Sanofi Pasteur
476 Fluzone® Intradermal Quadrivalent

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fluzone® Intradermal Quadrivalent safely and effectively. See full prescribing information for Fluzone Intradermal Quadrivalent.

Fluzone Intradermal Quadrivalent (Influenza Vaccine)
Suspension for Intradermal Injection
2017-2018 Formula
Initial US Approval (Fluzone Intradermal Quadrivalent): 2014

----------INDICATIONS AND USAGE----------

Fluzone Intradermal Quadrivalent is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. (1)

Fluzone Intradermal Quadrivalent is approved for use in persons 18 through 64 years of age. (1)

---------- DOSAGE AND ADMINISTRATION ----------

• **For intradermal use only** (2)

A single 0.1 mL dose for intradermal injection in adults 18 through 64 years of age. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------

Suspension for injection in a prefilled microinjection system, 0.1 mL. (3)

----------CONTRAINDICATIONS ----------

Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or after previous dose of any influenza vaccine. (4)

---------- WARNINGS AND PRECAUTIONS ----------

• If Guillain-Barré syndrome (GBS) has occurred within 6 weeks following previous influenza vaccination, the decision to give Fluzone Intradermal Quadrivalent should be based on careful consideration of the potential benefits and risks. (5.1)

---------- ADVERSE REACTIONS ----------

• In adults 18 through 64 years of age, the most common (≥10%) injection-site reactions were pain (53.3%), pruritus (52.1%), erythema (36.7%), swelling (19.5%), and induration (17.0%); the most common solicited systemic adverse reactions were myalgia (34.1%), headache (33.1%), malaise (27.7%), and shivering (12.1%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur Inc., at 1-800-822-2463 (1-800-VACCINE) or Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or www.vaers.hhs.gov.

---------- USE IN SPECIFIC POPULATIONS ----------

• Safety and effectiveness of Fluzone Intradermal Quadrivalent have not been established in pregnant women. (8.1)
• Pregnancy: Pregnancy registry available. Call Sanofi Pasteur Inc. at 1-800-822-2463. (8.1)

See **17 FOR PATIENT COUNSELING INFORMATION and FDA - approved patient labeling.**

Revised date: July 2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION:

1 INDICATIONS AND USAGE

Fluzone® Intradermal Quadrivalent is indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine.

Fluzone Intradermal Quadrivalent is approved for use in persons 18 through 64 years of age.

2 DOSAGE AND ADMINISTRATION

- **For intradermal use only**

2.1 Dose and Schedule

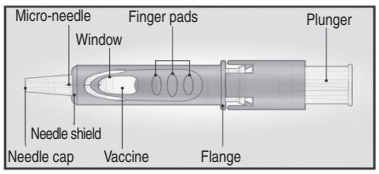
Fluzone Intradermal Quadrivalent should be administered as a single 0.1 mL injection by the intradermal route in adults 18 through 64 years of age.

2.2 Administration

Inspect Fluzone Intradermal Quadrivalent visually for particulate matter and/or discoloration prior to administration. If either of these conditions exist, the vaccine should not be administered.

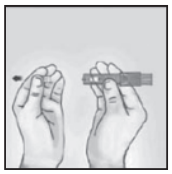
The preferred site of injection is the skin in the region of the deltoid. Note: A potential way to make vaccination more efficient is to have the patient place the hand of the arm being immunized on his/her hip, so the arm bends at the elbow. This can help create a more accessible angle to the skin in the deltoid region.

Fluzone Intradermal Quadrivalent should not be combined through reconstitution or mixed with any other vaccine.



1. Gently shake the device and remove needle cap

To prepare for vaccination, gently shake the device and remove needle cap before administering the vaccine.



2. Position the device in your hand between the thumb and middle finger, keeping the index finger free

Hold the device by placing the thumb and middle finger on the finger pads above device window. Keep the index finger free.

3. Gently pierce the skin over the deltoid region

Using light pressure, gently pierce the skin perpendicular to the deltoid region.

