PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

FLUCELVAX® QUAD

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

Suspension for Injection

Active Immunizing Agent for the Prevention of Influenza

ATC Code: J07BB02

2021/2022 strains

A/Wisconsin/588/2019 (H1N1)pdm09-like virus	15 micrograms HA
A/Cambodia/e0826360/2020 (H3N2)-like virus	15 micrograms HA
B/Washington/02/2019-like virus	15 micrograms HA
B/Phuket/3073/2013-like virus	15 micrograms HA

Sponsor:

Seqirus UK Limited

29 Market Street, Level 3

Maidenhead, Berkshire, UK

SL6 8AA

Distributed by:

Seqirus Canada Inc.

16766 TransCanada Highway, Suite 504

Kirkland, Québec

H9H 4M7

www.seqirus.ca

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RECENT MAJOR LABEL CHANGES

Indications, Pediatrics (1.1)	03/2021
Dosage and Administration, Recommended Dose (3.1)	03/2021

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

FLUCELVAX® QUAD is a quadrivalent inactivated vaccine indicated for active immunization of adults and children aged 2 years 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.

1.1 Pediatrics

Pediatrics (2 to < 18 years): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of FLUCELVAX® QUAD in pediatric patients has been established; therefore, Health Canada has authorized an indication for use in the pediatric population 2 years of age and older (see 8.2.1 ADVERSE REACTIONS, Clinical Trial Adverse Reactions - Pediatrics and 14 CLINICAL TRIALS).

2 CONTRAINDICATIONS

FLUCELVAX® QUAD is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose

The recommended dosage schedule for FLUCELVAX® QUAD is presented in Table 1.

Table 1: FLUCELVAX® QUAD Recommended Dosage, by Age Group

Age Group	Dose	Schedule
2 to < 9 years	One or two[a] 0.5 mL doses	If 2 doses, administer at least 4 weeks apart
≥ 9 years	One 0.5 mL dose	Not applicable

[a] Children less than 9 years of age who have not been previously vaccinated against influenza, should receive a second dose

4.4 Administration

The vaccine should be administered by intramuscular injection. The preferred site for intramuscular injection in older children and adults is the deltoid muscle of the upper arm. Younger children with insufficient deltoid mass should be vaccinated in the anterolateral aspect of the thigh.

Shake before use. After shaking, the normal appearance of the vaccine is a clear to slightly opalescent suspension.

Visually inspect the contents of each multi-dose vial or pre-filled syringe for particulate matter and/or variation in appearance prior to administration. If either condition exists, do not administer the

vaccine.

FLUCELVAX® QUAD must not be mixed with other products.

Multi-Dose Vial

Between uses, return the multi-dose vial to the recommended storage conditions.

Please refer to the Canadian Immunization Guide, Public Health Agency of Canada, for general information regarding vaccine administration practices.

5 OVERDOSAGE

There is no experience of overdose with FLUCELVAX® QUAD.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

Table 2: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular Injection	Pre-filled syringe/ Multi-dose vials Each 0.5 mL contains 15 mcg haemagglutinin (HA) of each influenza virus strain listed below	Excipients: Disodium phosphate dihydrate, Magnesium chloride hexahydrate, Potassium chloride, Potassium dihydrogen phosphate, Sodium chloride, Thimerosal*, Water for injections Residuals: beta-propiolactone, cetyltrimethylammonium bromide, polysorbate 80

*Multi-dose vials only

For the 2021/2022 Northern Hemisphere Influenza Season, FLUCELVAX® QUAD contains the following strains:

A/Wisconsin/588/2019 (H1N1)pdm09-like virus (A/Washington/19/2020 (H1N1))
A/Cambodia/e0826360/2020 (H3N2)-like virus (A/Tasmania/503/2020 (H3N2))
B/Washington/02/2019-like virus (B/Darwin/7/2019)
B/Phuket/3073/2013-like virus (B/Singapore/INFTT-16-0610/2016)

As recommended annually by the World Health Organization (WHO) and the National Advisory Committee on Immunization (NACI).

Packaging

FLUCELVAX® QUAD suspension for injection is supplied in two presentations:

- 0.5 mL suspension in needle-free pre-filled syringes (type I glass), with a plunger stopper (bromobutyl rubber) (needles not supplied)
- 5.0 mL multi-dose vial (type 1 glass), with rubber (bromobutyl) stopper

FLUCELVAX® QUAD 0.5 mL pre-filled syringes contain no preservative or antibiotics.

FLUCELVAX® QUAD 5 mL multi-dose vial formulation contains thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose from the multi-dose vial contains 25 mcg mercury. FLUCELVAX® QUAD 5 mL multi-dose vial formulation contains no antibiotics.

The tip caps and plungers of the pre-filled syringes and the multi-dose vial stopper are not made with natural rubber latex.

Both presentations of FLUCELVAX® QUAD are considered safe for use in persons with latex allergies.

7 WARNINGS AND PRECAUTIONS

General

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Immunization should be postponed in patients with febrile illness until the fever is resolved.

A protective immune response may not be elicited in all vaccine recipients.

Hematologic

As with other intramuscular injections, administration of FLUCELVAX® QUAD requires careful consideration in patients with clinically significant bleeding disorders.

Immune

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Neurologic

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUCELVAX® QUAD should be based on careful consideration of the potential benefits and risks.

Reproductive Health: Female and Male Potential

- **Fertility**

FLUCELVAX QUAD has not been evaluated for possible effect on fertility.

A reproductive and developmental toxicity study in female rabbits with a similar trivalent vaccine manufactured by Seqirus revealed no impairment of fertility.

7.1 Special Populations

7.1.1 Pregnant Women

Healthcare providers should assess the benefit and potential risks of administering the vaccine to pregnant women taking into consideration official recommendations.

The safety of FLUCELVAX® QUAD in pregnancy has not been assessed in clinical trials.

Reproductive and developmental toxicology data from trivalent influenza vaccines do not predict an increased risk of developmental abnormalities. See 16 NON-CLINICAL TOXICOLOGY.

Breast-feeding

FLUCELVAX® QUAD has not been evaluated in nursing mothers.

It is unknown if FLUCELVAX® QUAD is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

7.1.2 Pediatrics

Pediatrics (< 2 years): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for use in children less than 2 years of age.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Adverse event information is derived from clinical trials and worldwide post-marketing experience with FLUCELVAX® QUAD.

