PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

FLUVIRAL

(2025 – 2026)

Trivalent Influenza Vaccine (Split Virion, Inactivated)

Suspension for Injection

ATC Code J07BB02

Manufactured by:
ID Biomedical Corporation of Quebec
Quebec, Quebec, Canada

Distributed by:
GlaxoSmithKline Inc.
100 Milverton Drive
Mississauga, Ontario
L5R 4H1

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

FLUVIRAL (Trivalent Influenza Vaccine (Split-Virion, Inactivated)) is indicated for active immunization of adults and children from 6 months of age for the prevention of influenza disease caused by influenza virus types A and 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 published *Statement on Seasonal Influenza Vaccine* for the current season.

1.1 Pediatrics

Pediatrics (6 months – 17 years): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of FLUVIRAL in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use.

2 CONTRAINDICATIONS

FLUVIRAL should not be administered to subjects with known history of hypersensitivity to any component of the vaccine or following a previous dose of any influenza vaccine produced in eggs. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

FLUVIRAL should be administered as a single 0.5 mL injection.

Children 6 months to less than 9 years of age who have not previously been vaccinated against influenza should receive a second dose of 0.5 mL after an interval of at least 4 weeks.

4.4 Administration

For intramuscular use only. Do not inject intravascularly.

The preferred site for injection is the anterolateral aspect of the thigh in infants or the deltoid muscle of the upper arm in children and adults. The vaccine should not be injected in the gluteal area or areas where there may be a major nerve trunk and/or blood vessel.

Instructions for use:

FLUVIRAL should not be mixed with other vaccines/medicinal products (see 9.4 Drug-Drug Interactions, Use with Other Vaccines)

The vaccine presents as an opalescent translucent to off-white suspension that may sediment slightly.

The vial should be shaken prior to each administration and inspected visually for any foreign particulate matter and/or variation of physical aspect prior to administration. In the event of either being observed, discard the vaccine.

Each vaccine dose of 0.5 mL is withdrawn into a 1 mL syringe for injection and administered intramuscularly. It is recommended to equip the syringe with a needle gauge not larger than 23-G.

Between uses, the multidose vial should be stored in a refrigerator (2°C - 8°C).

5 OVERDOSAGE

Insufficient data are available.

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 1 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular (IM)	Suspension for Injection Each 0.5 mL dose contains 15 µg of influenza virus haemagglutinin/strain for each strain listed below (see Description)	Egg proteins, ethanol, formaldehyde, phosphate buffered saline, polysorbate 80, sodium deoxycholate, α-tocopheryl hydrogen succinate, sucrose. Thimerosal preservative in the multidose vial presentation

Description

FLUVIRAL is a trivalent influenza vaccine (split-virion, inactivated) prepared from virus grown in the allantoic cavity of embryonated hens' eggs. The virus is inactivated with ultraviolet light treatment followed by formaldehyde treatment, purified by centrifugation, and disrupted with sodium deoxycholate.

This vaccine complies with the World Health Organization (WHO) recommendation (Northern Hemisphere) for the 2025 – 2026 season. The trivalent vaccine contains 2 influenza A virus subtypes and one influenza B virus lineage.

Each 0.5 mL dose of vaccine contains 15 micrograms (µg) haemagglutinin (HA) of each of the following three influenza virus strains:

15 µg HA - A/Victoria/4897/2022 (H1N1)pdm09-like virus (A/Victoria/4897/2022 (H1N1) IVR-238)

15 µg HA - A/Croatia/10136RV/2023 (H3N2)-like virus (A/Croatia/10136RV/2023 (H3N2) X-425A)

15 µg HA - B/Austria/1359417/2021 (B/Victoria lineage)-like virus (B/Austria/1359417/2021 BVR-26)

The vaccine is formulated with phosphate buffered saline, which is composed of: sodium chloride, potassium chloride, disodium hydrogen phosphate heptahydrate, potassium dihydrogen phosphate and water for injection.

Each 0.5-mL dose contains, α-tocopheryl hydrogen succinate (200 µg), and polysorbate 80 (512 µg).

Each 0.5-mL dose may also contain residual amounts of egg proteins (ovalbumin $\leq$0.3 µg), sodium deoxycholate, ethanol, formaldehyde and sucrose from the manufacturing process.

Thimerosal, a mercury derivative, is added as a preservative in the multidose vial presentation. Each 0.5 mL dose contains 50 µg thimerosal (<25 µg mercury).

Antibiotics are not used in the manufacture of this vaccine.

