

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

**Fluzone (Influenza Virus Vaccine)
Suspension for Intramuscular Injection
2012-2013 Formula
Initial US Approval 1980**

INDICATIONS AND USAGE

Fluzone is indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccines. (1)
Fluzone is approved for use in persons 6 months of age and older. (1)

DOSAGE AND ADMINISTRATION

- For intramuscular use only

Age	Dose	Schedule
6 months through 35 months	One or two doses ^a , 0.25 mL each	If 2 doses, administer at least 1 month apart
36 months through 8 years	One or two doses ^a , 0.5 mL each	If 2 doses, administer at least 1 month apart
9 years and older	One dose, 0.5 mL	-

^a1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza with vaccines.

"-" indicates information is not applicable

DOSAGE FORMS AND STRENGTHS

Suspension for injection supplied in 4 presentations: prefilled syringe (pink plunger rod), 0.25 mL; prefilled syringe (clear plunger rod), 0.5 mL; single-dose vial, 0.5 mL; multi-dose vial, 5 mL. (3)

CONTRAINDICATIONS

Severe allergic reaction 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 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 reactions were pain or tenderness (>50%) and redness (>25%); the most common solicited systemic adverse events 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 reaction was pain (>50%); the most common solicited systemic adverse events were headache and myalgia (>30%). (6.1)
- In adults ≥65 years of age, the most common injection-site reaction was pain (>20%); the most common solicited systemic adverse events were headache, myalgia, and malaise (>10%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur Inc., Discovery Drive, Swiftwater, PA 18370 at 1-800-822-2463 (1-800-VACCINE) or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

USE IN SPECIFIC POPULATIONS

- Safety and effectiveness of Fluzone has not been established in pregnant women. (8.1).
- Antibody responses to Fluzone are lower in persons ≥65 years of age than in younger adults. (8.5)

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

Revised: May 2012

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1 **FULL PRESCRIBING INFORMATION:**

2 **1 INDICATIONS AND USAGE**

3 Fluzone® is an inactivated influenza virus vaccine indicated for active immunization against
4 influenza disease caused by influenza virus subtypes A and type B contained in the vaccine.

5

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

7

8 **2 DOSAGE AND ADMINISTRATION**

- 9 • For intramuscular use only

10 **2.1 Dose and Schedule**

11 The dose and schedule for Fluzone is presented in [Table 1](#).

12 **Table 1: Fluzone**

Age	Dose	Schedule
6 months through 35 months	One or two doses ^a , 0.25 mL each	If 2 doses, administer at least 1 month apart
36 months through 8 years	One or two doses ^a , 0.5 mL each	If 2 doses, administer at least 1 month apart
9 years and older	One dose, 0.5 mL	-

13 ^a1 or 2 doses depends on vaccination history as per Advisory Committee on Immunization Practices annual
14 recommendations on prevention and control of influenza with vaccines.

15 "-" indicates information is not applicable

16

17 **2.2 Administration**

18 Inspect Fluzone visually for particulate matter and/or discoloration prior to administration. If

19 either of these conditions exist, the vaccine should not be administered.

20

1 Before administering a dose of vaccine, shake the prefilled syringe or single-dose or multi-dose
2 vial. Withdraw a single dose of vaccine using a sterile needle and syringe. Use a separate sterile
3 needle and syringe for each dose withdrawn from the multi-dose vial.

4

5 The preferred sites for intramuscular injection are the anterolateral aspect of the thigh in infants 6
6 months through 11 months of age, the anterolateral aspect of the thigh (or the deltoid muscle if
7 muscle mass is adequate) in persons ≥ 12 months through 35 months of age, or the deltoid muscle
8 in persons ≥ 36 months of age. The vaccine should not be injected into the gluteal area or areas
9 where there may be a major nerve trunk.

10

11 Do not administer this product intravenously or subcutaneously.

12

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

14

15 **3 DOSAGE FORMS AND STRENGTHS**

16 Fluzone is a suspension for injection.

17

18 Fluzone is supplied in 4 presentations:

19 1) Prefilled syringe (pink syringe plunger rod), 0.25 mL, for persons 6 months through 35 months
20 of age.