8.2 Clinical Trial Adverse Reactions (Adults)

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The safety of FLUCELVAX® QUAD in adults 18 years and older was evaluated in a randomized, double-blind, controlled study conducted in the U.S. (Study 1). The safety population included a total of 2680 adults 18 years of age and older: 1340 adults 18 to less than 65 years of age and 1340 adults 65 years of age and older.

In this study, subjects received FLUCELVAX® QUAD or one of the two formulations of comparator trivalent influenza vaccine (FLUCELVAX N=1334, TIV1c N=677 or TIV2c N=669). Solicited local injection site and systemic adverse reactions were collected from subjects who completed a symptom diary card for 7 days following vaccination.

Solicited adverse reactions in the safety population of adults 18 to less than 65 years of age and 65 years of age and older are shown in Table 3. Overall, the most common (≥10%) local and systemic reactions in adults 18 to less than 65 years of age were injection site pain (45%), headache (19%), fatigue (18%), myalgia (15%), injection site erythema (13%), induration (12%) and nausea (10%). The

most common (≥10%) local and systemic reactions in adults 65 years of age and older were injection site pain (22%) and injection site erythema (12%).

Table 3: Incidence of Solicited Adverse Reactions[1] in the Adult and Elderly Safety Population[2] Reported Within 7 Days of Vaccination (Study 1)

	Percentages of Subjects with Any (Severe) Solicited Reactions[3]					
	18 to less than 65 years of age			≥ 65 years of age		
	FLUCELVAX® QUAD N=663	Trivalent Influenza Vaccine		FLUCELVAX® QUAD N=656	Trivalent Influenza Vaccine	
		TIV1c N=330	TIV2c N=327		TIV1c N=340	TIV2c N=336
Local Adverse Reactions						
Injection site pain	45 (<1)	37 (<1)	41 (0)	22 (0)	19 (0)	19 (0)
Injection site erythema	13 (0)	13 (0)	10 (0)	12 (0)	11 (0)	10 (0)
Injection site induration	12 (0)	10 (<1)	10 (0)	9 (0)	7 (0)	8 (0)
Injection site ecchymosis	4 (0)	3 (<1)	5 (0)	5 (0)	4 (0)	5 (0)
Systemic Adverse Reactions						
Headache	19 (<1)	19 (<1)	19 (<1)	9 (<1)	9 (<1)	8 (<1)
Fatigue	18 (<1)	22 (<1)	16 (2)	9 (<1)	11 (<1)	9 (<1)
Myalgia	15 (<1)	15 (<1)	15 (1)	8 (<1)	9 (<1)	8 (<1)
Nausea	10 (<1)	7 (<1)	9 (1)	4 (<1)	4 (0)	4 (<1)
Arthralgia	8 (<1)	8 (0)	10 (<1)	6 (<1)	5 (<1)	7 (<1)
Loss of appetite	8 (<1)	9 (<1)	8 (<1)	4 (<1)	5 (0)	4 (<1)
Diarrhea	7 (<1)	8 (0)	8 (<1)	4 (<1)	5 (<1)	5 (<1)
Chills	6 (<1)	6 (<1)	6 (0)	4 (<1)	4 (<1)	5 (<1)
Vomiting	3 (0)	2 (<1)	<1(0)	<1 (<1)	<1 (0)	<1 (0)
Fever: ≥38.0 °C (≥40.0°C)	<1 (0)	<1 (0)	<1 (0)	<1 (0)	<1 (0)	<1 (0)

[1] All solicited local and systemic adverse events reported within 7 days of vaccination are included.

[2] Safety population: all subjects in the exposed population who provided post-vaccination safety data.

[3] Percentage of severe adverse reactions are presented in parenthesis.

Definition of severe reactions: Erythema, Induration and Ecchymosis: >100 mm; Pain, Chills, Nausea, Myalgia, Arthralgia, Headache, Fatigue, Loss of appetite; unable to perform daily activity, Vomiting: requires outpatient hydration; Diarrhea: 6 or more stools or requires outpatient IV hydration.

Unsolicited adverse events (AEs) were collected for 21 days after vaccination. Comparable percentages of unsolicited events were reported in subjects in the FLUCELVAX® QUAD, TIV1c and TIV2c groups, (16.1%, 14.7% and 16.5% respectively).

Serious adverse events (SAEs) were collected throughout the study duration (until 6 months after vaccination). Comparable percentages of SAEs were reported in subjects in the FLUCELVAX® QUAD, TIV1c and TIV2c groups, (3.9%, 3.3% and 3.2% respectively). No SAE was assessed as being related to study vaccines.

8.2.1 Clinical Trial Adverse Reactions (Pediatrics)

Children 2 to less than 18 years of age

The safety of FLUCELVAX® QUAD in children 2 to less than 18 years of age has been evaluated in two clinical studies, V130_03 (Study 2) and V130_12 (Study 3).

Study 2 was a randomized, double-blind, controlled study conducted in the U.S.. The safety population included a total of 2332 children 4 to less than 18 years of age; 1161 children 4 to less than 9 years of age and 1171 children 9 to less than 18 years of age.

In this study, subjects 9 to less than 18 years received a single dose of FLUCELVAX® QUAD or one of the two formulations of comparator trivalent influenza vaccine (FLUCELVAX® QUAD N=1159, TIV1c N=593 or TIV2c N= 580).

Solicited local injection site and systemic adverse reactions were collected from subjects who completed a symptom diary card for 7 days following vaccination. Solicited adverse reactions in the safety population of children 9 years to less than 18 years of age are shown in Table 4.

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%).