4. Press the plunger to inject the vaccine

Using index finger, gently press the plunger to inject the vaccine. Do not aspirate. When the plunger stops, vaccination is complete. Note: Excessive pressure on the plunger may prematurely activate the needle shield on the patient's arm. Because the vaccine is injected into the skin, a wheal (superficial bump) and/or redness may be visible at the injection site.

5. Activate the needle shield and dispose

Remove the needle from the skin. Direct the needle away from you and others. Push very firmly with the thumb on the plunger to activate the needle shield. You will hear a click when the shield extends to cover the needle. Dispose the device in an appropriate container.

3 DOSAGE FORMS AND STRENGTHS

Fluzone Intradermal Quadrivalent is a suspension for injection.

Fluzone Intradermal Quadrivalent is supplied in a single-dose prefilled microinjection system, 0.1 mL, for adults 18 through 64 years of age.

4 CONTRAINDICATIONS

Do not administer Fluzone Intradermal Quadrivalent to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine [see *Description* (11)], including egg protein, or to a previous dose of any influenza vaccine.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome (GBS) has occurred within 6 weeks following previous influenza vaccination, the decision to give Fluzone Intradermal Quadrivalent should be based on careful consideration of the potential benefits and risks. The 1976 swine influenza vaccine was associated with an elevated risk of GBS. Evidence for a causal relation of GBS with other influenza vaccines is inconclusive; if an excess risk exists, it is probably slightly more than 1 additional case per 1 million persons vaccinated (See references 1 and 2).

5.2 Preventing and Managing Allergic Reactions

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of Fluzone Intradermal Quadrivalent.

5.3 Altered Immunocompetence

If Fluzone Intradermal Quadrivalent is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the expected immune response may not be obtained.

5.4 Limitations of Vaccine Effectiveness

Vaccination with Fluzone Intradermal Quadrivalent may not protect all recipients.

6 ADVERSE REACTIONS

In adults 18 through 64 years of age, the most common (≥10%) injection-site reactions were pain (53.3%), pruritus (52.1%), erythema (36.7%), swelling (19.5%), and induration (17.0%); the most common solicited systemic adverse reactions were myalgia (34.1%), headache (33.1%), malaise (27.7%), and shivering (12.1%).

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trial(s) of a vaccine cannot be directly compared to rates in the clinical trial(s) of another vaccine, and may not reflect the rates observed in practice.

Fluzone Intradermal Quadrivalent in Adults 18 Through 64 Years of Age

Study 1 (NCT01712984, see http://clinicaltrials.gov) was a randomized, double-blind, active-controlled, multi-center safety and immunogenicity study conducted in the US. In this study, adults 18 through 64 years of age received a single injection of either Fluzone Intradermal Quadrivalent or one of two formulations of a comparator trivalent influenza vaccine by the intradermal route (TIV-ID1 or TIV-ID2). Each of the trivalent formulations contained an influenza type B virus that corresponded to one of the two type B viruses in Fluzone Intradermal Quadrivalent (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). The safety analysis set, comprised of all participants who received a study vaccine, included 3355 recipients. Among participants in the three vaccine groups combined, 61.3% were female, 84.9% White, 11.9% Black, 1.1% Asian, and 2.1% were of other racial/ethnic groups. Table 1 summarizes solicited injection-site and systemic adverse reactions reported within 7 days post-vaccination via diary cards. Participants were monitored for unsolicited adverse events for 28 days after vaccination and serious adverse events (SAEs) for 6 months after vaccination.