Packaging

6 mL vial (type 1 glass) containing 5 mL of vaccine (10 doses of 0.5 mL)

Pack size of 1 or 10 vials.

The vial stopper does not contain latex.

7 WARNINGS AND PRECAUTIONS

General

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

FLUVIRAL should under no circumstances be administered intravascularly.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

FLUVIRAL is not effective against all possible strains of influenza virus. FLUVIRAL is intended to provide protection against those strains of virus from which the vaccine is prepared and to closely related strains.

Febrile or Acute Disease

As with other vaccines, vaccination with FLUVIRAL should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Hematologic
As with other vaccines administered intramuscularly, FLUVIRAL should be given with caution in individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these subjects.

Immune

It may be expected that in patients receiving immunosuppressive treatment or patients with immunodeficiency, an adequate immune response may not be elicited.

Local Skin Reactions at Vaccination Sites

Soreness and redness at the injection site may occur and may last for up to two days. Prophylactic acetaminophen may decrease the frequency of pain at the injection site.

Neurologic

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

Immunization should be delayed in a patient with an active neurologic disorder, but should be considered when the disease process has been stabilized.

Respiratory

Revaccination of individuals who have previously experienced oculo-respiratory symptoms is safe. Previously affected individuals should be encouraged to be revaccinated. The risk of recurrence of oculo-respiratory symptoms after revaccination is minimal compared to the serious threat posed by influenza. Please refer to the most current NACI recommendations regarding revaccination of subjects who experienced more severe oculo-respiratory syndrome.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of FLUVIRAL when administered to pregnant women has not been evaluated in clinical trials. A systematic literature review on inactivated influenza vaccines do not indicate an increased risk of adverse pregnancy outcomes. Animal studies with FLUVIRAL do not indicate direct or indirect harmful effects with respect to reproductive and developmental toxicity. The FLUVIRAL vaccine may be administered to pregnant women following an assessment of the risks and benefits.

7.1.2 Breast-feeding

The safety of FLUVIRAL when administered to breast-feeding women has not been evaluated. It is unknown whether FLUVIRAL is excreted in human breast milk. FLUVIRAL should only be used during breast-feeding when the possible advantages outweigh the potential risks.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most commonly reported adverse drug reactions from 6 pooled clinical studies in adults with FLUVIRAL are pain at the injection site (32%), fatigue (16%), headache (16%), myalgia (15%), and redness at the injection site (10%). The most commonly reported adverse drug reactions in 3-17 year-old children from the Flu Q-TIV-TF-008 study included pain at the injection site (53%), irritability (21%), appetite loss (19%), and drowsiness (14%). Reactions are generally mild and of limited duration.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, 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 may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

In six adult clinical studies conducted in the United States and Canada, FLUVIRAL was administered to more than 2,200 subjects at least 18 years of age and in one paediatric clinical study conducted in the United States, FLUVIRAL was administered to more than 1,000 children 3 to 17 years of age.

Local and general symptoms were solicited by a diary aid used by the subjects for at least the day of vaccination and 3 days post-vaccination. Subjects were also requested to report any clinical events occurring during the 21-day (for adults) and 28-day (for children) study period.

The clinical trial data with FLUVIRAL are supported by 2 studies conducted with FLULAVAL TETRA, a vaccine manufactured by the same process containing three influenza virus strains shared with FLUVIRAL plus a second influenza B virus lineage. Therefore, adverse reactions attributed to FLULAVAL TETRA (60 µg haemagglutinin per 0.5 mL) are likely to predict those expected with FLUVIRAL (45 µg haemagglutinin per 0.5 mL).

Safety data in FLULAVAL TETRA studies were collected by the same method used in FLUVIRAL studies, except that solicited local and general symptoms were collected over a 7-day rather than a 4-day period.

In more than 1200 adults, FLULAVAL TETRA had a similar safety profile to that observed for FLUVIRAL in adults. Additional adverse reactions were gastrointestinal symptoms (including nausea, vomiting, diarrhoea and /or abdominal pain) reported as common and injection site reactions (such as haemorrhage, haematoma, warmth), lymphadenopathy, pruritus and rash reported as uncommon.

In 299 children 6 to 35 months of age, FLULAVAL TETRA had a similar safety profile to that observed for FLUVIRAL in children 3 to 4 years of age. Additional adverse reactions were diarrhoea and vomiting reported as uncommon.

