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HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Fluzone (Influenza Vaccine) injectable suspension, for intramuscular use
2025 Formula
Initial U.S. Approval: 1980

----------RECENT MAJOR CHANGES----------

Dosage and Administration, Dose and Schedule (2.1)	03/2024
Warnings and Precautions, Syncope (5.5)	03/2024

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

Fluzone Southern Hemisphere is a vaccine indicated for active immunization for the prevention of disease caused by influenza A subtype viruses and type B virus contained in the vaccine. (1)
Fluzone Southern Hemisphere is approved for use in persons 6 months of age and older. (1)

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

- **For intramuscular use (2)**

Age	Vaccination Status	Dose	Schedule
6 months through 35 months	Not previously vaccinated with influenza vaccine or unknown vaccination history	Two doses, either 0.25 mL or 0.5mL*	Administer at least 4 weeks apart
	Previously vaccinated with influenza vaccine	One or two doses†, either 0.25 mL or 0.5 mL*	If two doses, administer at least 4 weeks apart
36 months through 8 years	Not previously vaccinated with influenza vaccine or unknown vaccination history	Two 0.5 mL doses	Administer at least 4 weeks apart
	Previously vaccinated with influenza vaccine	One or two 0.5 mL doses†	If two doses, administer at least 4 weeks apart
9 years and older	-	One 0.5 mL dose	-

*The schedule can be completed as two 0.25-mL doses ≥ 4 weeks apart, two 0.5-mL doses ≥ 4 weeks apart, or any combination of 2 doses (either 0.25 mL or 0.5 mL) administered ≥ 4 weeks apart.

†To determine if 1 or 2 doses are required, refer to Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines
"-" Indicates information is not applicable

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

Fluzone is an injectable suspension.

For individuals 6 months through 35 months, a single dose is 0.25 mL or 0.5 mL.

For individuals 36 months and older, a single dose is 0.5 mL. (3)

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

Do not administer Fluzone to anyone with a history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or after previous dose of any influenza vaccine. (4, 11)

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

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

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

- In children 6 months through 8 years of age, the most common injection-site adverse reactions were pain or tenderness (>50%) and redness (>25%); the most common solicited systemic adverse reactions were irritability and drowsiness (>25% of children 6 months through 35 months) and myalgia (>20% of children 3 years through 8 years). (6.1)
- In adults 18 through 64 years of age, the most common injection-site adverse reaction was pain (>50%); the most common solicited systemic adverse reactions were headache and myalgia (>30%). (6.1)
- In adults ≥65 years of age, the most common injection-site adverse reaction was pain (>20%); the most common solicited systemic adverse reactions were headache, myalgia, and malaise (>10%). (6.1)

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

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

- Antibody responses to Fluzone are lower in persons ≥65 years of age than in younger adults. (8.5)

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

Revised: x/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

Fluzone Southern Hemisphere is approved for use in persons 6 months of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular use

2.1 Dose and Schedule

The dose and schedule for Fluzone Southern Hemisphere are presented in Table 1.

Table 1: Dose and Schedule for Fluzone Southern Hemisphere

Age	Vaccination Status	Dose	Schedule
6 months through 35 months	Not previously vaccinated with influenza vaccine or unknown vaccination history	Two doses, either 0.25 mL or 0.5 mL*	Administer at least 4 weeksapart
	Previously vaccinated with influenza vaccine	One or two doses†, either 0.25 mL or 0.5 mL*	If two doses, administer at least 4 weeksapart
36 months through 8 years	Not previously vaccinated with influenza vaccine or unknown vaccination history	Two 0.5 mL doses	Administer at least 4 weeks apart
	Previously vaccinated with influenza vaccine	One or two 0.5 mL doses†	If two doses, administer at least 4 weeks apart
9 years and older	-	One 0.5 mL dose	-

* The schedule can be completed as two 0.25-mL doses ≥ 4 weeks apart, two 0.5-mL doses ≥ 4 weeks apart, or any combination of 2 doses (either 0.25 mL or 0.5 mL) administered ≥ 4 weeks apart

†To determine if 1 or 2 doses are required, refer to Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines

"-" Indicates information is not applicable

2.2 Administration

Fluzone Southern Hemisphere is clear and slightly opalescent in color. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exist, the vaccine should not be administered.

Before administering a dose of vaccine, shake the prefilled syringe or multi-dose vial.

A maximum of ten doses can be withdrawn from the multi-dose vial.

Administer each dose intramuscularly.

3 DOSAGE FORMS AND STRENGTHS

Fluzone Southern Hemisphere is an injectable suspension.

For individuals 6 months through 35 months, a single dose is 0.25 mL or 0.5 mL.

For individuals 36 months and older, a single dose is 0.5 mL.

4 CONTRAINDICATIONS

Do not administer Fluzone Southern Hemisphere to anyone with a history of 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 Southern Hemisphere 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. (1)

5.2 Preventing and Managing Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of Fluzone Southern Hemisphere.

5.3 Altered Immunocompetence

If Fluzone Southern Hemisphere 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 Southern Hemisphere may not protect all recipients.

5.5 Syncope

Syncope (fainting) has been reported following vaccination with Fluzone Southern Hemisphere. Procedures should be in place to avoid injury from fainting.

6 ADVERSE REACTIONS

Fluzone Southern Hemisphere and Fluzone are manufactured using the same process. This section summarizes data obtained from clinical studies with Fluzone and Fluzone Quadrivalent.

In children 6 months through 8 years of age, the most common injection-site adverse reactions were pain or tenderness (>50%) and redness (>25%); the most common solicited systemic adverse reactions were irritability and drowsiness (>25% of children 6 months through 35 months) and myalgia (>20% of children 3 years through 8 years).

In adults 18 through 64 years of age, the most common injection-site adverse reaction was pain (>50%); the most common solicited systemic adverse reactions were headache and myalgia (>30%).

In adults ≥65 years of age, the most common injection-site adverse reaction was pain (>20%); the most common solicited systemic adverse reactions were headache, myalgia, and malaise (>10%).

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.

Children 6 Months through 8 Years of Age

Study 1 (NCT00391391) was a multi-center study conducted in the US. In this study, children 6 months through 35 months of age received two 0.25 mL doses of Fluzone, and children 3 years through 8 years of age received two 0.5 mL doses of Fluzone, irrespective of previous influenza vaccination history. The two doses (2006-2007 formulation) were administered 26 to 30 days apart. The safety analysis set included 97 children 6 months through 35 months of age and 163 children 3 years through 8 years of age. Table 2 and Table 3 summarize solicited injection site adverse reactions and systemic adverse reactions reported within 7 days post-vaccination via diary cards.