Table 4: Incidence of Solicited Adverse Reactions[1] in the Safety Population[2] of Children 9 to less than 18 years of age Reported After Any Dose Within 7 Days of Vaccination (Study 2)

	Children 9 to <18 years		
	Percentages of Subjects with Any (Severe) Solicited Reactions[3]		
	FLUCELVAX® QUAD N=579	Trivalent Influenza Vaccine	
		TIV1c N=294	TIV2c N=281-282[4]
Local Adverse Reactions			
Injection site pain	58 (1)	51 (<1)	50 (0)
Injection site erythema	19 (< 1)	1 7(0)	15 (< 1)
Injection site induration	15 (0)	15 (0)	13 (< 1)
Injection site ecchymosis	4 (0)	5 (0)	5 (0)
Systemic Adverse Reactions			
Headache	22 (1)	23 (2)	18 (1)
Fatigue	18 (< 1)	16 (1)	16 (< 1)
Myalgia	16 (< 1)	17(< 1)	15 (< 1)
Loss of appetite	9 (0)	9 (< 1)	9 (0)
Nausea	9 (< 1)	8 (1)	7 (1)
Fever: ≥38.0 °C (≥40.0 °C)	1 (< 1)	3 (0)	1 (0)
Arthralgia	6 (0)	6 (0)	8 (< 1)
Vomiting	2 (0)	1 (0)	2 (0)
Diarrhea	4 (0)	4 (0)	3 (< 1)
Chills	7 (0)	6 (1)	4 (1)

[1] All solicited local and systemic adverse events reported within 7 days of vaccination are included.
[2] Safety population: all subjects in the exposed population who provided post-vaccination safety data.
[3] Percentage of severe adverse reactions are presented in parenthesis.
Definition of severe reactions: Erythema, Induration and Ecchymosis: Severe= >100 mm; Pain and systemic adverse reactions: Severe = unable to perform daily activity.
[4] 281 subjects provided data for Injection site ecchymosis.

Unsolicited adverse events were collected for 21 days after last vaccination. Comparable percentages of unsolicited events were reported in children 9 through 17 years of age in the FLUCELVAX® QUAD, TIV1c and TIV2c groups, (37.2%, 36.7% and 39.8% respectively).

Serious adverse events (SAEs) were collected throughout the study duration (until 6 months after last vaccination). Comparable percentages of SAEs were reported in children 9 through 17 years of age in the FLUCELVAX® QUAD, TIV1c and TIV2c groups, (0.9%, 1.3% and 0% respectively). No SAE was assessed as being related to study vaccines.

Study 3 (V130_12) was a multi-season, multi-national, randomized, observer-blind study in children 2 to less than 18 years of age. The solicited safety population included a total of 4509 children who received FLUCELVAX® QUAD (N=2255) or a non-influenza vaccine comparator vaccine (N=2254). In this study, children 2 to less than 9 years of age received one or two doses (separated by 4 weeks) of FLUCELVAX® QUAD or comparator vaccine depending on the subject's prior influenza vaccination history. Children 9 to less than 18 years received a single dose of FLUCELVAX® QUAD or comparator vaccine.

In this study, solicited local injection site and systemic adverse reactions were collected from subjects who completed a symptom diary card for 7 days following vaccination.

In children 2 to less than 18 years of age who received FLUCELVAX® QUAD, the incidence of local and systemic solicited adverse reactions were similar to or less than those reported in Study 2.

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%).

The most common (≥10%) local and systemic adverse reactions 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%).

The most common (≥10%) local and systemic adverse reactions 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%).

In Study 3, in children who received two doses, the rates of solicited local and systemic adverse reactions was generally lower after the second dose compared to the first dose.

The incidence of local and systemic solicited adverse reactions in children 2 to less than 18 years of age who received FLUCELVAX® QUAD and comparator are summarized in Table 5.

Table 5: Incidence of Solicited Adverse Reactions in the Safety Population[1] (2 to less than 18 years of age) Reported After Any Dose Within 7 Days of Vaccination (Study 3)

	Children 2 to < 6 years		Children 6 to <9 years		Children 9 to <18 years	
	Percentages of Subjects with Any (Severe) Solicited Reactions[2]					
	FLUCELVAX® QUAD N=580	Comparator[3] N=565	FLUCELVAX® QUAD N=564	Comparator[3] N=578	FLUCELVAX® QUAD N=1111	Comparator[3] N=1111
Local Adverse Reactions						
Injection site pain/Tenderness	28.7 (1.0)	25.4 (1.4)	27.9 (1.2)	20.3 (1.6)	21.7 (0.5)	18.3 (1.0)
Injection site erythema	20.2 (0.3)	24.5 (1.8)	22.4 (0.4)	22.8 (0.3)	17.2 (0)	18.7 (0.5)
Injection site induration	13.5 (0.2)	13.9 (0.7)	16.3 (0.2)	16.5 (0.2)	10.5 (0.1)	11 (0.2)
Injection site ecchymosis	9.2 (0)	6.9 (0)	10.9 (0)	8.0 (0.2)	5.0 (0)	5.2 (0)
Systemic Adverse Reactions						
Sleepiness	14.9 (0.9)	17.6 (1.8)	-	-	-	-
Irritability	13.8 (0.2)	10.8 (0.5)	-	-	-	-
Fatigue	-	-	13.8 (0.9)	12.7 (0.7)	17 (1.1)	18.2 (1.2)
Headache	-	-	13.8 (0.4)	11.8 (0.5)	18.1 (1.4)	17.4 (0.6)
Loss of appetite	-	-	10.6 (0.5)	8.0 (0.5)	8.5 (0.5)	7.5 (0.5)
Change of eating habits	9.9 (1.0)	10.1 (0.7)	-	-	-	-
Fever: ≥38.0 °C (≥40.0 °C)	8.8 (0.5)	7.7 (0.4)	6.4 (0.5)	4.5 (0)	2.8 (0.1)	3.0 (0.3)
Diarrhoea	8.3 (0.5)	8.5 (0.9)	4.6 (0.4)	5.2 (0.3)	7.4 (0.5)	8.1 (0.3)
Arthralgia	-	-	5.2 (0.4)	6.2 (0.3)	7.1 (0.4)	8.4 (0.5)
Nausea	-	-	5.2 (0)	4.5 (0.7)	6.0 (0.2)	6.1 (0.6)
Vomiting	4.8 (0.5)	4.1 (0.7)	5.0 (0.7)	4.2 (0.5)	3.0 (0.3)	3.0 (0.4)
Chills/Shivering	4.7 (0.7)	3.9 (0.4)	6.1 (0.5)	3.8 (0.3)	7.6 (0.4)	7.6 (0.3)
Myalgia	-	-	2.9 (0.2)	4.0 (0.3)	6.1 (0.5)	5.5 (0.5)

[1] Solicited Safety Population: subjects who were vaccinated and provided any solicited local or systemic adverse event safety data, from 6 hours through 7 days after vaccination

[2] Percentage of subjects with severe adverse reactions are presented in parenthesis.

