with a pre-vaccination HI titer ≥10 and a minimum 4-fold increase in serum HI antibody titer.
- Noninferiority criteria for GMT was defined as the upper bound of the 2-sided 95% CI for the ratio of GMTs (GMT TIV1c of TIV2c/GMT QIVc) for HI antibody should not exceed the noninferiority margin of 1.5.
- Noninferiority criteria for seroconversion was defined as the upper bound of the 2-sided 95% CI for the difference between seroconversion rates (% seroconversion TIV1c or TIV2c - % seroconversion QIVc) for HI antibody should not exceed the margin of 10%.

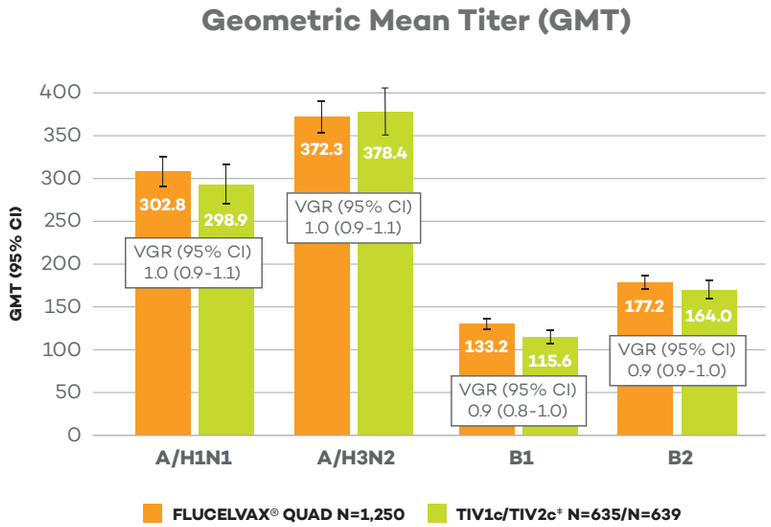
¶ Trivalent FLUCELVAX® is not available in Canada.

‡ Immunogenicity of FLUCELVAX® QUAD was evaluated in adults 18 years of age and older in a randomized, double-blind, controlled study conducted in the US (Study 1). In this study, subjects received FLUCELVAX® QUAD or one of the two formulations of comparator trivalent influenza vaccine (FLUCELVAX® QUAD N=1334, TIV1c N=677 or TIV2c N=669), each containing an influenza type B virus that corresponded to one of the two B viruses in QIV (a type B virus of the Massachusetts lineage [TIV1c] or a type B virus of the Brisbane lineage [TIV2c]), respectively, and the same influenza A subtype viruses.

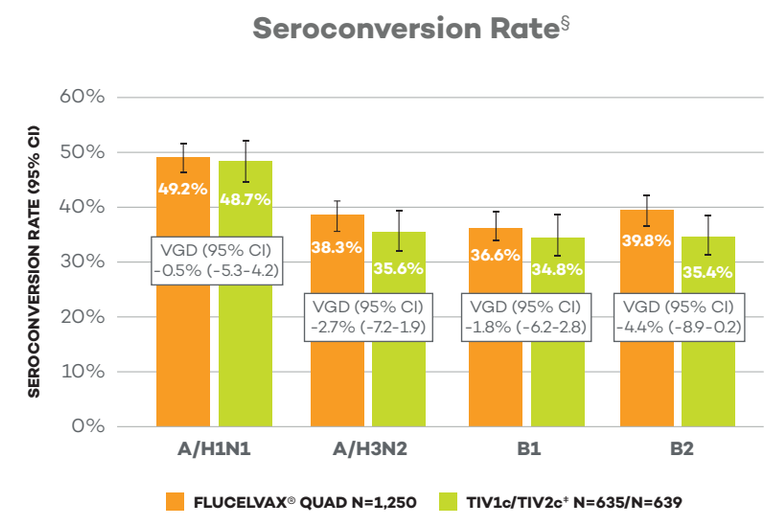
§ Immunogenicity of FLUCELVAX® QUAD was evaluated in children 9 to less than 18 years of age as part of a randomized, double-blind, controlled study conducted in the pediatric population 4 to less than 18 years of age in the US (Study 2). Enrolled subjects were first split into age cohorts based on age at time of enrollment (at least 4 to less than 9 years of age and at least 9 to less than 18 years of age). In this study, subjects received FLUCELVAX® QUAD or one of the two formulations of comparator trivalent influenza vaccine (FLUCELVAX® QUAD N=1159, TIV1c N=593 or TIV2c N=580).