21 2) Prefilled syringe (clear syringe plunger rod), 0.5 mL, for persons 36 months of age and older.

22 3) Single-dose vial, 0.5 mL, for persons 36 months of age and older.

23 4) Multi-dose vial, 5 mL, for persons 6 months of age and older.

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4 CONTRAINDICATIONS

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 is a contraindication to administration of Fluzone.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

The 1976 swine influenza vaccine was associated with an elevated risk of Guillain-Barré syndrome (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). If 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.

5.2 Preventing and Managing Allergic Reactions

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

5.3 Altered Immunocompetence

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

1 **5.4 Limitations of Vaccine Effectiveness**

2 Vaccination with Fluzone may not protect all recipients.

3

4 **6 ADVERSE REACTIONS**

5 **6.1 Clinical Trials Experience**

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

9

10 **Children 6 Months through 8 Years of Age**

11 In a multi-center study conducted in the US, children 6 months through 35 months of age received
12 two 0.25 mL doses of Fluzone, and children 3 years through 8 years of age received two 0.5 mL
13 doses of Fluzone, irrespective of previous influenza vaccination history. The two doses (year
14 2006-2007 formulation) were administered 26 to 30 days apart. The safety analysis set included
15 97 children 6 months through 35 months of age and 163 children 3 years through 8 years of age.
16 [Table 2](#) and [Table 3](#) summarize solicited injection site reactions and systemic adverse events
17 reported within 7 days post-vaccination via diary cards.

1 **Table 2: Frequency of Solicited Injection Site Reactions and Systemic Adverse Events**
2 **Within 7 Days After Vaccination with Fluzone, Children 6 Through 35 Months of Age**

	Dose 1 (N ^a =90-92) Percentage			Dose 2 (N ^a =86-87) Percentage		
	Any	Moderate ^b	Severe ^c	Any	Moderate ^b	Severe ^c
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^d	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

3 ^aN is the number of vaccinated subjects with available data for the events listed.

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

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

1 ^dFever - Any Fever indicates $\geq 100.4^{\circ}\text{F}$. The percentage of temperature measurements that were taken by rectal,
2 axillary, or oral routes, or not recorded were 69.2%, 17.6%, 13.2%, and 0.0%, respectively for Dose 1; and 69.0%,
3 13.8%, 16.1%, and 1.1%, respectively for Dose 2

4 **Table 3: Frequency of Solicited Injection Site Reactions and Systemic Adverse Events**
5 **Within 7 Days After Vaccination with Fluzone, Children 3 Through 8 Years of Age**

	Dose 1 (N ^a =150-151) Percentage			Dose 2 (N ^a =144-145) Percentage		
	Any	Moderate ^b	Severe ^c	Any	Moderate ^b	Severe ^c
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^d	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

6 ^aN is the number of vaccinated subjects with available data for the events listed.

7 ^bModerate - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-
8 site erythema, Injection-site swelling, Injection-site induration, and Injection-site ecchymosis: ≥ 2.5 cm to < 5 cm;
9 Fever: $> 100.4^{\circ}\text{F}$ to $\leq 102.2^{\circ}\text{F}$; Headache, Malaise, and Myalgia: interferes with daily activities

10 ^cSevere - Injection-site pain: incapacitating, unable to perform usual activities, may have/or required medical care or
11 absenteesim; Injection-site erythema, Injection-site swelling, Injection-site induration, and Injection-site
12 ecchymosis: ≥ 5 cm; Fever: $> 102.2^{\circ}\text{F}$; Headache, Malaise, and Myalgia: prevents daily activities

13 ^dFever - Any Fever indicates $\geq 99.5^{\circ}\text{F}$. The percentage of temperature measurements that were taken by oral or
14 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%,
15 respectively for Dose 2

1 "-" indicates information was not collected

2

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

6

7 **Adults**

8 Adults 18 through 64 years of age received Fluzone (year 2008-2009 formulation) in a multi-
9 center trial conducted in the US. The safety analysis set included 1421 Fluzone recipients. [Table 4](#)
10 summarizes solicited injection-site reactions and systemic adverse events reported within 7 days
11 post-vaccination via diary cards.