Table 2: Frequency of Solicited Injection Site and Systemic Adverse Reactions Within 7 Days After Vaccination with Fluzone, Children 6 Through 35 Months of Age (Study 1[#])

	Dose 1 (N[*]=90-92) Percentage			Dose 2 (N[*]=86-87) Percentage		
	Any	**Moderate[†]**	**Severe[‡]**	**Any**	**Moderate[†]**	**Severe[‡]**
Injection-Site Tenderness	47.3	8.8	0.0	56.3	3.4	1.1
Injection-Site Erythema	29.3	0.0	0.0	32.2	1.1	0.0
Injection-Site Swelling	16.7	0.0	0.0	14.9	0.0	0.0
Injection-Site Induration	14.4	0.0	0.0	16.1	0.0	0.0
Injection-Site Ecchymosis	14.4	1.1	0.0	14.9	2.3	0.0
Fever[§] (≥100.4°F)	11.0	4.4	0.0	10.3	3.4	1.1
Vomiting	6.6	1.1	0.0	8.1	5.8	0.0
Crying Abnormal	31.9	11.0	0.0	18.6	7.0	2.3
Drowsiness	26.4	1.1	0.0	26.7	4.7	0.0
Appetite Lost	23.1	8.8	0.0	19.8	5.8	1.2
Irritability	42.9	19.8	1.1	34.9	17.4	4.7

[#] (NCT00391391)

[*] N is the number of vaccinated participants with available data for the adverse reactions listed

[†] Moderate - Injection-site tenderness: cries and protests when injection site is touched; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥2.5 cm to <5 cm; Fever: >101.3°F to ≤103.1°F; Vomiting: 2 to 5 episodes per 24 hours; Crying abnormal: 1 to 3 hours; Drowsiness: not interested in surroundings or did not wake up for a meal; Appetite lost: missed 1 or 2 feeds completely; Irritability: requiring increased attention

[‡] Severe - Injection-site tenderness: cries when injected limb is moved or the movement of the injected limb is reduced; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥5 cm; Fever: >103.1°F; Vomiting: ≥6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal: >3 hours; Drowsiness: sleeping most of the time or difficulty to wake up; Appetite lost: refuses ≥3 feeds or refuses most feeds; Irritability: inconsolable

[§] Fever - The percentage of temperature measurements that were taken by rectal, axillary, or oral routes, or not recorded were 69.2%, 17.6%, 13.2%, and 0.0%, respectively, for Dose 1; and 69.0%, 13.8%, 16.1%, and 1.1%, respectively, for Dose 2

Table 3: Frequency of Solicited Injection Site and Systemic Adverse Reactions Within 7 Days After Vaccination with Fluzone, Children 3 Through 8 Years of Age (Study 1[#])

	Dose 1 (N[*]=150-151) Percentage			Dose 2 (N[*]=144-145) Percentage		
	Any	**Moderate[†]**	**Severe[‡]**	**Any**	**Moderate[†]**	**Severe[‡]**
Injection-Site Pain	59.3	8.0	0.0	62.1	9.7	0.7
Injection-Site Erythema	27.8	3.3	0.7	27.6	2.1	0.7
Injection-Site Swelling	19.9	5.3	0.0	14.5	2.8	0.0
Injection-Site Induration	16.6	2.0	0.0	11.7	1.4	0.0
Injection-Site Ecchymosis	12.6	0.7	0.7	15.2	0.7	0.0
Injection-Site Pruritus	7.3	-	-	13.2	-	-
Fever[§] (≥99.5°F)	11.9	2.6	2.0	9.7	1.4	1.4
Headache	16.7	2.0	0.7	11.8	1.4	1.4
Malaise	20.0	2.7	1.3	14.6	4.2	0.7
Myalgia	28.0	5.3	0.0	17.4	4.2	0.0

[#] (NCT00391391)

[*] N is the number of vaccinated participants with available data for the adverse reactions listed

[†] Moderate - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥2.5 cm to <5 cm; Fever: >100.4°F to ≤102.2°F; Headache, Malaise, and Myalgia: interferes with daily activities

[‡] Severe - Injection-site pain: incapacitating, unable to perform usual activities, may have/or required medical care or absenteeism; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥5 cm; Fever: >102.2°F; Headache, Malaise, and Myalgia: prevents daily activities

[§] Fever - The percentage of temperature measurements that were taken by oral or axillary routes, or not recorded were 93.4%, 6.6%, and 0.0%, respectively, for Dose 1; and 93.1%, 6.2%, and 0.7%, respectively, for Dose 2

"-" Indicates information was not collected

During the period from the first vaccination through 6 months following the second vaccination, there were no serious adverse events considered to be caused by vaccination and no deaths reported in this study.

Study 2 (NCT01240746) was a single-blind, randomized, active-controlled multi-center safety and immunogenicity study conducted in the US. In this study, children 6 months through 35 months of age received one or two 0.25 mL doses of either Fluzone Quadrivalent or one of two formulations of a comparator trivalent influenza vaccine (TIV-1 or TIV-2), and children 3 years through 8 years of age received one or two 0.5 mL doses of either Fluzone Quadrivalent, TIV-1, or TIV-2. Each of the trivalent formulations contained an influenza type B virus that corresponded to one of the two type B viruses in Fluzone Quadrivalent (a type B virus of the Victoria lineage or a type B virus of the Yamagata lineage). For participants who received two doses, the doses were administered approximately 4 weeks apart. The safety analysis set included 1841 children 6 months through 35 months of age and 2506 children 3 years through 8 years of age. Among participants 6 months through 8 years of age in the three vaccine groups combined, 49.3% were female (Fluzone Quadrivalent, 49.2%; TIV-1, 49.8%; TIV-2, 49.4%), 58.4% Caucasian (Fluzone Quadrivalent, 58.4%; TIV-1, 58.9%; TIV-2, 57.8%), 20.2% Black (Fluzone Quadrivalent, 20.5%; TIV-1, 19.9%; TIV-2, 19.1%), 14.1% Hispanic (Fluzone Quadrivalent, 14.3%; TIV-1, 13.2%; TIV-2, 14.7%), and 7.3% were of other racial/ethnic groups (Fluzone Quadrivalent, 6.8%; TIV-1, 8.0%; TIV-2, 8.5%). Table 4 and Table 5 summarize 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 each dose and serious adverse events (SAEs) during the 6 months following the last dose.