Adults: Study Q-QIV-007 (Immunogenicity Non-Inferiority):

A randomized, double-blind, active-controlled study evaluated 1,703 adults 18 years of age and older who received FLULAVAL TETRA, a quadrivalent seasonal vaccine, with two A strains and two B strains, one of Victoria lineage and one of Yamagata lineage (N = 1,272), or FLUVIRAL manufactured for the 2010-2011 season with a B strain of Victoria lineage (N = 213), or a TIV with the same two A strains as FLUVIRAL but with a B strain of Yamagata lineage (N = 218). The mean age of subjects was 50 years. Solicited local adverse reactions and systemic adverse events were collected using diary cards for 7 days (day of vaccination and the next 6 days).

Table 2 – Incidence of Solicited Local Adverse Reactions and Systemic Adverse Events within 7 Days of Vaccination in Adults[b] (Total Vaccinated Cohort)

	FLULAVAL Tetra[c] N = 1,260 %	FLUVIRAL (B Victoria)[d] N = 208 %	TIV (B Yamagata)[e] N = 216 %
Local			
Pain	60	45	41
Swelling	3	1	4
Redness	2	3	1
Systemic			
Myalgia	26	25	19
Headache	22	20	23
Fatigue	22	22	17
Arthralgia	15	17	15
Gastrointestinal symptoms[f]	9	10	7
Shivering	9	8	6
Fever ≥100.4°F (38.0°C)	2	1	1

TIV = trivalent influenza vaccine.
Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
[a] 7 days included day of vaccination and the subsequent 6 days.
[b] Study Q-QIV-007: NCT01196975.
[c] Contained two A strains and two B strains, one of Victoria lineage and one of Yamagata lineage.
[d] Contained two A strains and a B strain of Victoria lineage.
[e] Contained the same two A strains as FLUVIRAL and a B strain of Yamagata lineage.
[f] Gastrointestinal symptoms included nausea, vomiting, diarrhea, and/or abdominal pain.

Unsolicited adverse events: Unsolicited events that occurred within 21 days of vaccination (day 0-20) were recorded based on spontaneous reports or in response to queries about changes in health status. The incidence of unsolicited adverse events reported during the 21-day post-vaccination period for subjects who received FLULAVAL TETRA (N = 1,272), FLUVIRAL (N = 213), or TIV (B Yamagata) (N = 218) was 19%, 23%, and 23%, respectively. Unsolicited events reported for FLULAVAL TETRA considered as possibly related to vaccination and occurring in ≥0.1% of subjects included dizziness, injection site hematoma, injection site hemorrhage, injection site warmth, lymphadenopathy, pruritus, rash, and upper respiratory tract infection.

8.2.1 Clinical Trial Adverse Reactions - Pediatrics

Children: Study Q-TIV TF-008 (Immunogenicity Non-Inferiority):

An observer-blind, active-controlled study evaluated subjects 3 through 17 years of age who received FLUVIRAL (N = 1,055) or FLUZONE (N = 1,061), a licensed trivalent, inactivated influenza virus vaccine, manufactured by Sanofi Pasteur SA. In the overall population, 53% were male. The mean age of subjects was 8 years. Children 3 through 8 years of age with no history of influenza vaccination received 2 doses approximately 28 days apart. Children 3 through 8 years of age with a history of influenza vaccination and children 9 years of age and older received one dose. Solicited local adverse reactions

and systemic adverse events were collected using diary cards for 4 days (day of vaccination and the next 3 days) (Table 3).

Table 3 – Incidence of Solicited Local Adverse Reactions and Systemic Adverse Events Within 4 Days[a] of First Vaccination in Children 3 to 17 Years of Age[b] (Total Vaccinated Cohort)

	FLUVIRAL %	Comparator[c] %
	Age Group: 3 to 17 Years	
Local	**N = 1,042**	**N = 1,026**
Pain	56	53
Redness	4	5
Swelling	4	5
	Age Group: 3 to 4 Years	
Systemic	**N = 293**	**N = 279**
Irritability	25	27
Drowsiness	19	19
Loss of appetite	16	13
Fever ≥100.4°F (38.0°C)	5	3
	Age Group: 5 to 17 Years	
Systemic	**N = 749**	**N = 747**
Muscle aches	24	23
Headache	17	15
Fatigue	17	17
Arthralgia	8	10
Shivering	6	5
Fever ≥100.4°F (38.0°C)	5	4

Total vaccinated cohort for safety included all vaccinated subjects for whom safety data were available.
[a] 4 days included day of vaccination and the subsequent 3 days.
[b] Study Q-TIV TF-008: NCT00980005.
[c] Licensed trivalent, inactivated influenza virus vaccine (manufactured by Sanofi Pasteur SA).