[3] Non-influenza vaccine comparator

Definitions of severe reactions (subjects 2 to < 6 years of age): Erythema, Induration and Ecchymosis: > 50 mm; Tenderness and Shivering: prevents daily activity; Change of eating habits: Missed more than 2 feeds/meals; Sleepiness: Sleeps most of the time and is hard to arouse him/her; Vomiting: 6 or more times in 24 hours or requires intravenous hydration; Diarrhea: 6 or more loose stools in 24 hours or requires intravenous hydration; Irritability: unable to console.

Definitions of severe reactions (subjects 6 to < 18 years of age): Erythema, Induration and Ecchymosis: > 100 mm; Loss of appetite: Not eating at all; Vomiting: 6 or more times in 24 hours or requires intravenous hydration; Diarrhea: 6 or more loose stools in 24 hours or requires intravenous hydration; Pain, Nausea, Fatigue, Myalgia, Arthralgia, Headache and Chills: prevents daily activity

"-" denotes reaction was not solicited in this age group

Study 3: NCT03165617

All unsolicited adverse events were collected for 21 days after last vaccination. Comparable percentages of unsolicited events were reported in children 2 to less than 18 years of age in the FLUCELVAX® QUAD and non-influenza comparator vaccine groups, (28.0% and 27.9%, respectively).

Serious adverse events (SAEs) were collected throughout the study duration (until 6 months after last vaccination). Comparable percentages of SAEs were reported in children 2 to less than 18 years of age in the FLUCELVAX® QUAD and non-influenza comparator vaccine groups (1.1 and 1.3% respectively). No SAE was assessed as being related to study vaccines.

8.3 Less Common Clinical Trial Adverse Reactions

See 8 ADVERSE REACTIONS, Clinical Trial Adverse Reactions.

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

See 8 ADVERSE REACTIONS, Clinical Trial Adverse Reactions.

8.5 Post-Market Adverse Reactions

The following events have been identified during post-approval use of FLUCELVAX® QUAD:

Immune system disorders: Allergic or immediate hypersensitivity reactions, including anaphylactic shock.

Nervous system disorders: paraesthesia.

Skin and subcutaneous tissue disorders: Generalized skin reactions including pruritus, urticaria, or non-specific rash.

General disorders and administration site conditions: Extensive swelling of injected limb.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Not applicable.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

There are no data available on co-administration of FLUCELVAX® QUAD with other vaccines.

If FLUCELVAX® QUAD is to be given at the same time as another injectable vaccine(s), the vaccine(s) should always be administered to separate limbs. It should be noted that adverse reactions may be intensified.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

FLUCELVAX® QUAD provides active immunization against four influenza virus strains (two A subtypes and two B types) contained in the vaccine. FLUCELVAX® QUAD induces humoral antibodies against the haemagglutinins. These antibodies neutralize influenza viruses.

Influenza illness and its complications follow infection with influenza viruses. Global surveillance and analysis of influenza virus isolates permits identification of yearly antigenic variants. Since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation. Specific levels of hemagglutination inhibition (HI) antibody titers post-vaccination with inactivated influenza virus vaccine have not been correlated with protection from influenza virus. In some human studies, antibody titers of 1:40 or greater have been associated with protection from influenza illness in up to 50% of subjects.

Antibody against one influenza virus type or subtype confers limited or no protection against another. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype. Frequent development of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the usual change of one or more strains in each year's influenza vaccine. Therefore, inactivated influenza vaccines are standardized to contain the hemagglutinin of influenza virus strains representing the influenza viruses likely to circulate in Canada in the upcoming winter on the basis of the recommendations from the World Health Organization (WHO) and the National Advisory Committee on Immunization (NACI).

10.2 Pharmacodynamics

Seroprotection is generally obtained within 3 weeks following vaccination.

Annual revaccination with the current vaccine is recommended because immunity declines during the year after vaccination and circulating strains of influenza virus change from year to year.

10.3 Pharmacokinetics

Duration of Effect: Protection against influenza post-vaccination is expected throughout the influenza season for which the vaccine is indicated.

11 STORAGE, STABILITY AND DISPOSAL

Store under refrigeration at 2° to 8°C. Do not freeze. Protect from exposure to light. Do not use after the expiration date. Any unused product or waste material should be disposed of in compliance with local requirements.

The multi-dose vial must be used within 28 days from removal of the first dose, and between uses, should be returned to the recommended storage conditions.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

For the 2021-2022 season, FLUCELVAX® QUAD contains:

Influenza virus surface antigens (haemagglutinin and neuraminidase)*, inactivated, of the following strains:

A/Wisconsin/588/2019 (H1N1)pdm09-like virus (A/Washington/19/2020 (H1N1))	15 micrograms HA**
A/Cambodia/e0826360/2020 (H3N2)-like virus (A/Tasmania/503/2020 (H3N2))	15 micrograms HA**
B/Washington/02/2019-like virus (B/Darwin/7/2019)	15 micrograms HA**
B/Phuket/3073/2013-like virus (B/Singapore/INFTT-16-0610/2016)	15 micrograms HA**

per 0.5 mL dose

* propagated in Madin Darby Canine Kidney (MDCK) cells

** haemagglutinin

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

Pharmaceutical standard: FLUCELVAX® QUAD is standardized according to recommendations from the World Health Organization (WHO) and National Advisory Committee on Immunization (NACI) for the Northern Hemisphere 2021 – 2022 season.

Product Characteristics:

FLUCELVAX® QUAD is a clear to slightly opalescent liquid.

FLUCELVAX® QUAD is a subunit influenza vaccine prepared from virus propagated in Madin Darby Canine Kidney (MDCK) cells, a continuous cell line. These cells were adapted to grow freely in suspension in culture medium. The virus is inactivated with beta-propiolactone, disrupted by the detergent cetyltrimethylammonium bromide and purified through several process steps. Each of the 4 virus strains is produced and purified separately then pooled to formulate the quadrivalent vaccine.

Eggs are not used in the manufacturing process, therefore, FLUCELVAX® QUAD does not contain egg protein.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Three randomized clinical trials (V130_01, V130_03 and V130_12) were conducted with FLUCELVAX® QUAD. Two safety and immunogenicity clinical trials (V130_01 and V130_03) were conducted in the United States with FLUCELVAX® QUAD, one in adults 18 years and older, and one in children 4 to less than 18 years of age. One safety, efficacy and immunogenicity clinical trial (V130_12) was conducted across geographical regions in children 2 to less than 18 years of age. One safety, efficacy and immunogenicity clinical trial (V58P13) was conducted with TIVc in adults 18 to less than 50 years of age. The trial designs and demographics of the randomized clinical trial are presented in Table 6.