Table 4: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Study 2[*] Safety Analysis Set[†])

	Fluzone Quadrivalent[‡, §] (N[Þ]=1223)			TIV-1[§, ¶] (B Victoria) (N[Þ]=310)			TIV-2[§, #] (B Yamagata) (N[Þ]=308)		
	Any (%)	Grade 2[ß] (%)	Grade 3[à] (%)	Any (%)	Grade 2[ß] (%)	Grade 3[à] (%)	Any (%)	Grade 2[ß] (%)	Grade 3[à] (%)
Injection-site adverse reactions									
Pain[è]	57.0	10.2	1.0	52.3	11.5	0.8	50.3	5.4	2.7
Tenderness[ð]	54.1	11.3	1.9	48.4	8.2	1.9	49.7	10.3	0.0
Erythema	37.3	1.5	0.2	32.9	1.0	0.0	33.3	1.0	0.0
Swelling	21.6	0.8	0.2	19.7	1.0	0.0	17.3	0.0	0.0
Systemic adverse reactions									
Fever (≥100.4°F)[ø]	14.3	5.5	2.1	16.0	6.6	1.7	13.0	4.1	2.0
Malaise[è]	38.1	14.5	4.6	35.2	14.8	4.7	32.4	12.8	6.8
Myalgia[è]	26.7	6.6	1.9	26.6	9.4	1.6	25.0	6.8	2.7
Headache[è]	8.9	2.5	0.6	9.4	3.9	0.0	12.2	4.7	0.0
Irritability[ð]	54.0	26.4	3.2	52.8	20.1	3.1	53.5	22.9	2.8
Crying abnormal[ð]	41.2	12.3	3.3	36.5	8.2	1.9	29.9	10.4	2.1
Drowsiness[ð]	37.7	8.4	1.3	32.1	3.8	0.6	31.9	5.6	0.7
Appetite loss[ð]	32.3	9.1	1.8	33.3	5.7	1.9	25.0	8.3	0.7
Vomiting[ð]	14.8	6.2	1.0	11.3	4.4	0.6	13.9	6.3	0.0

[*] NCT01240746

[†] The safety analysis set includes all persons who received at least one dose of study vaccine

[‡] Fluzone Quadrivalent (0.25 mL) containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)

[§] Participants received 1 or 2 doses according to ACIP recommendations

[¶] 2010-2011 Fluzone TIV (0.25 mL) containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed

[#] Investigational TIV (0.25 mL) containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

[Þ] N is the number of participants in the safety analysis set

[ß] Grade 2 - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site tenderness: cries and protests when injection-site is touched; Injection-site erythema, Injection-site swelling: ≥2.5 cm to <5 cm; Fever: >101.3°F to ≤103.1°F (6 months through 23 months); ≥101.2°F to ≤102.0°F (24 months through 35 months); Malaise, Myalgia, and Headache: some interference with activity; Irritability: requiring increased attention; Crying abnormal: 1 to 3 hours; Drowsiness: not interested in surroundings or did not wake up for a feed/meal; Appetite loss: missed 1 or 2 feeds/meals completely; Vomiting: 2 to 5 episodes per 24 hours

[à] Grade 3 - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site tenderness: cries when injected limb is moved, or the movement of the injected limb is reduced; Injection-site erythema, Injection-site swelling: ≥5 cm; Fever: >103.1°F (6 months through 23 months); ≥102.1°F (24 months through 35 months); Malaise, Myalgia, and Headache: Significant; prevents daily activity; Irritability: inconsolable; Crying abnormal: >3 hours; Drowsiness: sleeping most of the time or difficult to wake up; Appetite loss: refuses ≥3 feeds/meals or refuses most feeds/meals; Vomiting: ≥6 episodes per 24 hours or requiring parenteral hydration

[è] Assessed in children 24 months through 35 months of age

[ð] Assessed in children 6 months through 23 months of age

[ø] Fever measured by any route

Table 5: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 3 Years Through 8 Years of Age (Study 2* Safety Analysis Set†)

	Fluzone Quadrivalent‡ (N#=1669)			TIV-1§ (B Victoria) (N#=424)			TIV-2¶ (B Yamagata) (N#=413)		
	Any (%)	Grade 2Þ (%)	Grade 3ß (%)	Any (%)	Grade 2Þ (%)	Grade 3ß (%)	Any (%)	Grade 2Þ (%)	Grade 3ß (%)
Injection-site adverse reactions									
Pain	66.6	15.8	2.1	64.6	9.5	2.0	63.8	11.6	2.8
Erythema	34.1	2.9	1.8	36.8	3.4	1.2	35.2	2.5	1.8
Swelling	24.8	2.8	1.4	25.4	1.5	1.2	25.9	2.5	1.8
Systemic adverse reactions									
Fever (≥100.4°F)à	7.0	2.1	2.1	7.1	2.2	1.2	7.6	2.8	0.8
Headache	23.1	6.8	2.2	21.2	5.1	2.7	24.4	7.5	2.0
Malaise	31.9	11.2	5.5	32.8	11.4	5.6	33.4	10.8	5.0
Myalgia	38.6	12.2	3.3	34.1	9.0	2.7	38.4	11.1	2.8

*NCT01240746

†The safety analysis set includes all persons who received at least one dose of study vaccine

‡Fluzone Quadrivalent containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)

§2010-2011 Fluzone TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 (Victoria lineage), licensed

¶Investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

#N is the number of participants in the safety analysis set

ÞGrade 2 - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site erythema, Injection-site swelling: ≥2.5 cm to <5 cm; Fever: ≥101.2°F to ≤102.0°F; Headache, Malaise, and Myalgia: some interference with activity

ßGrade 3 - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site erythema, Injection-site swelling: ≥5 cm; Fever: ≥102.1°F; Headache, Malaise, and Myalgia: Significant; prevents daily activity

à Fever measured by any route

Among children 6 months through 8 years of age, unsolicited non-serious adverse events were reported in 1360 (47.0%) recipients in the Fluzone Quadrivalent group, 352 (48.0%) recipients in the TIV-1 group, and 346 (48.0%) recipients in the TIV-2 group. The most commonly reported unsolicited non-serious adverse events were cough, vomiting, and pyrexia. During the 28 days following vaccination, a total of 16 (0.6%) recipients in the Fluzone Quadrivalent group, 4 (0.5%) recipients in the TIV-1 group, and 4 (0.6%) recipients in the TIV-2 group, experienced at least one SAE. Throughout the study period, a total of 41 (1.4%) recipients in the Fluzone Quadrivalent group, 7 (1.0%) recipients in the TIV-1 group, and 14 (1.9%) recipients in the TIV-2 group, experienced at least one SAE. Three SAEs were considered to be possibly related to vaccination: croup in a Fluzone Quadrivalent recipient and 2 episodes of febrile seizure, 1 each in a TIV-1 recipient and a TIV-2 recipient.