In children who received a second dose of FLUVIRAL or the comparator vaccine, the incidences of adverse events following the second dose were generally lower than those observed after the first dose.

Unsolicited adverse events that occurred within 28 days (day 0-27) of any vaccination were recorded based on spontaneous reports or in response to queries about changes in health status. The incidence of unsolicited adverse events reported in subjects who received FLUVIRAL (N = 1,055) or FLUZONE (N = 1,061) was 40% and 37%, respectively. Unsolicited events reported for FLUVIRAL considered as possibly related to vaccination and occurring in ≥0.1% of subjects included diarrhea, influenza-like illness, injection site hematoma, injection site rash, injection site warmth, rash, upper abdominal pain, and vomiting. The rates of SAEs were comparable between groups (0.9% and 0.6% for FLUVIRAL and the comparator, respectively); none of the SAEs were considered related to vaccination.

Children 6-35 months: Study Q-QIV-013 (Immunogenicity and Safety):

A randomized, double-blind, active controlled study in which subjects received one or two 0.5 mL doses of FLULAVAL TETRA (N = 299) or a comparator trivalent influenza vaccine (FLUARIX N = 302) containing one B strain from the B/Yamagata lineage. Children with no history of prior influenza vaccination received 2 doses approximately 28 days apart (92.6% and 93.0 % for FLULAVAL TETRA and FLUARIX, respectively). Children with a history of prior influenza vaccination received one dose of vaccine (7.4% and 7.0%, respectively). Solicited local adverse reactions and systemic adverse events were collected using diary cards for 7 days.

Table 4 – Incidence of Solicited Local and Systemic Adverse Events Within 7 Days[a] of Vaccination in Children 6 to 35 Months of Age[b] (Total Vaccinated Cohort)

Children 6-35 months	FLULAVAL TETRA[c] %	FLUARIX[d] %
Local	**N = 564 doses**	**N = 573 doses**
Pain	23.0	21.5
Swelling	1.1	1.2
Redness	1.2	1.0
Systemic	**N = 561 doses**	**N = 572 doses**
Irritability	29.1	29.5
Drowsiness	21.6	18.9
Loss of appetite	22.5	22.0
Fever ≥38.0°C	13.4	12.1

[a] 7 days included day of vaccination and the subsequent 6 days.
[b] Study Q-QIV-013: NCT01711736
[c] Contained two A strains and two B strains, one of Victoria lineage and one of Yamagata lineage.
[d] Contained two A strains and one B strain from the Yamagata lineage

Unsolicited adverse events

During the 28-day post-vaccination period, overall, unsolicited AEs were experienced after 33.5% of FLULAVAL TETRA doses and 35.8% of FLUARIX doses. The most frequently reported unsolicited AEs were nasopharyngitis (16.1% and 17.7% respectively) followed by diarrhoea (7.5% and 7.2% respectively).

8.5 Post-Market Adverse Reactions

The following adverse reactions have been identified during post approval use of FLUVIRAL or FLULAVAL TETRA (quadrivalent influenza vaccine). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

Immune system disorders

Allergic reactions including anaphylactic and anaphylactoid reactions

Nervous system disorders
Guillain-Barré syndrome

Spontaneous reports of Guillain-Barré syndrome have been received following vaccination with FLUVIRAL. However, a causal association between vaccination and the Guillain-Barré syndrome has not been established.

Skin and subcutaneous tissue disorders

Angioedema, urticaria

There have been reports of other neurological illnesses, including facial paralysis, encephalitis, encephalopathy, demyelinating disease and labyrinthitis, associated with other influenza vaccines. Any relationship, other than temporal, to the vaccine has not been established.

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

The vaccine is unlikely to produce an effect on the ability to drive and use machines.

9.4 Drug-Drug Interactions

Use with Other Vaccines

No interaction studies have been performed. If FLUVIRAL is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

9.7 Drug-Laboratory Test Interactions

False positive ELISA serologic tests for HIV-1, Hepatitis C, and especially HTLV-1 may occur following influenza vaccination. These transient false-positive results may be due to cross-reactive IgM elicited by the vaccine. For this reason, a definitive diagnosis of HIV-1, Hepatitis C, or HTLV-1 infection requires a positive result from a virus-specific confirmatory test (e.g. Western Blot or immunoblot).

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

FLUVIRAL provides active immunization against the three influenza virus strains (two A subtypes and one B type) contained in the vaccine. Although multiple mechanisms, including cellular immunity, may contribute to vaccine-induced protection against influenza, the humoral components of the immune response, in particular antibodies against virus haemagglutinin (HA) and neuraminidase (NA) antigens is best understood. Specific levels of vaccine-induced haemagglutination-inhibiting HI antibodies that protect against naturally occurring influenza disease have not been established in randomized, controlled trials.