Table 6: Summary of Trial Designs and Study Demographics for Clinical Trials with FLUCELVAX® QUAD and TIVc.

Study #	Trial design	Dosage, route of administration and duration	Study subjects (N)*	Mean age (Range)**	Sex**
1 (V130_01)	Randomized, double-blind, controlled study with FLUCELVAX® QUAD and two formulations of comparator trivalent influenza vaccine (TIV1c or TIV2c)	Single dose 0.5 mL IM	FLUCELVAX® QUAD=1335 TIV1c=676 TIV2c=669	57.4 years (18-96)	Male: 603 (45%) Female: 732 (55%)
2 (V130_03)	Randomized, double-blind, controlled study with FLUCELVAX® QUAD and two formulations of comparator trivalent influenza vaccine (TIV1c or TIV2c)	Single dose*** 0.5 mL IM	FLUCELVAX® QUAD=1159 TIV1c=593 TIV2c=581	9.5 years (4-17)	Male: 603 (52%) Female: 556 (48%)
3 (V130_12)	Randomized, observer-blind, controlled, multi-national study with FLUCELVAX® QUAD and non-influenza vaccine comparator	Single dose*** 0.5 mL IM	FLUCELVAX® QUAD=2258 Comparator = 2256	8.7 years (2-17)	Male: 1152 (51%) Female: 1106 (49%)
4 (V58P13)	Randomized, observer-blind, placebo-controlled, multicenter study with TIVc and egg-derived comparator influenza vaccine (TIVeA) and placebo	Single dose 0.5 mL IM	TIVc=3828 TIVeA=3676 PLACEBO=3900	32.7 years (18-49)	Male: 1740 (45%) Female: 2088 (55%)

*All randomized subjects.
** Age and gender data are presented only for subjects who received FLUCELVAX® QUAD in studies 1, 2 and 3 and TIVc in study 4.
***Previously unvaccinated subjects <9 years of age received a second dose after 4 weeks.
TIVeA = egg-based trivalent influenza vaccine (Agriflu)

14.2 Study Results

Efficacy against Culture-Confirmed Influenza in Adults 18 years of age and above

The efficacy experience with trivalent influenza vaccine (FLUCELVAX, TIVc) is relevant to FLUCELVAX® QUAD because both vaccines are manufactured using the same process and have overlapping compositions.

A multi-national (U.S., Finland and Poland), randomized, observer-blinded, placebo-controlled trial (Study 4) was performed to assess the clinical efficacy and safety of TIVc during the 2007-2008

influenza season in adults aged 18 to 49 years. A total of 11,404 subjects were enrolled to receive TIVc (N=3828), Agriflu (N=3676) or placebo (N=3900) in a 1:1:1 ratio. Among the overall study population enrolled, the mean age was 33 years, 55% were female, 84% were Caucasian, 7% were Black, 7% were Hispanic, and 2% were of other ethnic origin.

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. Influenza cases were identified by active and passive surveillance of influenza-like illness (ILI). ILI was defined according to Centers for Disease Control and Prevention (CDC) case definition, i.e., a fever (oral temperature ≥100.0°F / 38°C) and cough or sore throat. After an episode of ILI, nose and throat swab samples were collected for analysis. Vaccine efficacies against vaccine-matched influenza viral strains, against all influenza viral strains, and against individual influenza viral subtypes were calculated (Tables 7 and 8).

Table 7: Vaccine Efficacy against Culture-Confirmed Influenza

	Number of subjects per protocol[1]	Number of subjects with influenza	Attack Rate (%)	Vaccine Efficacy[2]	
				%	Lower Limit of One-Sided 97.5% CI
Antigenically Matched Strains					
TIVc	3776	7	0.19	83.8	61.0[3]
Placebo	3843	44	1.14	--	--
All Culture-Confirmed Influenza					
TIVc	3776	42	1.11	69.5	55.0
Placebo	3843	140	3.64	--	--

Abbreviations: CI = confidence interval.

1. Per Protocol (PP) Population, Efficacy: All subjects in the Exposed/MITT Efficacy population who correctly received the vaccine, provided evaluable swab samples within the 120 hour time window, and had no major protocol violation as defined prior to unblinding. Exposed/Modified Intention-to-Treat (MITT) Efficacy Population: All subjects in the enrolled population who received a study vaccination. PP population: 52 (1.4%) and 57 (1.5%) of the enrolled subjects were excluded for TIVc and placebo groups, respectively.

2. 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%.

3. 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%.

Table 8: Vaccine Efficacy of Trivalent Influenza Vaccine versus Placebo against Culture-Confirmed Influenza by Influenza Viral Subtype (Per Protocol Analysis Set[1])

	TIVc (N=3776)		Placebo (N=3843)		Vaccine Efficacy[2, 4]	
	Attack Rate (%)	Number of Subjects with Influenza	Attack Rate (%)	Number of Subjects with Influenza	%	Lower Limit of One-Sided 97.5% CI
Antigenically Matched Strains						
A/H3N2[3]	0.05	2	0	0	--	--
A/H1N1	0.13	5	1.12	43	88.2	67.4
B[3]	0	0	0.03	1	--	--
All Culture-Confirmed Influenza						
A/H3N2	0.16	6	0.65	25	75.6	35.1
A/H1N1	0.16	6	1.48	57	89.3	73.0
B	0.79	30	1.59	61	49.9	18.2

Abbreviations: CI = confidence interval.

1. Per Protocol (PP) Population, Efficacy: All subjects in the Exposed/MITT Efficacy population who correctly received the vaccine, provided evaluable swab samples within the 120 hour time window, and had no major protocol violation as defined prior to unblinding. Exposed/Modified Intention-to-Treat (MITT) Efficacy Population: All subjects in the enrolled population who received a study vaccination. PP population: 52 and 57 of the enrolled subjects were excluded for TIVc and placebo groups, respectively.
2. 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%.
3. There were too few cases of influenza due to vaccine-matched influenza A/H3N2 or B to adequately assess vaccine efficacy. Vaccine efficacy criterion were not pre-specified in the protocol for individual virus subtypes.
4. Vaccine efficacy criterion were not pre-specified in the protocol for individual virus subtypes.