Study 3 (NCT02915302) was a randomized, observer-blinded, 2-arm, multi-center safety and immunogenicity study conducted in the US. In this study, 1950 children 6 months through 35 months of age were randomly assigned to receive Fluzone Quadrivalent administered in either a volume of 0.25 mL (Group 1) or 0.5 mL

(Group 2). For participants recommended to receive two doses of influenza vaccine as per Advisory Committee on Immunization Practices guidance, the same dose was administered 4 weeks after the first. The safety analysis set included 1941 participants who received at least 1 dose of study vaccine. Of these participants, 49.7% were female, 74.3% were Caucasian, 19.2% were Black, 6.5% were of other racial groups, and 22.0% were Hispanic/Latino. Data for Fluzone Quadrivalent are relevant to Fluzone because both vaccines are manufactured using the same process and have overlapping compositions.

Table 6 summarizes solicited injection-site and systemic adverse reactions reported within 7 days post-vaccination via diary cards for the 0.25 mL and 0.5 mL volumes of Fluzone Quadrivalent in children 6 months through 35 months of age.

Table 6: Percentage of Solicited Injection Site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Month of Age (Study 3[*] Safety Analysis Set[†])

	Fluzone Quadrivalent 0.25 mL[‡] (N[§]=949)		**Fluzone Quadrivalent 0.5 mL[‡] (N[§]=992)**	
	Any (%)	**Grade 3[¶] (%)**	**Any (%)**	**Grade 3[¶] (%)**
Injection-site adverse reactions				
Tenderness	47.3	1.7	50.4	1.2
Redness	23.1	0.0	24.3	0.2
Swelling	12.9	0.1	14.7	0.0
Systemic adverse reactions				
Irritability	47.4	3.6	48.6	4.0
Abnormal Crying	33.3	3.1	34.1	2.6
Drowsiness	31.9	2.1	31.3	1.6
Loss of Appetite	27.3	1.4	28.3	2.2
Fever (≥100.4°F) [#]	11.3	0.6	12.2	1.2
Vomiting	10.0	0.4	10.2	0.5

[*]NCT02915302

[†]The safety analysis set includes all persons who received at least one dose of study vaccine

[‡]Participants received 1 or 2 doses according to ACIP recommendations

[§]N is the number of participants in the safety analysis set

[¶]Grade 3 - Injection-site tenderness: Cries when injected limb is moved, or the movement of the injected limb is reduced; Injection-site redness, Injection-site swelling: ≥ 50 mm; Irritability: inconsolable; Abnormal Crying: > 3 hours; Drowsiness: sleeping most of the time or difficult to wake up; Loss of Appetite: refuses ≥ 3 feeds/meals or refuses most feeds/meals; Fever: >103.1°F; Vomiting: ≥ 6 episodes per 24 hours or requiring parenteral hydration

[#]Fever measured by any route

The difference in fever rate (Group 2 minus Group 1) was 0.84% (95% CI: -2.13%; 3.80%), meeting the prespecified non-inferiority criterion (upper limit of the 2-sided 95% CI of the difference in fever rates < 5%). Participants were monitored for unsolicited adverse events and SAEs during the 28 days following vaccination.

Unsolicited non-serious adverse events were reported in 417 (44%) participants in Group 1 and 394 (40%) participants in Group 2. The most commonly reported unsolicited non-serious adverse events in both groups were cough and rhinorrhea. Ten SAEs were reported during the 28-day follow-up period: 5 (0.5%) in Group 1 and 5 (0.5%) in Group 2.

Adults

Study 4 (NCT00772109) was a multi-center trial conducted in the US. In this study adults 18 through 64 years of age received Fluzone (2008-2009 formulation). The safety analysis set included 1421 Fluzone recipients. Table 7 summarizes solicited injection-site reactions and systemic adverse reactions reported within 7 days post-vaccination via diary cards.

Table 7: Frequency of Solicited Injection Site and Systemic Adverse Reactions Within 7 Days After Vaccination with Fluzone, Adults 18 Through 64 Years of Age (Study 4[#])

	(N[*]=1392-1394) Percentage		
	Any	**Grade 2[†]**	**Grade 3[‡]**
Injection-Site Erythema	13.2	2.1	0.9
Injection-Site Induration	10.0	2.3	0.5
Injection-Site Swelling	8.4	2.1	0.9
Injection-Site Pain	53.7	5.8	0.8
Injection-Site Pruritus	9.3	0.4	0.0
Injection-Site Ecchymosis	6.2	1.1	0.4
Headache	30.3	6.5	1.6
Myalgia	30.8	5.5	1.4
Malaise	22.2	5.5	1.8
Shivering	6.2	1.1	0.6
Fever[§] (≥99.5°F)	2.6	0.4	0.2

[#] NCT00772109

[*] N is the number of vaccinated participants with available data for the adverse reactions listed

[†] 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

[‡] 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

[§] Fever - The percentage of temperature measurements that were taken by oral or axillary routes, or not recorded were 99.6%, 0.0%, and 0.4%, respectively

Within 28 days and 6 months post-vaccination, a serious adverse event was reported by 5 (0.4%) and 20 (1.4%) Fluzone recipients, respectively. No serious adverse event was considered to be caused by vaccination. No deaths were reported during the 6 months post-vaccination.

In Study 5 (NCT00391053) adults 65 years of age and older received Fluzone (2006-2007 formulation). The study was a multi-center, double-blind trial conducted in the US. The safety analysis set included 1260 Fluzone recipients.

Table 8 summarizes solicited injection-site reactions and systemic adverse reactions reported within 7 days post-vaccination via diary cards. Onset was usually within the first 3 days after vaccination and a majority of the adverse reactions resolved within 3 days.