In human challenge studies, HI antibody titers of $\geq$ 1:40 have been associated with reductions in influenza illness. In addition, HI antibody responses are used as a measure of vaccine activity. The effectiveness of inactivated influenza virus vaccines is influenced by the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains used to prepare the vaccines and those circulating in the population.

10.3 Pharmacokinetics

Duration of Effect

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

11 STORAGE, STABILITY AND DISPOSAL

Store in a refrigerator ($2^oC – 8^oC$).

Do not freeze.

Store in the original package in order to protect from light.

The vaccine in multidose vials is stable for 13 months.

Once entered, the multidose vial should be discarded within 28 days.

12 SPECIAL HANDLING INSTRUCTIONS

Any unused product or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

FLUVIRAL contains three split-virion, inactivated influenza virus strains prepared from virus propagated in the allantoic cavity of embryonated hens' eggs. Each of the influenza virus strains is produced and purified separately. The virus is inactivated with ultraviolet light followed by formaldehyde treatment, purified by centrifugation, and disrupted with sodium deoxycholate.

Product Characteristics:

FLUVIRAL is a sterile, opalescent translucent to off-white suspension in a phosphate-buffered saline solution and may sediment slightly. The vaccine has been formulated to contain 45 micrograms (µg) haemagglutinin (HA) per 0.5-mL dose in the recommended ratio of 15 µg HA of each of the 3 influenza virus strains. Antibiotics are not used in the manufacture of this vaccine.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The immunogenicity of FLUVIRAL has been evaluated as a trivalent or as a quadrivalent thimerosal-free formulation (FLULAVAL TETRA) in controlled and open-label clinical trials involving adults 18 years and older, and children aged 3 to 17 years. Adults and children 9 years and older received a single 0.5 mL dose of FLUVIRAL or a quadrivalent formulation of the vaccine (FLULAVAL TETRA). Children 6 months through 8 years with a history of influenza vaccination received one 0.5 mL dose. Children 6 months through 8 years of age with no history of influenza vaccination received 2 doses approximately 28 days apart.

The humoral immune response was assessed in terms of a serum haemagglutinin-inhibiting (HI) antibody titer against each virus strain included in the vaccine. In adult studies the immune response was assessed 21 days following vaccination. In pediatric studies, the immune response was assessed 28 days following the last vaccination.

Table 5 – Summary of Patient* Demographics for Clinical Trials

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
Q-QIV-007	randomized, double-blind, immunogenicity and safety	0.5 mL, IM	1703 ≥18 years	50.0 years (18-97 years)	F = 1044 M = 659
Q-TIV-TF-008	randomized, observer-blind, immunogenicity and safety.	0.5 mL, IM (unprimed: 2x0.5 mL IM, 28 days apart)	1055	7.8 years (3-17 years)	F = 500 M = 555

*Total Vaccinated Cohort

14.2 Study Results

Adults 18 years of age and older

In clinical study Q-QIV-007, approximately 1,200 adults 18 years of age and older received a single dose of a quadrivalent formulation of FLUVIRAL (FLULAVAL TETRA) and approximately 200 subjects received a single dose of FLUVIRAL.

The study assessed the non-inferiority of FLULAVAL TETRA versus FLUVIRAL for HI Geometric mean antibody titer (GMT) at Day 21 and HI seroconversion rate (4-fold rise in reciprocal titer or change from undetectable [< 10] to a reciprocal titer of ≥ 40) in adults 18 years of age and older.

Table 6 – Non-inferiority of Q-QIV versus FLUVIRAL for the common strains in terms of adjusted GMT ratios at Day 21

Strain	Comparator		Q-QIV		Adjusted GMT ratio (Comparator / QIV)		
					Value	95% CI	
	N	Adjusted GMT	N	Adjusted GMT		LL	UL
TIV-VB+TIV-YB vs. QIV							
A/California/7/2009 (H1N1)	414	160.0	1238	205.1	0.78	0.68	0.90
A/Victoria/210/2009 (H3N2)	415	147.6	1237	124.2	1.19	1.05	1.35
TIV-VB vs. QIV							
B/Brisbane/60/2008 (Victoria)	203	133.0	1240	177.2	0.75	0.65	0.87
TIV-YB vs. QIV							
B/Florida/4/2006 (Yamagata)	211	311.7	1241	396.2	0.79	0.69	0.90