Efficacy of FLUCELVAX® QUAD in Children 2 to less than 18 years of age

Absolute efficacy of FLUCELVAX® QUAD was evaluated in children 2 to less than 18 years of age in Study 3. This was a multi-national, 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. The study enrolled 4,514 subjects. Out of the 4514 enrolled, 4513 received either FLUCELVAX® QUAD (N=2,258) or a non-influenza vaccine comparator vaccine (N=2255). The full analysis set (FAS) for efficacy consisted of 4509 subjects.

Children 2 to less than 9 years of age received either one or two doses (separated by 4 weeks) of FLUCELVAX® QUAD or comparator vaccine depending on the subject's prior influenza vaccination history. Children 9 to less than 18 years of age received a single dose of FLUCELVAX® QUAD or comparator vaccine. Among all enrolled subjects (N=4514), the mean age was 8.8 years, 48% were female, 51% were 2 to less than 9 years of age, 50% were Caucasian and 49% were Asian. There were no notable differences in the distribution of demographic and baseline characteristics between the two treatment groups.

The primary efficacy objective of the study was to demonstrate the absolute vaccine efficacy (VE) of FLUCELVAX® QUAD versus a non-influenza comparator determined by the first occurrence of RT-PCR or culture-confirmed influenza, due to any influenza Type A and B strain in subjects 2 to less than 18 years

of age. The success criterion for this primary objective was as follows: The efficacy of FLUCELVAX® QUAD was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) for VE was above 20%.

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 antigenically similar to the subtypes in the vaccine were calculated. (Table 9)

Table 9: Vaccine Efficacy of FLUCELVAX® QUAD Against First Occurrence RT-PCR Confirmed or Culture Confirmed Influenza in Subjects 2 to less than 18 years of age– FAS Efficacy[1] (Study 3).

	Number of subjects per protocol[1]	Number of cases of influenza	Attack Rate (%)	Vaccine Efficacy (VE)[2]	
				VE %	95% Confidence Interval[3]
RT-PCR or Culture Confirmed Influenza					
FLUCELVAX® QUAD	2257	175	7.8	54.6	45.7, 62.1
Non-Influenza Comparator	2252	364	16.2	-	-
Culture Confirmed Influenza					
FLUCELVAX® QUAD	2257	115	5.1	60.8	51.3, 68.5
Non-Influenza Comparator	2252	279	12.4	-	-
Antigenically Matched Culture-Confirmed Influenza					
FLUCELVAX® QUAD	2257	90	4.0	63.6	53.6, 71.5
Non-Influenza Comparator	2252	236	10.5	-	-

[1]Number of subjects in the Full-Analysis Set (FAS) – Efficacy, which included all subjects randomized, received a study vaccination and provided efficacy data.

[2]Efficacy against influenza was evaluated over three influenza seasons, SH 2017, NH 2017-18 and NH 2018-19

[3]FLUCELVAX® QUAD met the pre-defined success criterion defined as the lower limit of the two-sided 95% CI of absolute vaccine efficacy greater than 20%

Study 3: NCT03165617

Vaccine efficacy by viral subtype is described in Table 10.

Table 10: Vaccine Efficacy of FLUCELVAX QUAD against RT-PCR Confirmed or Culture-Confirmed Influenza by Influenza Viral Subtype in Subjects 2 to less than 18 years of age - FAS Efficacy[1] (Study 3)

	FLUCELVAX® QUAD (N=2257)		Non-influenza Comparator (N=2252)		Vaccine Efficacy[2, 3]	
	Attack Rate (%)	Number of Subjects with Influenza	Attack Rate (%)	Number of Subjects with Influenza	VE %	95% Confidence Interval[4]
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

Abbreviations: CI = confidence interval.

[1] Number of subjects in the Full-Analysis Set (FAS) – Efficacy, which included all subjects randomized, received a study vaccination and provided efficacy data.

[2] Efficacy against influenza was evaluated over three influenza seasons, SH 2017, NH 2017-18 and NH 2018-19

[3] 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.

[4] Vaccine efficacy criterion were not pre-specified in the protocol for individual virus subtypes.

Study 3: NCT03165617

14.4 Immunogenicity

Immunogenicity of FLUCELVAX® QUAD in Adults 18 years of age and above

Immunogenicity of FLUCELVAX® QUAD was evaluated in adults 18 years of age and older in a randomized, double-blind, controlled study conducted in the U.S. (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. The treatment randomization ratio was 2:1:1 (FLUCELVAX® QUAD:TIV1c:TIV2c). In the per protocol set, the mean age of subjects who received FLUCELVAX® QUAD was 57.5 years; 55.1% of subjects were female and 76.1% of subjects were Caucasian, 13% were black and 9% were Hispanics. The immune response to each of the vaccine antigens was assessed 21 days after vaccination.

The immunogenicity endpoints were geometric mean antibody titers (GMTs) of HI antibodies response and percentage of subjects who achieved seroconversions, defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or with a pre-vaccination HI titer of ≥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% confidence interval (CI) for the ratio of GMTs (GMT TIV1c or 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%.

FLUCELVAX® QUAD was noninferior to trivalent influenza vaccine. Noninferiority was established for all 4 influenza strains included in FLUCELVAX® QUAD, as assessed by ratios of GMTs and the differences in the percentages of subjects achieving seroconversion at 3 weeks following vaccination (Table 11).