12 **Table 4: Frequency of Solicited Injection-Site Reactions and Systemic Adverse Events**
13 **Within 7 Days After Vaccination with Fluzone, Adults 18 Through 64 Years of Age**

	(N ^a =1392-1394) Percentage		
	Any	Grade 2 ^b	Grade 3 ^c
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^d	2.6	0.4	0.2

1 ^aN is the number of vaccinated subjects with available data for the events listed.

2 ^bGrade 2 - Injection-site erythema, Injection-site induration, Injection-site swelling, and Injection-site ecchymosis: ≥
3 2.5 cm to <5 cm; Injection-site pain and Injection-site pruritus: sufficiently discomforting to interfere with normal
4 behavior or activities; Fever: >100.4°F to ≤102.2°F; Headache, Myalgia, Malaise, and Shivering: interferes with
5 daily activities

6 ^cGrade 3 - Injection-site erythema, Injection-site induration, Injection-site swelling, and Injection-site ecchymosis: ≥5
7 cm; Injection-site pain: incapacitating, unable to perform usual activities; Injection-site pruritus: incapacitating,
8 unable to perform usual activities, may have/or required medical care or absenteeism; Fever: >102.2°F; Headache,
9 Myalgia, Malaise, and Shivering: prevents daily activities

10 ^dFever - Any Fever indicates ≥99.5°F. The percentage of temperature measurements that were taken by oral or
11 axillary routes, or not recorded were 99.6%, 0.0%, and 0.4%, respectively

12

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

16

17 **Geriatric Adults**

18 Adults 65 years of age and older received Fluzone (year 2006-2007 formulation) in a multi-
19 center, double-blind trial conducted in the US. The safety analysis set included 1260 Fluzone
20 recipients.

21

22 [Table 5](#) summarizes solicited injection-site reactions and systemic adverse events reported within
23 7 days post-vaccination via diary cards. Onset was usually within the first 3 days after vaccination
24 and a majority of the reactions resolved within 3 days.

1 **Table 5: Frequency of Solicited Injection-Site Reactions and Systemic Adverse Events**
2 **Within 7 Days After Vaccination with Fluzone, Adults 65 Years of Age and Older**

	N ^a =1258-1260 Percentage		
	Any	Moderate ^b	Severe ^c
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^d	2.3	0.2	0.1

3 ^aN is the number of vaccinated subjects with available data for the events listed

4 ^bModerate - Injection-site pain: sufficiently discomforting to interfere with normal behavior or activities; Injection-
5 site erythema and Injection-site swelling: ≥ 2.5 cm to < 5 cm; Fever: $> 100.4^{\circ}\text{F}$ to $\leq 102.2^{\circ}\text{F}$; Myalgia, Malaise, and
6 Headache: interferes with daily activities

7 ^cSevere - Injection-site pain: incapacitating, unable to perform usual activities; Injection-site erythema and Injection-
8 site swelling: ≥ 5 cm; Fever: $> 102.2^{\circ}\text{F}$; Myalgia, Malaise, and Headache: prevents daily activities

9 ^dFever –Any Fever indicates $\geq 99.5^{\circ}\text{F}$. The percentage of temperature measurements that were taken by oral route or
10 not recorded were 98.6% and 1.4%, respectively

11

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

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6.2 Post-Marketing Experience

The following events have been spontaneously reported during the post-approval use 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, vasodilatation/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

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7 DRUG INTERACTIONS

Data evaluating the concomitant administration of Fluzone with other vaccines are not available.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with Fluzone. It is also not known whether Fluzone can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Fluzone should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether Fluzone is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Fluzone is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of Fluzone in children below the age of 6 months have not been established. Safety and immunogenicity of Fluzone was evaluated in children 6 months through 8 years of age. [See *Adverse Reactions (6.1) and Clinical Studies (14.1).*]