DEMONSTRATED IN STUDY 1: NONINFERIORITY OF FLUCELVAX® QUAD RELATIVE TO TRIVALENT INFLUENZA VACCINE IN ADULTS ≥18 YEARS OF AGE, PER PROTOCOL ANALYSIS SET†

DATA FROM NON-INFERIORITY TRIAL:



Adapted from the FLUCELVAX® QUAD Product Monograph[1]



Adapted from the FLUCELVAX® QUAD Product Monograph[1]

VGR=vaccine group ratio; VGD=vaccine group difference

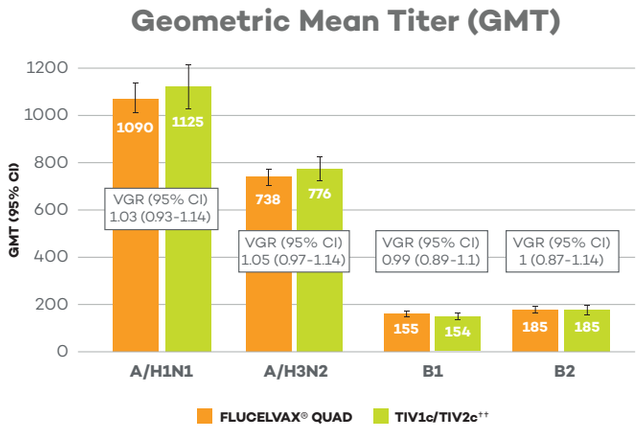
† The per protocol (PP) analysis set is defined as all subjects in the FAS Immunogenicity who correctly received the vaccine (i.e., received the vaccine to which the subjects are randomized and at the scheduled time points), had no major protocol deviations leading to exclusion as defined prior to unblinding/analysis and are not excluded due to other reasons defined prior to unblinding or analysis. PP population: 85 (6.4%), 41 (6.1%) and 31 (4.5%) enrolled subjects were excluded for QIVc, TIV1c and TIV2c groups, respectively.

‡ The comparator vaccine for noninferiority comparisons for A/H1N1, A/H3N2 and B1 is TIV1c, for B2 it is TIV2c.

§ Seroconversion rate = percentage of subjects with either a prevaccination HI titer <1:10 and postvaccination HI titer ≥1:40 or with a prevaccination HI titer ≥1:10 and a minimum 4-fold increase in postvaccination HI antibody titer.

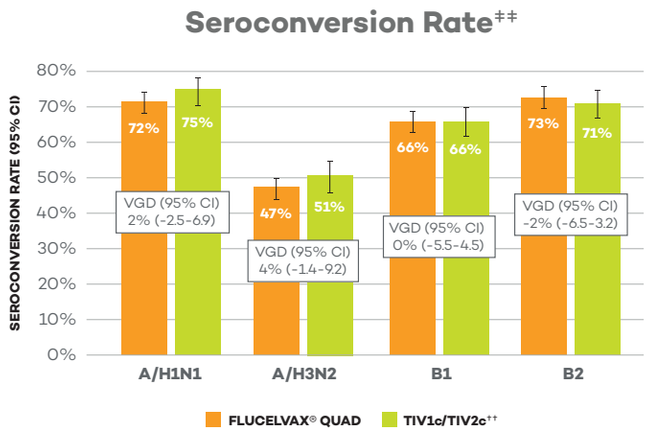
DEMONSTRATED IN STUDY 2: NONINFERIORITY¶ OF FLUCELVAX® QUAD RELATIVE TO TRIVALENT INFLUENZA VACCINE IN CHILDREN AND ADOLESCENTS 4 TO LESS THAN 18 YEARS OF AGE, PER PROTOCOL ANALYSIS SET

DATA FROM NON-INFERIORITY TRIAL:



FLUCELVAX® QUAD	N=1014	N=1013	N=1013	N=1009
TIV1c/TIV2c	N=510	N=510	N=510	N=510

Adapted from the FLUCELVAX® QUAD Product Monograph[1]



FLUCELVAX® QUAD	N=1014	N=1013	N=1013	N=1009
TIV1c/TIV2c	N=510	N=510	N=510	N=510

Adapted from the FLUCELVAX® QUAD Product Monograph[1]

CI = confidence interval; GR=vaccine group ratio; VGD=vaccine group difference
¶ Analyses are performed on data for day 22 for previously vaccinated subjects and day 50 for not previously vaccinated subjects.
†† The comparator vaccine for noninferiority comparisons for A/H1N1, A/H3N2 and B1 is TIV1c, for the B2 strain the comparator vaccine is TIV2c.
‡‡ Seroconversion rate = percentage of subjects with either a prevaccination HI titer <1:10 and postvaccination HI titer ≥1:40 or with a prevaccination HI titer ≥1:10 and a minimum 4-fold increase in postvaccination HI antibody titer. The definition of the PP analysis set in study V130_03 is the same as in V130_01, see the table for the adult population above. PP population: 145 (12.5%), 83 (14.0%) and 79 (13.6%) enrolled subjects were excluded for QIVc, TIV1c and TIV2c groups, respectively.