Table 11: Noninferiority of FLUCELVAX® QUAD Relative to Trivalent Influenza Vaccine in Adults 18 Years of Age and Above, Per Protocol Analysis Set[c]

		FLUCELVAX® QUAD N = 1250	TIV1c/TIV2c[a] N = 635/N =639	Vaccine group Ratio (95% CI)	Vaccine Group Difference (95% CI)
A/H1N1	GMT (95% CI)	302.8 (281.8-325.5)	298.9 (270.3-330.5)	1.0 (0.9-1.1)	-
	Seroconversion Rate[b] (95% CI)	49.2% (46.4-52.0)	48.7% (44.7-52.6)	-	-0.5% (-5.3-4.2)
A/H3N2	GMT (95% CI)	372.3 (349.2-396.9)	378.4 (345.1-414.8)	1.0 (0.9-1.1)	-
	Seroconversion Rate[b] (95% CI)	38.3% (35.6-41.1)	35.6% (31.9-39.5)	-	-2.7% (-7.2-1.9)
B1	GMT (95% CI)	133.2 (125.3-141.7)	115.6 (106.4-125.6)	0.9 (0.8-1.0)	-
	Seroconversion Rate[b] (95% CI)	36.6% (33.9-39.3)	34.8% (31.1-38.7)	-	-1.8% (-6.2-2.8)
B2	GMT (95% CI)	177.2 (167.6-187.5)	164.0 (151.4-177.7)	0.9 (0.9-1.0)	-
	Seroconversion Rate[b] (95% CI)	39.8% (37.0-42.5)	35.4% (31.7-39.2)	-	-4.4% (-8.9-0.2)

Abbreviations: CI = confidence interval, GMT = geometric mean titer.

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

[b] 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.

[c] The per protocol (PP) analysis set is defined as all subjects in the FAS Immunogenicity who correctly received the vaccine (i.e., receive the vaccine to which the subjects is 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.

Immunogenicity in Children and Adolescents 4 to less than 18 years of age

Immunogenicity of FLUCELVAX® QUAD was evaluated in children 4 to less than 18 years of age as part of a randomized, double-blind, controlled study conducted in U.S. (Study 2). 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). Subjects were randomized at an approximately 2:1:1 ratio to receive QIVc, TIV1c, or TIV2c vaccine. 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 the per protocol set, the mean age was 9.8 years; 47% of subjects were female and 54% of subjects were Caucasian, 22% were black and 19% were Hispanics. The immune response to each of the vaccine antigens was assessed, 21 days after vaccination.

The immunogenicity endpoints were GMTs of HI antibodies response and percentage of subjects who

achieved seroconversions, defined as a pre-vaccination HI titer of <1:10 with a post-vaccination titer ≥1:40 or with a pre-vaccination HI titer ≥ 1:10 and a minimum 4-fold increase in serum HI antibody titer. The definition of noninferiority criteria for GMT and seroconversion was the same as for Study 1.

FLUCELVAX® QUAD was noninferior to trivalent influenza vaccine. Noninferiority was established for all 4 influenza strains included in the FLUCELVAX® QUAD, as assessed by ratios of GMTs and the differences in the percentages of subjects achieving seroconversion at 3 weeks following vaccination (Table 12).

Table 12: Noninferiority[a] of FLUCELVAX® QUAD Relative to Trivalent Influenza Vaccine in Children and Adolescents 4 to less than 18 Years of Age, Per Protocol Analysis Set

		FLUCELVAX® QUAD	TIV1c/TIV2c[b]	Vaccine Group Ratio	Vaccine Group Difference
A/H1N1		N=1014	N=510		
	GMT (95% CI)	1090 (1027-1157)	1125 (1034-1224)	1.03 (0.93-1.14)	-
	Seroconversion Rate[c] (95% CI)	72% (69-75)	75% (70-78)	-	2% (-2.5- 6.9)
A/H3N2		N=1013	N=510		
	GMT (95% CI)	738 (703-774)	776 (725-831)	1.05 (0.97-1.14)	-
	Seroconversion Rate[c] (95% CI)	47% (44-50)	51% (46-55)	-	4% (-1.4- 9.2)
B1		N=1013	N=510		
	GMT (95% CI)	155 (146-165)	154 (141-168)	0.99 (0.89-1.1)	-
	Seroconversion Rate[c] (95% CI)	66% (63-69)	66% (62-70)	-	0% (-5.5- 4.5)
B2		N=1009	N= 501		
	GMT (95% CI)	185 (171-200)	185 (166-207)	1 (0.87-1.14)	-
	Seroconversion Rate[c] (95% CI)	73% (70-76)	71% (67-75)	-	-2% (-6.5- 3.2)

Abbreviations: CI = confidence interval, GMT = geometric mean titer.

[a] Analyses are performed on data for day 22 for previously vaccinated subjects and day 50 for not previously vaccinated subjects.

[b] The comparator vaccine for noninferiority comparisons for A/H1N1, A/H3N2 and B1 is TIV1c, for the B2 strain the comparator vaccine is TIV2c.

[c] Seroconversion rate = percentage of subjects with either a pre-vaccination 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 Table 7 above. PP population: 145 (12.5%), 83 (14.0%) and 79 (13.6%) enrolled subjects were excluded for QIVc, TIV1c and TIV2c groups, respectively.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Non-clinical data reveal no special hazard for humans based on a repeat dose toxicity study and a reproductive and developmental toxicity study with FLUCELVAX (trivalent formulation).

General Toxicology: In a repeat-dose toxicity study, male and female rabbits received 2 intramuscular doses of trivalent vaccine (45 mcg HA/dose) 1 week apart. There was no evidence of systemic toxicity and trivalent vaccine was locally well tolerated.

Reproductive and Developmental Toxicology: In a reproductive and developmental toxicity study, the effect of cell culture-derived antigens on embryo-foetal and postnatal development was evaluated in pregnant rabbits. Female rabbits were administered vaccine (45 mcg HA/dose) by intramuscular injection 3 times prior to gestation, during the period of organogenesis (gestation day 7) and later in pregnancy (gestation day 20), 0.5 mL/rabbit/occasion (approximately 11-fold excess relative to the projected adult human dose (60 mcg) on a body weight basis). No adverse effects on mating, female fertility, pregnancy, embryo-foetal development, or post-natal development were observed. There were no vaccine-related foetal malformations or other evidence of teratogenesis.

Genotoxicity and carcinogenic potential were not assessed.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

FLUCELVAX® QUAD

Influenza Vaccine, suspension for injection

Read this carefully before you are given **FLUCELVAX® QUAD**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FLUCELVAX® QUAD**.

What is FLUCELVAX® QUAD used for?

FLUCELVAX® QUAD is used in adults and children 2 years and older to prevent influenza, often called "the flu."

Influenza is caused by infection with specific influenza viruses. New types of influenza viruses can appear each year. FLUCELVAX® QUAD vaccine contains fragments of four different types of influenza virus. Each year the World Health Organization decides which four types of viruses are most suitable to include in the vaccine.