Table 8: Frequency of Solicited Injection Site and Systemic Adverse Reactions Within 7 Days After Vaccination with Fluzone, Adults 65 Years of Age and Older (Study 5[#])

	N[*]=1258-1260 Percentage		
	Any	**Moderate[†]**	**Severe[‡]**
Injection-Site Pain	24.3	1.7	0.2
Injection-Site Erythema	10.8	0.8	0.6
Injection-Site Swelling	5.8	1.3	0.6
Myalgia	18.3	3.2	0.2
Malaise	14.0	3.7	0.6
Headache	14.4	2.5	0.3
Fever[§] (≥99.5°F)	2.3	0.2	0.1

[#] NCT00391053

[*] N is the number of vaccinated participants with available data for the adverse reactions listed

[†] Moderate - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-site erythema and Injection-site swelling: ≥2.5 cm to <5 cm; Fever: >100.4°F to ≤102.2°F; Myalgia, Malaise, and Headache: interferes with daily activities

[‡] Severe - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site erythema and Injection-site swelling: ≥5 cm; Fever: >102.2°F; Myalgia, Malaise, and Headache: prevents daily activities

[§] Fever - The percentage of temperature measurements that were taken by oral route or not recorded were 98.6% and 1.4%, respectively

Within 6 months post-vaccination, 93 (7.4%) Fluzone recipients experienced a serious adverse event (N=1260). No deaths were reported within 28 days post-vaccination. A total of 7 deaths were reported during the period Day 29-180 post-vaccination: 7 (0.6%) among Fluzone recipients (N=1260). The majority of these participants had a medical history of cardiac, hepatic, neoplastic, renal, and/or respiratory diseases. No deaths were considered to be caused by vaccination.

6.2 Postmarketing Experience

The following adverse events have been spontaneously reported during the post-approval use of Fluzone or Fluzone Quadrivalent. 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 or Fluzone Quadrivalent.

- *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, vasodilatation/flushing
- *Respiratory, Thoracic and Mediastinal Disorder*s: Dyspnea, oropharyngeal pain, rhinorrhea, 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

Fluzone Southern Hemisphere and Fluzone are manufactured using the same process. Data in this section were obtained in studies with Fluzone.

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Fluzone. Healthcare providers are encouraged to enroll women who receive Fluzone during pregnancy in Sanofi Pasteur Inc.'s vaccination pregnancy registry at sanofipasteurpregnancyregistry.com or by calling 1-800-822-2463 (1-800-VACCINE).

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Available data with Fluzone use in pregnant women are insufficient to inform vaccine-associated risk of adverse developmental outcomes.

There were no developmental studies of Fluzone performed in animals. The developmental effects of Fluzone Quadrivalent are relevant to Fluzone because both vaccines are manufactured using the same process and have overlapping compositions. A developmental toxicity study was performed in female rabbits administered Fluzone Quadrivalent prior to mating and during gestation. The dose was 0.5 mL on each of five occasions (a single human dose is 0.5 mL). This study revealed no adverse effects to the fetus or pre-weaning development and no evidence of impaired female fertility due to Fluzone Quadrivalent (see Data).

Data

Animal Data: A developmental toxicity study was performed in female rabbits administered Fluzone Quadrivalent by intramuscular injection on 24 and 10 days before insemination, and on Days 6, 12, and 27 of gestation. The dose was 0.5 mL on each occasion (a single human dose is 0.5 mL). This study revealed no vaccine related fetal malformations and no adverse effects on pre-weaning development or female fertility.

Clinical Considerations

Disease-associated Maternal and/or Embryo/Fetal Risk

Pregnant women are at increased risk of complications associated with influenza infection compared to non-pregnant women. Pregnant women who contract influenza may be at increased risk for adverse pregnancy outcomes, including preterm labor and delivery.

8.2 Lactation

It is not known if Fluzone is excreted in human milk. Data are not available to assess the effects of Fluzone on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Fluzone and any potential adverse effects on the breastfed child from Fluzone or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to the disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of Fluzone in children below the age of 6 months have not been established. Safety and effectiveness of Fluzone in children 9 through 17 years of age is based on safety and effectiveness in children 6 months through 8 years of age and adults 18 years of age and older.

8.5 Geriatric Use

Safety and immunogenicity of Fluzone were evaluated in adults 65 years of age and older. [See *Adverse Reactions (6.1) and Clinical Studies (14.3)*] Antibody responses to Fluzone are lower in persons ≥65 years of age than in younger adults. [See *Clinical Studies (14.5, 14.6)*]

11 DESCRIPTION

Fluzone Southern Hemisphere (Influenza Vaccine) for intramuscular use 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 containing hemagglutinin (HA) antigen is further purified and then suspended in sodium phosphate-buffered isotonic sodium chloride solution. The purified split virus from the three strains included in the vaccine are produced separately and then combined to make the trivalent formulation.

Fluzone Southern Hemisphere is an injectable suspension and is clear and slightly opalescent in color.

Antibiotics are not used in the manufacture of Fluzone Southern Hemisphere.

No presentation of Fluzone Southern Hemisphere is made with natural rubber latex.

Fluzone Southern Hemisphere is standardized according to United States Public Health Service requirements and is formulated to contain HA of each of the following three influenza strains recommended for the 2025-Southern Hemisphere influenza season: A/Victoria/4897/2022 IVR-238 (H1N1), A/Croatia/10136RV/2023 X-425A (H3N2), and B/Michigan/01/2021 (a B/Austria/1359417/2021-like virus, B Victoria lineage). The amounts of HA and other ingredients per dose of vaccine are listed in Table 9. The 0.5 mL single-dose, pre-filled syringe presentation is manufactured and formulated without thimerosal or any other preservative. The 5 mL multi-dose vial presentation contains thimerosal, a mercury derivative, added as a preservative. Each 0.5 mL dose from the multi-dose vial contains 25 mcg mercury. Each 0.25 mL dose from the multi-dose vial contains 12.5 mcg mercury.

Table 9: Fluzone Southern Hemisphere Ingredients

Ingredient	**Quantity (per dose)**	
	Fluzone 0.25 mL Dose	**Fluzone 0.5 mL Dose**
Active Substance: Split influenza virus, inactivated strains*:	22.5 mcg HA total	45 mcg HA total
A (H1N1)	7.5 mcg HA	15 mcg HA
A (H3N2)	7.5 mcg HA	15 mcg HA
B	7.5 mcg HA	15 mcg HA

Ingredient	Quantity (per dose)	
	Fluzone 0.25 mL Dose	Fluzone 0.5 mL Dose
Other:		
Sodium phosphate-buffered isotonic sodium chloride solution	QS† to appropriate volume	QS† to appropriate volume
Formaldehyde	≤50 mcg	≤100 mcg
Octylphenol ethoxylate	≤75 mcg	≤150 mcg
Preservative		
Single-dose presentations	-	-
Multi-dose presentation (thimerosal)	12.5 mcg mercury	25 mcg mercury

* per United States Public Health Service (USPHS) requirement

† Quantity Sufficient

"-" Indicates information is not applicable

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Specific levels of hemagglutination inhibition (HI) antibody titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza virus infection. In some human studies, antibody titers ≥1:40 have been associated with protection from influenza illness in up to 50% of participants. (2) (3)

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.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Fluzone has not been evaluated for carcinogenic or mutagenic potential or for impairment of fertility in males.