Table 1: Study 1[a]: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Adults 18 Through 64 Years of Age (Safety Analysis Set)[b]

	Fluzone Intradermal Quadrivalent (N[e]=1649-1656)			TIV-ID1[c] (B Yamagata) (N[e]=819-820)			TIV-ID2[d] (B Victoria) (N[e]=836-838)		
	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)	Any (%)	Grade 2[f] (%)	Grade 3[g] (%)
Injection-site adverse reactions									
Pain	53.3	9.7	1.4	48.2	7.9	1.2	50.1	7.5	1.4
Pruritis	52.1	9.4	2.8	45.4	9.0	1.8	44.6	7.5	2.3
Erythema	36.7	10.9	0.4	34.0	9.8	0.1	32.1	6.3	0.4
Swelling	19.5	4.8	0.1	14.8	3.9	0.0	14.7	2.0	0.0
Induration	17.0	2.8	<0.1	13.5	1.8	0.0	11.2	2.2	0.0
Ecchymosis	2.6	0.4	0.0	1.8	0.4	0.0	1.8	0.1	0.0
Systemic adverse reactions									
Myalgia	34.1	8.1	2.6	29.0	8.2	1.5	31.1	7.4	2.5
Headache	33.1	9.1	3.2	31.3	9.6	2.4	33.2	8.9	1.8
Malaise	27.7	9.2	3.0	26.3	6.6	1.8	30.4	8.4	2.5
Shivering	12.1	2.0	1.4	10.4	2.2	0.6	11.2	3.3	1.6
Fever (≥100.4°F)[h]	0.8	0.2	0.2	0.7	0.2	0.1	0.5	0.0	0.0

[a]NCT01712984
[b]The safety analysis set includes all persons who received study vaccine
[c]TIV-ID1: 2012-2013 Fluzone Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Texas/6/2011 (Yamagata lineage), licensed
[d]TIV-ID2: Investigational Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), non-licensed
[e]N is the number of vaccinated participants with available data for the events listed
[f]Grade 2 - Injection-site pain and injection-site pruritus: Some interference with activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥51 to ≤100 mm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, Malaise, and Shivering: Some interference with activity
[g]Grade 3 - Injection-site pain and injection-site pruritus: Significant – prevents daily activity; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: >100 mm; Fever: ≥102.1°F; Myalgia, Headache, Malaise, and Shivering: Significant – prevents daily activity
[h]Fever measured by any route

Unsolicited non-serious adverse events were reported in 382 (22.8%) recipients in the Fluzone Intradermal Quadrivalent group, 169 (20.2%) recipients in the TIV-ID1 group, and 212 (25.1%) recipients in the TIV-ID2 group. The most commonly reported unsolicited non-

serious adverse events were cough, headache, and oropharyngeal pain. During the 28 days following vaccination, a total of 6 (0.4%) recipients in the Fluzone Intradermal Quadrivalent group, 2 (0.2%) recipients in the TIV-ID1 group, and 3 (0.4%) recipients in the TIV-ID2 group experienced at least one SAE; no deaths occurred. Throughout the study period (6 months post-vaccination), a total of 20 (1.2%) recipients in the Fluzone Intradermal Quadrivalent group, 14 (1.7%) recipients in the TIV-ID1 group, and 11 (1.3%) recipients in the TIV-ID2 group experienced at least one SAE. One death (177 days post-vaccination due to acute coronary myocardial infarction) occurred in the Fluzone Intradermal Quadrivalent group. This death was considered not related to the study vaccine by the Investigator.

Fluzone Intradermal (Trivalent Influenza Vaccine) in Adults 18 Through 64 Years of Age
The safety experience with Fluzone Intradermal (trivalent influenza vaccine) is relevant to Fluzone Intradermal Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions. In a study of adults 18 through 64 years of age (NCT00772109), safety was evaluated in 2855 Fluzone Intradermal recipients compared to 1421 Fluzone (trivalent influenza vaccine) recipients. Rates of solicited injection-site reactions and systemic adverse events in adults are shown in Table 2.