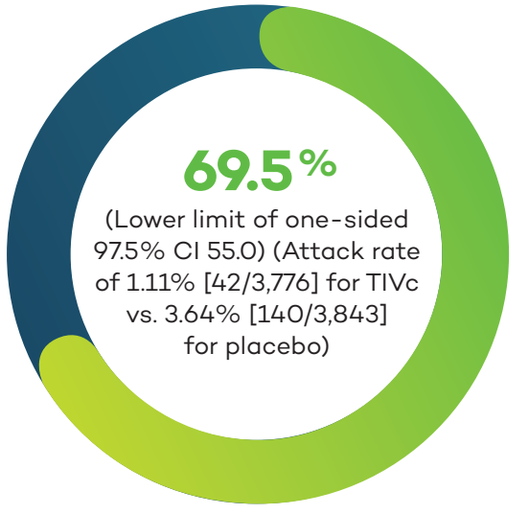
CONSIDER THE DATA FOR TRIVALENT FLUCELVAX® IN ADULTS.

THIS DATA IS RELEVANT AND CAN BE CONSIDERED FOR FLUCELVAX® QUAD.

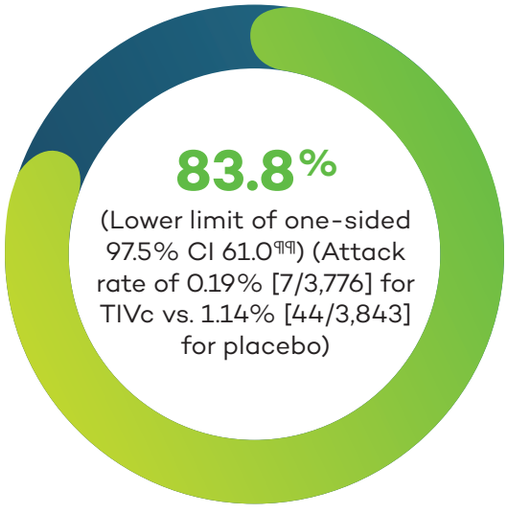
DEMONSTRATED EFFICACY OF TRIVALENT FLUCELVAX® AGAINST CULTURE-CONFIRMED INFLUENZA[1§§]

The efficacy data of trivalent FLUCELVAX® are relevant to FLUCELVAX® QUAD, as both vaccines are manufactured using the same process and have overlapping compositions. Vaccine efficacy was assessed by the prevention of culture-confirmed symptomatic influenza illness caused by viruses antigenically matched to those in the vaccine compared to placebo.[1]

There are no efficacy data demonstrating prevention of influenza disease after vaccination with FLUCELVAX® in the pediatric age group.[1]



EFFICACY††† AGAINST ALL CULTURE-CONFIRMED INFLUENZA STRAINS



EFFICACY††† AGAINST ANTIGENICALLY MATCHED CULTURE-CONFIRMED INFLUENZA STRAINS

Adapted from the FLUCELVAX® QUAD Product Monograph[1]

CI = confidence interval
§§ In a multinational, randomized, observer-blind, placebo-controlled trial, the clinical efficacy and safety of trivalent FLUCELVAX® was assessed during the 2007-2008 influenza season in adults aged 18 through 49 years. A total of 11,404 subjects were enrolled to receive FLUCELVAX® (n=3,828), AGRIFLU® (n=3,676), or placebo (n=3,900) in a 1:1:1 ratio.
¶¶ Simultaneous one-sided 97.5% confidence intervals for the vaccine efficacy of each influenza vaccine relative to placebo based on the Sidak-corrected score confidence intervals for the two relative risks. Vaccine Efficacy = (1 - Relative Risk) x 100%.
††† Vaccine Efficacy: Each vaccine was considered statistically compliant with the May 2007 CBER guidance for industry criteria for estimating VE against placebo if the lower limit of the one-sided simultaneous 97.5% Confidence Interval (CI) for the estimate of VE relative to placebo was greater than 40%.

THE MOST COMMON (≥10%) LOCAL AND SYSTEMIC REACTIONS:[1]

Adults – Study 1

In adults 18 to <65 years of age were injection-site pain (45%), headache (19%), fatigue (18%), myalgia (15%), injection-site erythema (13%), induration (12%) and nausea (10%).

In adults ≥65 years of age were injection-site pain (22%) and injection-site erythema (12%).