8.5 Geriatric Use

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

4

5 **11 DESCRIPTION**

6 Fluzone (Influenza Virus Vaccine) for intramuscular injection, is an inactivated influenza virus
7 vaccine, prepared from influenza viruses propagated in embryonated chicken eggs. The virus-
8 containing allantoic fluid is harvested and inactivated with formaldehyde. Influenza virus is
9 concentrated and purified in a linear sucrose density gradient solution using a continuous flow
10 centrifuge. The virus is then chemically disrupted using a non-ionic surfactant, Octylphenol
11 Ethoxylate (Triton® X-100), producing a “split virus”. The split virus is further purified and then
12 suspended in sodium phosphate-buffered isotonic sodium chloride solution.

13

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

15

16 Antibiotics are not used in the manufacture of Fluzone.

17

18 No presentation of Fluzone contains latex.

19

20 Fluzone is standardized according to United States Public Health Service requirements and is
21 formulated to contain HA of each of the following three influenza strains recommended for the
22 2012-2013 influenza season: A/California/07/2009 NYMC X-179A (H1N1), A/Victoria/361/2011

1 IVR-165 (H3N2) and B/Texas/6/2011 (a B/Wisconsin/1/2010-like virus). The amounts of HA and
2 other ingredients per dose of vaccine are listed in [Table 6](#).

3 **Table 6: Fluzone Ingredients**

Ingredient	Quantity (per dose)	
	Fluzone 0.25 mL Dose	Fluzone 0.5 mL Dose
Active Substance: Split influenza virus, inactivated strains^a:	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
Other:		
Sodium phosphate-buffered isotonic sodium chloride solution	QS ^b to appropriate volume	QS ^b to appropriate volume
Formaldehyde	≤50 mcg	≤100 mcg
Octylphenol Ethoxylate	≤75 mcg	≤150 mcg
Gelatin	0.05%	0.05%
Preservative		
Single-Dose Presentations	None	None
Multi-Dose Presentation (Thimerosal)	N/A	25 mcg mercury

4 ^aper United States Public Health Service (USPHS) requirement

5 ^bQuantity Sufficient

6 N/A not applicable

7

8 **12 CLINICAL PHARMACOLOGY**

9 **12.1 Mechanism of Action**

10 Influenza illness and its complications follow infection with influenza viruses. Global surveillance
11 of influenza identifies yearly antigenic variants. For example, since 1977, antigenic variants of
12 influenza A (H1N1 and H3N2) viruses and influenza B viruses have been in global circulation.

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

5
6 Antibodies against one influenza virus type or subtype confer limited or no protection against
7 another. Furthermore, antibodies to one antigenic variant of influenza virus might not protect
8 against a new antigenic variant of the same type or subtype. Frequent development of antigenic
9 variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the
10 usual change of one or more new strains in each year's influenza vaccine. Therefore, influenza
11 vaccines are standardized to contain the hemagglutinins of influenza virus strains, representing the
12 influenza viruses likely to be circulating in the US in the upcoming winter.

13
14 Annual vaccination with the current vaccine is recommended because immunity during the year
15 after vaccination declines, and because circulating strains of influenza virus change from year to
16 year.

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18 **13 NON-CLINICAL TOXICOLOGY**

19 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

20 Fluzone has not been evaluated for carcinogenic or mutagenic potential, or for impairment of
21 fertility.

22

23 **14 CLINICAL STUDIES**

1 **14.1 Immunogenicity of Fluzone in Children 6 Months through**
2 **8 Years of Age**

3 In a multi-center study conducted in the US, 68 children 6 months through 35 months of age
4 given two 0.25 mL doses of Fluzone and 120 children 3 years through 8 years of age given two
5 0.5 mL doses of Fluzone were included in the per-protocol analysis set. The two doses (year
6 2006-2007 formulation) were administered 26 to 30 days apart. Females accounted for 42.6% of
7 the participants in the 6 months through 35 months age group and 53.3% of the participants in the
8 3 years through 8 years age group. Most participants in the 6 months through 35 months and 3
9 years through 8 years age groups, respectively, were Caucasian (70.6% and 79.2%), followed by
10 Hispanic (19.1% and 13.3%), and Black (7.4% and 4.2%).