Table 2: Frequency of Solicited Injection-Site Reactions and Systemic Adverse Events Within 7 Days After Vaccine Injection, Adults 18 Through 64 Years of Age

	Fluzone Intradermal (N[a]=2798-2802) Percentage			Fluzone (N[a]=1392-1394) Percentage		
	Any	Grade 2[b]	Grade 3[c]	Any	Grade 2[b]	Grade 3[c]
Injection-Site Erythema	76.4	28.8	13.0	13.2	2.1	0.9
Injection-Site Induration	58.4	13.0	3.4	10.0	2.3	0.5
Injection-Site Swelling	56.8	13.4	5.4	8.4	2.1	0.9
Injection-Site Pain	51.0	4.4	0.6	53.7	5.8	0.8
Injection-Site Pruritus	46.9	4.1	1.1	9.3	0.4	0.0
Injection-Site Ecchymosis	9.3	1.4	0.4	6.2	1.1	0.4
Headache	31.2	6.4	1.5	30.3	6.5	1.6
Myalgia	26.5	4.6	1.5	30.8	5.5	1.4
Malaise	23.3	5.5	2.2	22.2	5.5	1.8
Shivering	7.3	1.5	0.7	6.2	1.1	0.6
Fever[d] (≥99.5°F)	3.9	0.6	0.1	2.6	0.4	0.2

[a] N is the number of vaccinated subjects with available data for the events listed
[b] Grade 2 - Injection-site erythema, Injection-site induration, Injection-site swelling, and Injection-site ecchymosis: ≥2.5 cm to <5 cm; Injection-site pain and Injection-site pruritus: sufficiently discomforting to interfere with normal behavior or activities; Fever: >100.4°F to ≤102.2°F; Headache, Myalgia, Malaise, and Shivering: interferes with daily activities
[c] Grade 3 - Injection-site erythema, Injection-site induration, Injection-site swelling, and Injection-site ecchymosis: ≥5 cm; Injection-site pain: incapacitating, unable to perform usual activities; Injection-site pruritus: incapacitating, unable to perform usual activities, may have/or required medical care or absenteeism; Fever: >102.2°F; Headache, Myalgia, Malaise, and Shivering: prevents daily activities
[d] Fever - The percentage of temperature measurements that were taken by oral or axillary routes, or not recorded were 99.9%, <0.1%, and 0.1%, respectively, for Fluzone Intradermal; and 99.6%, 0.0%, and 0.4%, respectively, for Fluzone

6.2 Post-Marketing Experience
The following events have been spontaneously reported during the post-approval use of the trivalent formulation of Fluzone. Because these events 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 vaccine exposure. Adverse events were included based on one or more of the following factors: severity, frequency of reporting, or strength of evidence for a causal relationship to Fluzone.

- *Blood and Lymphatic System Disorders*: Thrombocytopenia, lymphadenopathy
- *Immune System Disorders*: Anaphylaxis, other allergic/hypersensitivity reactions (including urticaria, angioedema)
- *Eye disorders*: Ocular hyperemia
- *Nervous System Disorders*: Guillain-Barré syndrome (GBS), convulsions, febrile convulsions, myelitis (including encephalomyelitis and transverse myelitis), facial palsy (Bell's palsy), optic neuritis/neuropathy, brachial neuritis, syncope (shortly after vaccination), dizziness, paresthesia
- *Vascular Disorders*: Vasculitis, vasodilation/flushing
- *Respiratory, Thoracic and Mediastinal Disorders*: Dyspnea, pharyngitis, rhinitis, cough, wheezing, throat tightness
- *Skin and Subcutaneous Tissue Disorders*: Stevens-Johnson syndrome
- *General Disorders and Administration Site Conditions*: Pruritus, asthenia/fatigue, pain in extremities, chest pain
- *Gastrointestinal Disorders*: Vomiting

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category B: The developmental and reproductive toxicity study performed with the trivalent formulation of Fluzone Intradermal is relevant to Fluzone Intradermal Quadrivalent because both vaccines share the same manufacturing process and route of administration. The study, in which the trivalent formulation of Fluzone Intradermal (27 mcg) was administered to female rabbits at a dose approximately 20 times the human dose (on a mg/kg basis), revealed no evidence of impaired female fertility or harm to the fetus. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Fluzone Intradermal Quadrivalent should be used during pregnancy only if clearly needed.

Sanofi Pasteur Inc. is maintaining a prospective pregnancy exposure registry to collect data on pregnancy outcomes and newborn health status following vaccination with Fluzone Intradermal Quadrivalent during pregnancy. Healthcare providers are encouraged to enroll women who receive Fluzone Intradermal Quadrivalent during pregnancy in Sanofi Pasteur Inc.'s vaccination pregnancy registry by calling 1-800-822-2463.