Pediatric – Studies 2 and 3

In Study 2, the most common (≥10%) local and systemic adverse reactions in children and adolescents 9 to less than 18 years of age were pain at the injection site (58%), headache (22%), injection-site erythema (19%), fatigue (18%), myalgia (16%) and injection-site induration (15%).

In Study 3, the most common (≥10%) local and systemic adverse reactions:

- in children 2 to less than 6 years of age were injection-site tenderness (29%), injection-site erythema (20%), sleepiness (15%), irritability (14%) and injection-site induration (14%).
- in children 6 to less than 9 years of age were injection-site pain (28%), injection-site erythema (22%), injection-site induration (16%), fatigue (14%), headache (14%), injection-site ecchymosis (11%) and loss of appetite (11%).
- in children and adolescents 9 to less than 18 years of age were injection-site pain (22%), headache (18%), injection-site erythema (17%), fatigue (17%) and injection-site induration (11%).

WHAT DO I NEED TO CONSIDER IF MY PATIENT IS ALLERGIC TO EGG OR CHICKEN PROTEIN?†

FLUCELVAX® QUAD is prepared in cell culture. Eggs are not used in the manufacturing process; therefore, FLUCELVAX® QUAD does not contain egg protein.[1†]

† Clinical significance has not been established.

Relevant warnings and precautions:

- As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event
- Postpone in patients with febrile illness
- Clinically significant bleeding disorders
- Endogenous or iatrogenic immunosuppression
- Guillain-Barré syndrome
- Syncope, presyncope
- Pregnant and nursing women
- A protective immune response may not be elicited in all vaccine recipients

For more information:

Please consult the Product Monograph at https://www.cslseqirus.ca/flucelvaxmonograph for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling us at 1-855-358-8966.

References:

1. FLUCELVAX® QUAD Product Monograph. Jan 23, 2023.
2. Data on file (1).
3. PHAC. An Advisory Committee Statement (ACS). National Advisory Committee on Immunization (NACI). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2020-2021.
4. PHAC. Seasonal influenza vaccine coverage in Canada, 2017-2018.
5. CDC. How Flu Vaccine Effectiveness and Efficacy is Measured Questions & Answers. https://www.cdc.gov/flu/vaccines work/effectivenessqa.htm (accessed Feb 1, 2020).
6. Government of Canada. Flu (influenza): For health professionals. https://www.canada.ca/en/public-health/services diseases/flu-influenza/health-professionals.html (accessed Feb 1, 2020).
7. CDC. Antigenic Characterization. https://www.cdc.gov/flu/about/professionals/antigenic.htm (accessed Oct. 20, 2020)
8. Belongia *et al*. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test negative design studies. *Lancet Infect Dis*. 2016;16(8):942-951.
9. CDC. Cell-Based Flu Vaccines. www.cdc.gov/flu/prevent/cell-based.htm (accessed Feb 1, 2020).
10. WHO. Biologicals – Influenza. https://www.who.int/biologicals/vaccines/influenza/en/ (accessed Feb 1, 2020).
11. CDC. How influenza (flu) vaccines are made. https://www.cdc.gov/flu/prevent/how-fluvaccine-made.htm (accessed Feb 1, 2020).
12. Data on file (2) (TIV1c/TIV2c).

FLUCELVAX® QUAD
Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures)

FLUCELVAX® QUAD

Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures)

FLUCELVAX® QUAD - INDICATED IN ADULTS AND CHILDREN AGED 6 MONTHS OR OLDER

FLUCELVAX® QUAD is a quadrivalent inactivated vaccine indicated for active immunization of adults and children aged 6 months or older for the prevention of influenza disease caused by influenza virus subtypes A and B contained in the vaccine.

The first influenza vaccine available in Canada made using cell-based manufacturing[1,2†]

Available as:[1]

- 0.5 mL suspension in pre-filled syringes (PFS) (type I glass) (needles not supplied)

FLUCELVAX® QUAD:

- Helps protect against 4 influenza strains[1†]
- Demonstrated safety profile
- Indicated in patients aged 6 months or older

Visit https://flucelvax.ca/hcp for even more information

Customer relations
1-844-392-8582
customerservice.ca@seqirus.com

Medical information
1-855-358-8966
ca.medicalinformation@seqirus.com

To order FLUCELVAX® QUAD
salescanada.ca@seqirus.com

FLUCELVAX® QUAD (6 months+)
DIN 02494248 **UPC** 818944020240

†Clinical significance has not been established.

CSL Seqirus

Seqirus Canada Inc.
Kirkland, Québec
https://www.cslseqirus.ca/
1.844.392.8582 514.221.4877

CAN-IV-23-0007

REVIEWED BY PAAB

FLUCELVAX® QUAD