1. Q-QIV = Subjects received Q-QIV; TIV-VB = Subjects received TIV with B strain of Victoria lineage; TIV-YB = Subjects received TIV with B strain of Yamagata lineage; TIV-VB+TIV-YB = Pooled TIV-VB and TIV-YB groups;
2. Adjusted GMT = geometric mean antibody titer adjusted for baseline titer;
3. N = Number of subjects with both pre- and post-vaccination results available;
4. 95% CI = 95% confidence interval for the adjusted GMT ratio (ANCOVA model: adjustment for baseline titer - pooled variance); LL = lower limit, UL = upper limit

FLULAVAL TETRA met the non-inferiority criteria based on GMT's (upper limit of 2-sided 95% CI for GMT ratio (comparator / FLUVIRAL ≤1.5)

14.4 Immunogenicity

Table 7 – Post-vaccination GMTs and seroconversion rates from Study Q-QIV-007 in adults 18 years of age and older (ATP Cohort for analysis of immunogenicity)

Influenza Strain	FLULAVAL Tetra N=1246	FLUVIRAL[1] N=204
	GMT[4] (95% confidence interval)	
A/H1N1	204.6 (190.4;219.9)	176.0 (149.1;207.7)
A/H3N2	125.4 (117.4;133.9)	147.5 (124.1;175.2)
B (Victoria)[2]	177.7 (167.8;188.1)	135.9 (118.1;156.5)
B (Yamagata)[3]	399.7 (378.1;422.6)	176.9 (153.8;203.5)
	Seroconversion rate (95% confidence interval)	
A/H1N1	74.5% (71.9;76.9)	66.7% (59.7;73.1)
A/H3N2	66.5% (63.8;69.2)	73.0% (66.4;79.0)
B (Victoria)[2]	55.2% (52.4;58.0)	48.8% (41.7;55.9)
B (Yamagata)[3]	54.8% (52.0;57.6)	33.3% (26.9;40.3)

ATP = according to protocol. ATP cohort for immunogenicity included all evaluable subjects for whom assay results were available after vaccination for at least one study vaccine antigen.

[1] containing A/H1N1, A/H3N2 and B (Victoria lineage)

[2] recommended strain by WHO during the season 2010-2011

[3] additional B strain contained in FLULAVAL TETRA recommended in season 2008-2009

[4] GMT is reported as the absolute value

The respective post-vaccination seroprotection rates (Day 21 reciprocal titer of ≥ 40) for FLUVIRAL and FLULAVAL TETRA in adults 18 years of age and older were 92.6% and 93.7% against A/H1N1, 92.2% and 90.8% against A/H3N2, 94.6% and 96.4% against B (Victoria) and 98.0% and 99.8% against B (Yamagata).

Children (Immunogenicity Non-Inferiority)

In study Q-TIV-TF-008, the immune response of FLUVIRAL (N = 987) was compared to FLUZONE, a licensed trivalent, inactivated influenza virus vaccine (N = 979), manufactured by Sanofi Pasteur SA, in an observer-blind, randomized study in children 3 through 17 years of age. The immune responses to each of the antigens contained in FLUVIRAL formulated for the 2009-2010 season were evaluated in sera obtained after one or 2 doses of FLUVIRAL and were compared to those following the comparator influenza vaccine.

Immune responses, specifically HI antibody titers to each virus strain in the vaccine, were evaluated in sera 28 days following one or 2 doses. The non-inferiority endpoints were geometric mean antibody titers (GMTs) adjusted for baseline, and the percentage of subjects who achieved seroconversion, defined as at least a 4-fold increase in serum HI titer over baseline to ≥1:40, following vaccination, performed on the According-to-Protocol (ATP) cohort. FLUVIRAL was non-inferior to the comparator influenza for all strains based on adjusted GMTs and seroconversion rates.

Table 8 – Immune Responses to Each Antigen 28 Days After Last Vaccination in Children 3 to 17 Years of Age (ATP Cohort for Immunogenicity)[a]

GMTs Against	FLUVIRAL	Comparator[b]	GMT Ratio[c] (95% CI)
	N = 987 (95% CI)	N = 979 (95% CI)	
A/H1N1	320.9 (298.3, 345.2)	329.4 (306.8, 353.7)	1.03 (0.94, 1.13)
A/H3N2	414.7 (386.5, 444.9)	451.9 (423.8, 481.8)	1.05 (0.96, 1.13)
B	213.7 (198.5, 230.1)	200.2 (186.1, 215.3)	0.93 (0.85, 1.02)
Seroconversion[d]	**N = 987 % (95% CI)**	**N = 978 % (95% CI)**	**Difference in Seroconversion Rates[e] (95% CI)**
A/H1N1	59.8 (56.6, 62.9)	58.2 (55.0, 61.3)	-1.6 (-5.9, 2.8)
A/H3N2	68.2 (65.2, 71.1)	66.2 (63.1, 69.1)	-2.0 (-6.1, 2.1)
B	81.1 (78.5, 83.5)	78.6 (75.9, 81.2)	-2.4 (-6.0, 1.1)