8.3 Nursing Mothers
It is not known whether Fluzone Intradermal Quadrivalent is excreted in human milk. Because many drugs are excreted in human milk, the decision to give Fluzone Intradermal Quadrivalent to a nursing woman should be based on careful consideration of the potential benefits and risks.

8.4 Pediatric Use
Safety and effectiveness of Fluzone Intradermal Quadrivalent in persons <18 years of age have not been established. In a clinical trial, 97 infants and toddlers 6 months through 35 months of age and 160 children 3 years through 8 years of age were enrolled to receive two injections of the trivalent formulation of Fluzone Intradermal. Infants and children in a control group received two injections of Fluzone. Fluzone Intradermal was associated with increased local reactogenicity relative to Fluzone. The size of the study was not adequate to reliably evaluate serious adverse events or the immune response elicited by Fluzone Intradermal relative to Fluzone.

8.5 Geriatric Use
Safety and effectiveness of Fluzone Intradermal Quadrivalent in persons 65 years of age and older have not been established.

11 DESCRIPTION
Fluzone Intradermal Quadrivalent (Influenza Vaccine) for intradermal injection is an inactivated influenza vaccine, prepared from influenza viruses propagated in embryonated chicken eggs. The virus-containing allantoic fluid is harvested and inactivated with formaldehyde. Influenza virus is concentrated and purified in a linear sucrose density gradient solution using a continuous flow centrifuge. The virus is then chemically disrupted using a non-ionic surfactant, octylphenol ethoxylate (Triton® X-100), producing a "split virus". The split virus is further purified and then suspended in sodium phosphate-buffered isotonic sodium chloride solution. The Fluzone Intradermal Quadrivalent process uses an additional concentration factor after the ultrafiltration step in order to obtain a higher hemagglutinin (HA) antigen concentration. Antigens from the four strains included in the vaccine are produced separately and then combined to make the quadrivalent formulation.

Fluzone Intradermal Quadrivalent suspension for injection is clear and slightly opalescent in color.

Neither antibiotics nor preservative are used in the manufacture of Fluzone Intradermal Quadrivalent.

The Fluzone Intradermal Quadrivalent microinjection system is not made with natural rubber latex.

Fluzone Intradermal Quadrivalent is standardized according to United States Public Health Service requirements and is formulated to contain the following four influenza strains recommended for the 2017-2018 influenza season: A/Michigan/45/2015 X-275 (H1N1), A/Hong Kong/4801/2014 X-263B (H3N2), B/Phuket/3073/2013 (B Yamagata lineage), and B/Brisbane/60/2008 (B Victoria lineage). The amounts of HA and other ingredients per dose of vaccine are listed in Table 3.

Table 3: Fluzone Intradermal Quadrivalent Ingredients

Ingredient	Quantity per 0.1 mL Dose
Active Substance: Split influenza virus, inactivated strains[a]:	36 mcg HA total
A (H1N1)	9 mcg HA
A (H3N2)	9 mcg HA
B/(Victoria lineage)	9 mcg HA
B/(Yamagata lineage)	9 mcg HA
Other:	
Sodium phosphate-buffered isotonic sodium chloride solution	QS[b] to appropriate volume
Formaldehyde	≤20 mcg
Octylphenol ethoxylate	≤55 mcg

[a] per United States Public Health Service (USPHS) requirement
[b] Quantity Sufficient

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Influenza illness and its complications follow infection with influenza viruses. Global surveillance of influenza identifies yearly antigenic variants. Since 1977, antigenic variants of influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation. Since 2001, two distinct lineages of influenza B (Victoria and Yamagata lineages) have co-circulated worldwide. Protection from influenza virus infection has not been correlated with a specific level of hemagglutination inhibition (HAI) antibody titer post-vaccination. However, in some human studies, antibody titers ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects (See references 3 and 4).