14 CLINICAL STUDIES

Fluzone Southern Hemisphere and Fluzone are manufactured using the same process. Data in this section were obtained in studies with Fluzone and Fluzone Quadrivalent.

14.1 Efficacy of Fluzone in Children 6 through 24 Months of Age

Study 6 (NCT not available) was a randomized, double-blind, placebo-controlled study conducted at a single US center during the 1999-2000 (Year 1) and 2000-2001 (Year 2) influenza seasons. The intent-to-treat analysis set included a total of 786 children 6 through 24 months of age. Participants received two 0.25ml doses of either Fluzone (N = 525) or a placebo (N = 261) 4 weeks apart. Among all randomized participants in both years, the mean age was 13.8 months; 52.5% were male, 50.8% were Caucasian, 42.0% were Black, and 7.2% were of other racial groups. Cases of influenza were identified through active and passive surveillance for influenza-like illness or acute otitis media and confirmed by culture. Influenza-like illness was defined as fever with signs or

symptoms of an upper respiratory infection. Vaccine efficacy against all influenza viral types and subtypes was a secondary endpoint and is presented in Table 10.

Table 10: Estimated Efficacy of Fluzone Against Culture-Confirmed Influenza in Children Aged 6 through 24 Months during the 1999-2000 and 2000-2001 Influenza Seasons – Intent-to-Treat Analysis Set[*] (Study 6)

	Fluzone[†]				Placebo[‡]				Fluzone vs. Placebo	
Year	n[§]	N[¶]	Rate (n/N)[#]	(95% CI)	n[§]	N[¶]	Rate (n/N)[#]	(95% CI)	Relative Risk (95% CI)	Percent Relative Reduction[Þ] (95% CI)
Year 1[ß] (1999-2000)	15	273	5.5	(3.1; 8.9)	22	138	15.9	(10.3; 23.1)	0.34 (0.18; 0.64)	66 (36; 82)
Year 2[χ] (2000-2001)	9	252	3.6	(1.6; 6.7)	4	123	3.3	(0.9; 8.1)	1.10 (0.34; 3.50)	-10 (-250; 66)

[*]The intent-to-treat analysis set includes all enrolled participants who were randomly assigned to receive Fluzone or placebo and vaccinated[†]Fluzone: 1999-2000 formulation containing A/Beijing/262/95 (H1N1), A/Sydney/15/97 (H3N2), and B/Yamanashi/166/98 (Yamagata lineage) and 2000-2001 formulation containing A/New Caledonia/20/99 (H1N1), A/Panama/2007/99 (H3N2), and B/Yamanashi/166/98 (Yamagata lineage)

[‡]Placebo: 0.4% NaCl

[§]n is the number of participants with culture-confirmed influenza for the given year of study as listed in the first column

[¶]N is the number of participants randomly assigned to receive Fluzone or placebo for the given year of study as listed in the column headers (intent-to-treat analysis set)

[#]Rate (%) = (n/N) * 100

[Þ]Relative reduction in vaccine efficacy was defined as (1-relative risk) x 100

[ß]Includes all culture confirmed influenza cases throughout the study duration for Year 1 (12 months of follow-up)

[χ]Includes all culture-confirmed influenza cases throughout the study duration for Year 2 (6 months of follow-up)

14.2 Efficacy of Fluzone in Adults

Study 7 (NCT00538512) was a randomized, double-blind, placebo-controlled study conducted in a single US center during the 2007-2008 influenza season. Participants received one dose of either Fluzone vaccine (N = 813), an active comparator (N = 814), or placebo (N = 325). The intent-to-treat analysis set included 1138 healthy adults who received Fluzone or placebo. Participants were 18 through 49 years of age (mean age was 23.3 years); 63.3% were female, 83.1% were Caucasian, and 16.9% were of other racial/ethnic groups. Cases of influenza were identified through active and passive surveillance and confirmed by cell culture and/or real-time polymerase chain reaction (PCR). Influenza-like illness was defined as an illness with at least 1 respiratory symptom (cough or nasal congestion) and at least 1 constitutional symptom (fever or feverishness, chills, or body aches). Vaccine efficacy of Fluzone against all influenza viral types and subtypes is presented in Table 11.

Table 11: Estimated Efficacy of Fluzone Vaccine Against Influenza in Adults Aged 18 through 49 Years during the 2007-2008 Influenza Season – Intent-to-Treat Analysis Set* (Study 7[β])

Laboratory-Confirmed Symptomatic Influenza	Fluzone[†] (N=813) [§]			Placebo[‡] (N=325) [§]			Fluzone vs. Placebo	
	n[¶]	Rate (%)[#]	(95% CI)	n[¶]	Rate (%)[#]	(95% CI)	Relative Risk (95% CI)	Percent Relative Reduction[Þ] (95% CI)
Positive culture	21	2.6	(1.6; 3.9)	31	9.5	(6.6; 13.3)	0.27 (0.16; 0.46)	73 (54; 84)
Positive PCR	28	3.4	(2.3; 4.9)	35	10.8	(7.6; 14.7)	0.32 (0.20; 0.52)	68 (48; 80)
Positive culture, positive PCR, or both	28	3.4	(2.3; 4.9)	35	10.8	(7.6; 14.7)	0.32 (0.20; 0.52)	68 (48; 80)

*The intent-to-treat analysis set includes all enrolled participants who were randomly assigned to receive Fluzone or placebo and vaccinated

[β]NCT00538512

[†]Fluzone: 2007-2008 formulation containing A/Solomon Islands/3/2006 (H1N1), A/Wisconsin/67/2005 (H3N2), and B/Malaysia/2506/2004 (Victoria lineage)

[‡]Placebo: 0.9% NaCl

[§]N is the number of participants randomly assigned to receive Fluzone or placebo

[¶]n is the number of participants satisfying the criteria listed in the first column

[#]Rate (%) = (n/N) * 100

[Þ]Relative reduction in vaccine efficacy was defined as (1 - relative risk) x 100

14.3 Immunogenicity of Fluzone in Children 6 Months through 8 Years of Age

In Study 1, a multi-center study conducted in the US, 68 children 6 months through 35 months of age given two 0.25 mL doses of Fluzone and 120 children 3 years through 8 years of age given two 0.5 mL doses

of Fluzone were included in the per-protocol analysis set. The two doses (2006-2007 formulation) were administered 26 to 30 days apart. Females accounted for 42.6% of the participants in the 6 months through 35 months age group and 53.3% of the participants in the 3 years through 8 years age group. Most participants in the 6 months through 35 months and 3 years through 8 years age groups, respectively, were Caucasian (70.6% and 79.2%), followed by Hispanic (19.1% and 13.3%), and Black (7.4% and 4.2%).