For this season (2021 – 2022) the viruses are A/Wisconsin/588/2019 (H1N1)pdm09-like virus, A/Cambodia/e0826360/2020 (H3N2)-like virus, B/Washington/02/2019-like virus and B/Phuket/3073/2013-like virus.

You cannot catch influenza from the vaccine, as the virus in the vaccine has been killed and split into small non-infectious particles.

The National Advisory Committee on Immunization (NACI) encourages annual influenza vaccination for all Canadians who are able to have the vaccine.

Vaccination against influenza is recommended every year, for anyone wanting to lower their chance of catching influenza. FLUCELVAX® QUAD has been used by many people to lower their risk of catching the flu.

How does FLUCELVAX® QUAD work?

FLUCELVAX® QUAD vaccine works by helping your body to protect itself against infection by the types of influenza viruses that are in the vaccine. The vaccine stimulates the body to make substances called antibodies. Antibodies fight the influenza virus. If you have been vaccinated, when you come into contact with the influenza viruses in the vaccine, your body is usually able quickly to destroy the virus, which may prevent you from getting influenza.

Your body takes a few weeks after vaccination to fully develop effective protection against the influenza virus.

Protection against influenza generally requires one dose of FLUCELVAX® QUAD vaccine, however, some children less than 9 years of age may require two doses (see section **Usual dose**).

As with all vaccines, 100% protection cannot be guaranteed.

What are the ingredients in FLUCELVAX® QUAD?

Medicinal ingredients:

Each 0.5 mL dose of the vaccine contains 15 mcg haemagglutinin (HA) from each influenza strain:

- A/Wisconsin/588/2019 (H1N1)pdm09-like virus (A/Washington/19/2020 (H1N1))
- A/Cambodia/e0826360/2020 (H3N2)-like virus (A/Tasmania/503/2020 (H3N2))
- B/Washington/02/2019-like virus (B/Darwin/7/2019)
- B/Phuket/3073/2013-like virus (B/Singapore/INFTT-16-0610/2016)

Non-medicinal ingredients:

- Beta-propiolactone**,
- Cetyltrimethylammonium bromide**,
- Disodium phosphate dihydrate,
- Magnesium chloride hexahydrate,
- Polysorbate 80**,
- Potassium chloride,
- Potassium dihydrogen phosphate,
- Sodium chloride,
- Thimerosal,
- Water for injections

*Thimerosal is included in multi-dose vials only.
**Residuals

FLUCELVAX® QUAD is not made using eggs, therefore, there are no egg proteins in the vaccine.

The syringe and vial components do not contain latex. FLUCELVAX® QUAD is considered safe for use in persons with latex allergies.

FLUCELVAX® QUAD pre-filled syringes contain no preservative or antibiotics. FLUCELVAX® QUAD multi-dose vial formulation contains a preservative, but does not contain any antibiotics.

FLUCELVAX® QUAD comes in the following dosage forms:

FLUCELVAX® QUAD is supplied as a suspension for intramuscular injection in either a 0.5 mL single-dose, pre-filled syringe or a 5 mL multi-dose vial.

Do not use FLUCELVAX® QUAD if:

- Your child is under 2 years of age. FLUCELVAX® QUAD vaccine is only approved for use in children aged 2 years and older.
- You or your child have or previously have had an allergy to FLUCELVAX® QUAD or any ingredient listed in this leaflet.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take FLUCELVAX® QUAD. Talk about any health conditions or problems you may have, including if you or your child:

- **have or have had a reaction to vaccination with any of the following:**
  - severe allergic reaction
  - difficulty breathing
  - swelling of the throat
  - fainting or collapse

- fits or convulsions
- high temperature (greater than 38.5°C)
- severe skin reaction at the injection site, including severe bruising

- **have an infection or temperature higher than 38.5°C.** Your doctor may decide to delay vaccination until the illness has passed. A minor illness such as a cold is not usually a reason to delay vaccination.
- **have low immunity due to treatment with certain medicines**
- **have or have had Guillain-Barré Syndrome (GBS)**, an illness which affects the nervous system and causes paralysis.
- **have allergies to other medicines or substances**
- **are pregnant or breastfeeding.** Your healthcare professional will be able to discuss the potential risks and benefits of having FLUCELVAX® QUAD while you are pregnant or breastfeeding.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with FLUCELVAX® QUAD:

No data are available on administration of FLUCELVAX® QUAD with other vaccines.

How FLUCELVAX® QUAD is given:

FLUCELVAX® QUAD is given as an injection into a muscle, usually in the upper arm.

Usual dose:

FLUCELVAX® QUAD is given once every year as follows:

- Adults and children 9 years and over: one injection of 0.5 mL.

For children 2 to less than 9 years old who are receiving influenza vaccine for the first time, it is recommended that a follow-up (booster) dose of FLUCELVAX® QUAD is given 4 weeks after the first dose.

If the follow-up dose is missed, talk to your healthcare professional and arrange another visit as soon as possible.

Overdose:

If you think you have been given too many doses of FLUCELVAX® QUAD or have been given it by mistake, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using FLUCELVAX® QUAD?

These are not all the possible side effects you may have when taking FLUCELVAX® QUAD. If you experience any side effects not listed here, tell your healthcare professional.

The following are common or very common side effects of FLUCELVAX® QUAD. Most of these side effects are mild and do not last long. Tell your doctor if you or your child have side effects that bother you:

- Injection site pain, reddening, hardening or swelling
- Headache
- Muscle or joint pain
- Tiredness
- Nausea, vomiting, diarrhea
- Loss of appetite
- Bruising
- Shivering

Children may also experience the following common side effect:

- Fever

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
RARE			
Anaphylaxis Difficulty breathing, dizziness, a weak and rapid pulse, skin rash		✓	
Allergic reaction Rash, itching or hives on the skin, swelling of the face, lips, tongue, or other parts of the body		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Seqirus cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:

Store in a refrigerator between 2° to 8°C. Do not freeze. Protect from light. Do not use after the expiration date. The multi-dose vial must be used within 28 days from the initial removal of the first

dose and between uses, return the multi-dose vial to the recommended storage conditions.

Keep out of reach and sight of children.

If you want more information about FLUCELVAX® QUAD:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.seqirus.ca, or by calling 1-855-358-8966.

This leaflet was prepared by Seqirus UK Limited, 29 Market Street, Level 3, Maidenhead, Berkshire, SL6 8AA, UK.

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