Antibodies against one influenza virus type or subtype confer limited or no protection against another. Furthermore, antibodies 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 new strains in each year's influenza vaccine. Therefore, influenza vaccines are standardized to contain the hemagglutinins of influenza virus strains, representing the influenza viruses likely to be circulating in the US during the influenza season.

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

13 NON-CLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Fluzone Quadrivalent has not been evaluated for carcinogenic or mutagenic potential. A reproductive study of female rabbits vaccinated with Fluzone Quadrivalent was performed and revealed no evidence of impaired female fertility [see *Pregnancy* (8.1)].

14 CLINICAL STUDIES

14.1 Immunogenicity of Fluzone Intradermal Quadrivalent in Adults 18 through 64 Years of Age

In Study 1 (NCT01712984), study participants were randomized to receive one dose of Fluzone Intradermal Quadrivalent, TIV-ID1, or TIV-ID2. Of the 2249 participants randomized to provide blood samples for immunogenicity analyses, 2113 adults 18 through 64 years of age were included in the per-protocol analysis set. The distribution of demographics was similar to that of the safety analysis set [see *Clinical Trials Experience* (6.1)].

HAI antibody geometric mean titers (GMTs) and seroconversion rates 28 days following vaccination with Fluzone Intradermal Quadrivalent were non-inferior to those following each TIV-ID for all four strains, based on pre-specified criteria (see Table 4 and Table 5).

Table 4: Study 1[a]: Non-inferiority of Fluzone Intradermal Quadrivalent Relative to TIV-ID for Each Strain by HAI Antibody GMTs at 28 Days Post-Vaccination, Adults 18 Through 64 Years of Age (Per-protocol Analysis Set)[b]

Antigen Strain	Fluzone Intradermal Quadrivalent		Pooled TIV-ID[c]				GMT Ratio (95% CI)[d]
	M[e]	GMT	M[e]		GMT		
A (H1N1)	1041	589	1072		680		0.87 (0.78; 0.97)
A (H3N2)	1041	368	1071		430		0.86 (0.77; 0.96)
	Fluzone Intradermal Quadrivalent		TIV-ID1[f] (B Yamagata)		TIV-ID2[g] (B Victoria)		GMT Ratio (95% CI)[d]
	M[e]	GMT	M[e]	GMT	M[e]	GMT	
B/Texas/6/2011 (B Yamagata)	1041	105	539	93.5	533	(54.0)[h]	1.13 (1.02; 1.25)
B/Brisbane/60/2008 (B Victoria)	1041	136	538	(66.7)[i]	533	130	1.05 (0.94; 1.16)

[a]NCT01712984
[b]Per-protocol analysis set included all persons who underwent serologic testing and had no study protocol deviations
[c]Pooled TIV-ID group includes participants vaccinated with either TIV-ID1 or TIV-ID2
[d]Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the ratio of GMTs (Fluzone Intradermal Quadrivalent divided by pooled TIV-ID for the A strains, or the TIV-ID containing the corresponding B strain) was >2/3
[e]M is the number of participants in the per-protocol analysis set with available data for the considered endpoint
[f]TIV-ID1: 2012-2013 Fluzone Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Texas/6/2011 (Yamagata lineage), licensed
[g]TIV-ID2: Investigational Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), non-licensed
[h]TIV-ID2 did not contain B/Texas/6/2011
[i]TIV-ID1 did not contain B/Brisbane/60/2008

Table 5: Study 1[a]: Non-inferiority of Fluzone Intradermal Quadrivalent Relative to TIV-ID for Each Strain by Seroconversion Rates at 28 Days Post-Vaccination, Adults 18 Through 64 Years of Age (Per-protocol Analysis Set)[b]