The percentage of participants who received influenza vaccination during the previous influenza season was 54.4% for the 6 months through 35 months age group and 27.5% for the 3 years through 8 years age group. Table 12 shows seroconversion rates and the percentage of participants with an HI titer ≥1:40 pre-vaccination and one month following the second dose of Fluzone.

Table 12: Percentage (%) with Pre and Post-Vaccination HI Titers ≥1:40 and Seroconversion Following the Second Vaccine Injection with Fluzone* in Children 6 Months Through 35 Months and 3 Years Through 8 Years of Age (Study 1§)

Antigen	Age Group	Pre-Vaccination Titer ≥1:40 % (95% CI)	Post-Vaccination† Titer ≥1:40 % (95% CI)	Seroconversion‡ % (95% CI)
		N=68 (6 to 35 months); N=120 (3 through 8 years)		
A (H1N1)	6 through 35 months	11.8 (5.2; 21.9)	92.6 (83.7; 97.6)	88.2 (78.1; 94.8)
	3 through 8 years	40.0 (31.2; 49.3)	99.2 (95.4; 100.0)	78.3 (69.9; 85.3)
A (H3N2)	6 through 35 months	29.4 (19.0; 41.7)	100.0 (94.7; 100.0)	91.2 (81.8; 96.7)
	3 through 8 years	80.0 (71.7; 86.7)	100.0 (97.0; 100.0)	61.7 (52.4; 70.4)
B	6 through 35 months	1.5 (0.0; 7.9)	20.6 (11.7; 32.1)	20.6 (11.7; 32.1)
	3 through 8 years	3.3 (0.9; 8.3)	58.3 (49.0; 67.3)	53.3 (44.0; 62.5)

* Children received two doses of Fluzone administered 26 to 30 days apart, irrespective of previous influenza vaccination history

§ NCT00391391† Post-vaccination HI titers drawn at 28 days post-dose

‡ Seroconversion: Paired samples with pre-vaccination HI titer <1:10 and post-vaccination (28 days post-dose 2) titer ≥1:40 or a minimum 4-fold increase for participants with pre-vaccination titer ≥1:10

14.4 Immunogenicity of a 0.5 mL Dose of Fluzone Quadrivalent in Children 6 Months through 35 Months of Age

In Study 3 (NCT02915302) [see *Adverse Reactions* (6.1)], 1027 children, 6 months through 35 months of age, were included in the per-protocol immunogenicity analysis. The distribution of demographic characteristics was similar to that of the safety analysis set [see *Adverse Reactions* (6.1)].

In this study, children 6 months through 35 months of age received one or two doses of either 0.25 mL or 0.5 mL of Fluzone Quadrivalent. Non-inferiority of the 0.5 mL dose(s) relative to the 0.25 mL dose(s) of Fluzone Quadrivalent was demonstrated for all four strains based on pre- specified criteria (lower limit of the 2-sided 95% CI of the ratio of GMTs between groups >0.667; lower limit of the 2-sided 95% CI of the difference in seroconversion rates >-10%). GMT ratios ($GMT_{0.5\text{-mL dose}}$ divided by $GMT_{0.25\text{-mL dose}}$) for the A/H1N1, A/H3N2, B Victoria lineage, and B Yamagata lineage strains were 1.42 (95% CI: 1.16; 1.74), 1.48 (95% CI: 1.21; 1.82), 1.33 (95% CI: 1.09; 1.62), and 1.41 (95% CI: 1.17; 1.70), respectively. Seroconversion rate (SCR) differences ($SCR_{0.5\text{-mL dose}}$ minus $SCR_{0.25\text{-mL dose}}$) for the A/H1N1, A/H3N2, B Victoria lineage, and B Yamagata lineage strains were 4.6% (95% CI: -0.4%; 9.6%), 5.1% (95% CI: 0.4%; 9.8%), 1.3% (95% CI: -2.9%; 5.6%), and 2.6%

(95% CI: -1.4%; 6.5%). Data for Fluzone Quadrivalent are relevant to Fluzone because both vaccines are manufactured using the same process and have overlapping compositions.

14.5 Immunogenicity of Fluzone in Adults

Adults 18 through 64 years of age received Fluzone (2008-2009 formulation) in Study 4, a multi-center trial conducted in the US. For immunogenicity analyses, there were 1287 participants who received Fluzone in the per-protocol analysis set. There were fewer males (35.8%) than females. The mean age was 42.6 years (ranged from 18.2 through 65.0 years). Most participants were Caucasian (80.0%), followed by Hispanic (11.0%), and Black (6.3%). Table 13 shows seroconversion rates at 28 days following vaccination and the percentage of participants with an HI titer ≥1:40 prior to vaccination and 28 days following vaccination.

Table 13: Percentage (%) with Pre and Post-Vaccination HI Titers ≥1:40 and Seroconversion in Adult Fluzone Recipients 18 Through 64 Years of Age (Study 4[§])

Antigen	Pre-Vaccination Titer ≥1:40 % (95% CI) N[‡]=1285-1286	Post-Vaccination[*] Titer ≥1:40 % (95% CI) N[‡]=1283-1285	Seroconversion[†] % (95% CI) N[‡]=1283-1285
A (H1N1)	39.1 (36.4; 41.8)	91.7 (90.0; 93.1)	60.5 (57.7; 63.2)
A (H3N2)	33.6 (31.0; 36.2)	91.4 (89.8; 92.9)	74.8 (72.3; 77.1)
B	41.2 (38.5; 44.0)	89.3 (87.4; 90.9)	54.2 (51.4; 56.9)

[§] NCT00772109

[*] Post-vaccination HI titers drawn at 28 days post-dose

[†] Seroconversion: Paired samples with pre-vaccination HI titer <1:10 and post-vaccination (28 days post-dose) titer ≥1:40 or a minimum 4-fold increase for participants with pre-vaccination titer ≥1:10

[‡] N is the number of vaccinated participants with available data for the immunologic endpoint listed

14.6 Immunogenicity of Fluzone in Geriatric Adults

Adults 65 years of age and older received Fluzone (2006-2007 formulation) in Study 5, a multi-center trial conducted in the US. For immunogenicity analyses, there were 1275 participants who received Fluzone in the immunogenicity analysis set. Females accounted for 54.7% of participants. The mean age was 72.9 years (ranged from 65 through 94 years of age); 36% of participants were 75 years of age or older. Most participants were Caucasian (92.9%), followed by Hispanic (3.7%), and Black (2.7%). Table 14 shows seroconversion rates at 28 days following vaccination and the percentage of participants with an HI titer ≥1:40 prior to vaccination and 28 days following vaccination.