ATP = according to protocol; CI = Confidence Interval.
ATP cohort for immunogenicity included all evaluable subjects for whom assay results were available after vaccination for at least one study vaccine antigen.
[a] Results obtained following vaccination with influenza vaccines formulated for the 2009-2010 season.
[b] licensed trivalent, inactivated influenza virus vaccine (Sanofi Pasteur SA).
[c] FLUVIRAL met non-inferiority criteria based on GMTs (upper limit of 2-sided 95% CI for GMT ratio [comparator vaccine/FLUVIRAL] $\leq$1.5).
[d] Seroconversion defined as at least a 4-fold increase in serum titers of HI antibodies to $\geq$1:40.
[e] FLUVIRAL met non-inferiority criteria based on seroconversion rates (upper limit of 2-sided 95% CI for difference of the comparator vaccine minus FLUVIRAL $\leq$10%).

16 NON-CLINICAL TOXICOLOGY

Non-clinical data reveal no special hazards for humans based on conventional studies of acute toxicity, local tolerance, repeated dose toxicity and reproductive/developmental toxicity.

The potential for toxicity of the trivalent vaccine was evaluated with FLULAVAL TETRA, a quadrivalent thimerosal-free (Q-QIV TF) vaccine that was manufactured by the same process as the trivalent FLUVIRAL. The Q-QIV TF vaccine was used as a representative formulation for the toxicology assessment of thimerosal-plus and thimerosal-free formulations. The vaccine has not been evaluated for carcinogenicity or mutagenic potential.

Table 9 – Toxicity Studies with Q-QIV TF Vaccine

Study	Species or Substrate	Route	Dosing Regimen	Tested Material
Single dose and local tolerance	New Zealand White rabbits	Intramuscular	Single dose: FHD	Q-QIV TF [a] Phosphate buffer saline
Repeated dose	New Zealand White rabbits	Intramuscular	3 doses at 2 weeks interval; FHD	Q-QIV TF [a] Phosphate buffer saline
Repeated dose	New Zealand White rabbits	Intramuscular	3 doses at 2 weeks interval; FHD	Q-QIV TF Phosphate buffer saline
Reproduction and development	Sprague-Dawley rats (Crl:CD (SD) IGS BR)	Intramuscular	Day -28 and -14 before pairing, then Days 3, 8, 11, 15 after mating and Day 7 of lactation; 2/5th HD	Q-QIV TF D-QIV TF [b] Phosphate buffer saline
Female fertility and embryo-fetal survival	Sprague-Dawley rats (Crl:CD (SD) IGS BR)	Intramuscular	Day -28 and -14 before pairing, and then Days 3, 8, 11, 15 after mating; 2/5th HD	Q-QIV TF Phosphate buffer saline

a. B strains from both lineages were not available at the time of testing: a trivalent influenza virus candidate vaccine was tested: 2 "A" strains + 1 "B" strain, with double the amount of antigen, in order to mimic the total amount of antigen included in the quadrivalent vaccine.
b. D-QIV TF: Dresden (Germany) manufactured antigens.
FHD: Full Human Dose
HD: Human Dose

Single Dose Toxicity

In the single dose/local tolerance study, a full human dose of Q-QIV TF vaccine was administered to New Zealand White rabbits. There were no deaths, clinical signs, or changes in body weights that could be attributed to the administration of the vaccine. There was no associated toxicity after treatment with the vaccine. Minor inflammation was seen in both treated groups; however there were no clear differences between the Q-QIV TF vaccine and the saline control group.

Repeat Dose Toxicity

In the two repeated dose studies, a full human dose of the Q-QIV-TF vaccine was administered three times within a 2-week interval. The repeated intramuscular treatment of rabbits with the vaccine induced mild, transient local effects in the injected muscles. A few hematology and clinical chemistry parameters related to the local inflammation were transiently affected. The inflammation diminished distinctly over time and a clear recovery process was observed at the end of the 28-day observation period.