Antigen Strain	Fluzone Intradermal Quadrivalent		Pooled TIV-ID[c]				Difference of Seroconversion Rates (95% CI)[f]
	M[d]	Seroconversion[e] (%)	M[d]		Seroconversion[e] (%)		
A (H1N1)	1041	57.6	1072		60.4		-2.72 (-6.90; 1.47)
A (H3N2)	1040	58.5	1071		59.8		-1.30 (-5.48; 2.89)
	Fluzone Intradermal Quadrivalent		TIV-ID1[g] (B Yamagata)		TIV-ID2[h] (B Victoria)		Difference of Seroconversion Rates (95% CI)[f]
	M[d]	Seroconversion[e] (%)	M[d]	Seroconversion[e] (%)	M[d]	Seroconversion[e] (%)	
B/Texas/6/2011 (B Yamagata)	1041	55.7	539	46.9	533	(24.6)[i]	8.78 (3.58; 13.9)
B/Brisbane/60/2008 (B Victoria)	1041	50.4	538	(22.1)[j]	533	44.1	6.34 (1.13; 11.5)

[a]NCT01712984
[b]Per-protocol analysis set included all persons who underwent serologic testing and had no study protocol deviations
[c]Pooled TIV group includes participants vaccinated with either TIV-ID1 or TIV-ID2
[d]M is the number of participants in the per-protocol analysis set with available data for the considered endpoint
[e]Seroconversion: Paired samples with pre-vaccination HAI titer <1:10 and post-vaccination titer ≥1:40 or a minimum 4-fold increase for participants with pre-vaccination titer ≥1:10
[f]Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference in seroconversion rates (Fluzone Intradermal Quadrivalent minus pooled TIV-ID for the A strains, or the TIV-ID containing the corresponding B strain) was >-10%
[g]TIV-ID1: 2012-2013 Fluzone Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Texas/6/2011 (Yamagata lineage), licensed
[h]TIV-ID2: Investigational Intradermal TIV containing A/California/7/2009 (H1N1), A/Victoria/361/2011 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), non-licensed
[i]TIV-ID2 did not contain B/Texas/6/2011
[j]TIV-ID1 did not contain B/Brisbane/60/2008

15 REFERENCES

1 Lasky T, Terracciano GJ, Magder L, et al. The Guillain-Barré syndrome and the 1992-1993 and 1993-1994 influenza vaccines. N Engl J Med 1998;339:1797-802.
2 Baxter, R, et al. Lack of Association of Guillain-Barré Syndrome with Vaccinations. Clin Infect Dis 2013;57(2):197-204.
3 Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza vaccination. Virus Res 2004;103:133-138.
4 Hobson D, Curry RL, Beare AS, Ward-Gardner A. The role of serum haemagglutination-inhibiting antibody in protection against challenge infection with influenza A2 and B viruses. J Hyg Camb 1972;70:767-777.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Single-dose prefilled microinjection system, 0.1 mL (NDC 49281-712-48) (not made with natural rubber latex). Supplied as package of 10 (NDC 49281-712-40).

16.2 Storage and Handling

Store Fluzone Intradermal Quadrivalent refrigerated at 2° to 8°C (35° to 46°F). DO NOT FREEZE. Discard if vaccine has been frozen.

Do not use after the expiration date shown on the label.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information). Inform the vaccine recipient or guardian:

- Fluzone Intradermal Quadrivalent contains killed viruses and cannot cause influenza.
- Fluzone Intradermal Quadrivalent stimulates the immune system to protect against influenza, but does not prevent other respiratory infections.
- Annual influenza vaccination is recommended.
- Because the vaccine is injected into the skin, patients may experience visible reactions at the injection site, such as a wheal (superficial bump), redness, and swelling. Patients may also experience pain, itching, and induration at the injection site.
- Report adverse reactions to their healthcare provider and/or to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or *http://vaers.hhs.gov*.
- Sanofi Pasteur Inc. is maintaining a prospective pregnancy exposure registry to collect data on pregnancy outcomes and newborn health status following vaccination with Fluzone Intradermal Quadrivalent during pregnancy. Women who receive Fluzone Intradermal Quadrivalent during pregnancy are encouraged to contact Sanofi Pasteur Inc. directly or have their healthcare provider contact Sanofi Pasteur Inc. at 1-800-822-2463.

Manufactured by:
Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

SANOFI PASTEUR