Table 14: Percentage (%) with Pre and Post-Vaccination HI Titers ≥1:40 and Seroconversion in Adult Fluzone Recipients 65 Years of Age and Older (Study 5[§])

Antigen	Pre-Vaccination HI Titer ≥1:40 % (95% CI) N[‡]=1267-1268	Post-Vaccination[*] Titer ≥1:40 % (95% CI) N[‡]=1252	Seroconversion[†] % (95% CI) N[‡]=1248-1249
A (H1N1)	45.9 (43.2; 48.7)	76.8 (74.3; 79.1)	23.1 (20.8; 25.6)
A (H3N2)	68.6 (66.0; 71.2)	96.5 (95.3; 97.4)	50.7 (47.9; 53.5)
B	27.3 (24.9; 29.9)	67.6 (64.9; 70.2)	29.9 (27.4; 32.6)

[§] NCT00391053

[*] Post-vaccination HI titers drawn at 28 days post-dose

[†] Seroconversion: Paired samples with pre-vaccination HI titer <1:10 and post-vaccination (28 days post-dose) titer ≥1:40 or a minimum 4-fold increase for participants with pre-vaccination titer ≥1:10

[‡] N is the number of vaccinated participants with available data for the immunologic endpoint listed

15 REFERENCES

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2 Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza vaccination. Virus Res 2004;103:133-138.

3 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

Multi-dose vial, 5 mL (NDC 49281-356-78) (not made with natural rubber latex). Supplied as package of one (NDC 49281-356-15). A maximum of ten doses can be withdrawn from the multi-dose vial.

Single-dose, prefilled syringe (clear plunger rod), without needle, 0.5 mL (NDC 49281-325-88) (not made with natural rubber latex). Supplied as package of 10 (NDC 49281-325-50).

16.2 Storage and Handling

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

Between uses, return the multi-dose vial to the recommended storage conditions at 2° to 8°C (35° to 46°F).

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

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Inform the patient or guardian that Fluzone Southern Hemisphere contains killed viruses and cannot cause influenza.
- Fluzone Southern Hemisphere stimulates the immune system to produce antibodies that help protect against influenza, but does not prevent other respiratory infections.
- Annual influenza vaccination is recommended.

- Instruct vaccine recipients and guardians to report adverse reactions to their healthcare provider and/or to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967.
- Sanofi Pasteur Inc. is maintaining a prospective pregnancy exposure registry to collect data on pregnancy outcomes and newborn health status following vaccination with Fluzone Southern Hemisphere during pregnancy. Women who receive Fluzone Southern Hemisphere during pregnancy are encouraged to contact directly or have their healthcare provider contact Sanofi Pasteur Inc. at sanofipasteurpregnancyregistry.com or by calling 1-800-822-2463 (1-800-VACCINE).
- Vaccine Information Statements must be provided to vaccine recipients or their guardians, as required by the National Childhood Vaccine Injury Act of 1986 prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Fluzone is a registered trademark of Sanofi Pasteur Inc.

Manufactured by:

Sanofi Pasteur Inc.
Swiftwater PA 18370 USA

This product's labeling may have been updated. For the most recent prescribing information, please visit https://dailymed.nlm.nih.gov/dailymed/.

Patient Information Sheet
Fluzone® Southern Hemisphere
Influenza Vaccine

Please read this information sheet before getting Fluzone Southern Hemisphere vaccine. This summary is not intended to take the place of talking with your healthcare provider. If you have questions or would like more information, please talk with your healthcare provider.

What is Fluzone Southern Hemisphere vaccine?

Fluzone Southern Hemisphere is a vaccine that helps protect against influenza illness (flu).
Fluzone Southern Hemisphere vaccine is for people who are 6 months of age and older.
Vaccination with Fluzone Southern Hemisphere vaccine may not protect all people who receive the vaccine.

Who should not get Fluzone Southern Hemisphere vaccine?

You should not get Fluzone Southern Hemisphere vaccine if you:

- ever had a severe allergic reaction to eggs or egg products.
- ever had a severe allergic reaction after getting any influenza vaccine.
- are younger than 6 months of age.

Tell your healthcare provider if you or your child have or have had:

- Guillain-Barré syndrome (severe muscle weakness) after getting an influenza vaccine.
- problems with your immune system as the immune response may be diminished.

How is the Fluzone Southern Hemisphere vaccine given?

Fluzone Southern Hemisphere vaccine is given as an injection into the muscle.

What are the possible side effects of Fluzone Southern Hemisphere vaccine?

The most common side effects of Fluzone Southern Hemisphere vaccine are:

- pain, redness, swelling, bruising and hardness where you got the injection
- muscle aches
- tiredness
- headache

- fever

These are not all of the possible side effects of Fluzone Southern Hemisphere vaccine. Ask your healthcare provider about other side effects.

Call your healthcare provider for advice about any side effects that concern you. You may report side effects to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or http://vaers.hhs.gov. Sanofi Pasteur Inc. is collecting information on pregnancy outcomes and the health of newborns following vaccination with Fluzone Southern Hemisphere during pregnancy. Women who receive Fluzone Southern Hemisphere during pregnancy are encouraged to contact directly or have their healthcare provider contact Sanofi Pasteur Inc. at sanofipasteurpregnancyregistry.com or by calling 1-800-822-2463 (1-800-VACCINE).

What are the ingredients in Fluzone Southern Hemisphere vaccine?

Fluzone Southern Hemisphere vaccine contains 3 killed influenza virus strains.

Other ingredients include formaldehyde and octylphenol ethoxylate. The preservative thimerosal is only in the multi-dose vial of Fluzone Southern Hemisphere vaccine.

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