Reproductive and Developmental Toxicity

Vaccination of female rats with Q-QIV TF vaccine, at doses shown to be immunogenic in the rat, had no effect on F0 female clinical condition, food consumption, weight, mating performance, fertility, or ability to produce a live litter. There was no effect on pre- or post-natal development of F1 offspring.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

FLUVIRAL (2025 – 2026)

Trivalent Influenza Vaccine (Split Virion, Inactivated)

Read this carefully before you receive **FLUVIRAL.** This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **FLUVIRAL**.

What is FLUVIRAL used for?

FLUVIRAL is a trivalent vaccine for use in adults and children from 6 months of age for the prevention of influenza disease caused by influenza virus types A and B contained in the vaccine.

Influenza is a disease of the upper airways and lungs caused by infection with a flu virus. The most common symptoms are: high temperature (fever), sore throat, coughing, general aches and pains, headaches, weakness and tiredness.

How does FLUVIRAL work?

FLUVIRAL causes the body's immune system to make antibodies to protect the person from being infected by certain types of influenza virus. This vaccine is only effective against infection by type A and B viruses. None of the ingredients in the vaccine can cause influenza. As with all vaccines, FLUVIRAL may not fully protect all people who are vaccinated.

What are the ingredients in FLUVIRAL?

Medicinal ingredients: This vaccine complies with the World Health Organization (WHO) recommendation (Northern Hemisphere) for the 2025 – 2026 season.

Each 0.5 mL dose of the vaccine contains 15 micrograms of haemagglutinin, a type of protein that has been purified from killed and split influenza viruses. The three virus strains in this vaccine are:

- A/Victoria/4897/2022 (H1N1)pdm09-like virus
- A/Croatia/10136RV/2023 (H3N2)-like virus
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus

Non-medicinal ingredients: Phosphate buffered saline, polysorbate 80, α-tocopheryl hydrogen succinate, thimerosal. Trace amounts of: egg proteins, ethanol, formaldehyde, sodium deoxycholate, and sucrose.

FLUVIRAL comes in the following dosage forms:

- 6 mL multidose vial (type 1 glass) containing 5 mL of vaccine (10 doses of 0.5 mL)

The packaging does not contain latex.

Do not use FLUVIRAL if:

- You had a severe allergic reaction (e.g., anaphylaxis) to any ingredient in the vaccine, including egg protein, or following a previous dose of any influenza vaccine.

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

- You have a **severe infection** with a high temperature. In these cases, the vaccination will be postponed until you recover. A minor infection should not be a problem.
- You have a **bleeding problem** or **bruise easily**.
- You have a **weakened immune system** due to HIV infection or due to medicines that suppress the immune system.
- You have **fainted** before or after a previous injection.
- You are **taking any other medicines** or you have recently received any other vaccine.
- Guillain-Barré (GBS) has occurred within 6 weeks of receiving a previous influenza vaccination.
- You are **pregnant or breast-feeding** seek advice from your doctor.

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 FLUVIRAL:

FLUVIRAL must not be mixed with any other vaccine in the same syringe. If FLUVIRAL is to be given at the same time as another injectable vaccine, the vaccines should always be administered at different injection sites.

How to take FLUVIRAL:

Usual dose:

One injection of 0.5 mL into the shoulder muscle or the mid-thigh muscle.

Children 6 months to less than 9 years of age who have not been vaccinated against influenza in the past will receive a second injection at least one month after the first injection.

Overdose:

If you think you, or a person you are caring for, have received too much FLUVIRAL, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using FLUVIRAL?

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

Very common (may occur with more than 1 in 10 doses):

- Pain and redness at the injection site
- Fatigue
- Headache
- Aching muscles
- Loss of appetite
- Drowsiness
- Irritability

Common (may occur with up to 1 in 10 doses)

- Red eyes
- Feeling sick, vomiting, diarrhea, stomach pain
- Swelling at the injection site, fever, chills, malaise, chest tightness
- Joint pain
- Sore throat, cough

Contact your doctor, nurse or pharmacist urgently if you experience:

- Allergic reaction (including anaphylactic and anaphylactoid reactions). These can be recognized by:
  - itchy rash of the hands and feet
  - swelling of the eyes and face
  - difficulty in breathing or swallowing
  - sudden drop in blood pressure and loss of consciousness.
- Temporary inflammation of the nerves causing pain, weakness and paralysis called Guillain-Barré syndrome

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 GlaxoSmithKline Inc. 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°C and 8°C.

Do not freeze.

Keep out of reach and sight of children.

If you want more information about FLUVIRAL:

- 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.gsk.com, or by calling 1-800-387-7374.

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