11
12 The percentage of participants who received influenza vaccination during the previous influenza
13 season was 54.4% for the 6 months through 35 months age group and 27.5% for the 3 years
14 through 8 years age group. [Table 7](#) shows seroconversion rates and the percentage of participants
15 with an HI titer $\geq 1:40$ pre-vaccination and one month following the second dose of Fluzone.

1 **Table 7: Percentage (%) with Pre and Post-Vaccination HI Titers \geq 1:40 and Seroconversion**
 2 **Following the Second Vaccine Injection with Fluzone^a in Children 6 Months Through 35**
 3 **Months and 3 Years Through 8 Years of Age**

Antigen	Age Group	Pre-Vaccination Titer \geq 1:40 % (95% CI)	Post-Vaccination ^b Titer \geq 1:40 % (95% CI)	Seroconversion ^c % (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)

4 ^aChildren received two doses of Fluzone administered 26 to 30 days apart, irrespective of previous influenza
 5 vaccination history

6 ^bPost-vaccination HI titers drawn at 28 days post-dose

7 ^cSeroconversion: Paired samples with pre-vaccination HI titer $<$ 1:10 and post-vaccination (28 days post-dose 2) titer
 8 \geq 1:40 or a minimum 4-fold increase for participants with pre-vaccination titer \geq 1:10

9

10 **14.2 Immunogenicity of Fluzone in Adults**

11 Adults 18 through 64 years of age received Fluzone (year 2008-2009 formulation) in a multi-
 12 center trial conducted in the US. For immunogenicity analyses, there were 1287 participants who
 13 received Fluzone in the per-protocol analysis set. There were fewer males (35.8%) than females.
 14 The mean age was 42.6 years (ranged from 18.2 through 65.0 years). Most participants were
 15 Caucasian (80.0%), followed by Hispanic (11.0%), and Black (6.3%). [Table 8](#) shows

1 seroconversion rates at 28 days following vaccination and the percentage of participants with an
2 HI titer $\geq 1:40$ prior to vaccination and 28 days following vaccination.

3

4 **Table 8: Percentage (%) with Pre and Post-Vaccination HI Titers $\geq 1:40$ and Seroconversion**
5 **in Adult Fluzone Recipients 18 through 64 Years of Age**

Antigen	Pre-Vaccination Titer $\geq 1:40$ % (95% CI) N ^c =1285-1286	Post-Vaccination ^a Titer $\geq 1:40$ % (95% CI) N ^c =1283-1285	Seroconversion ^b % (95% CI) N ^c =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)

6 ^a Post-vaccination HI titers drawn at 28 days post-dose

7 ^b Seroconversion: Paired samples with pre-vaccination HI titer $< 1:10$ and post-vaccination (28 days post-dose) titer
8 $\geq 1:40$ or a minimum 4-fold increase for participants with pre-vaccination titer $\geq 1:10$

9 ^c N is the number of vaccinated subjects with available data for the immunologic endpoint listed

10

11 **14.3 Immunogenicity of Fluzone in Geriatric Adults**

12 Adults 65 years of age and older received Fluzone (year 2006-2007 formulation) in a multi-center
13 trial conducted in the US. For immunogenicity analyses, there were 1,275 participants who
14 received Fluzone in the immunogenicity analysis set. Females accounted for 54.7% of
15 participants. The mean age was 72.9 years (ranged from 65 through 94 years of age); 36% of
16 participants were 75 years of age or older. Most participants were Caucasian (92.9%), followed by
17 Hispanic (3.7%), and Black (2.7%). [Table 9](#) shows seroconversion rates at 28 days following

1 vaccination and the percentage of participants with an HI titer $\geq 1:40$ prior to vaccination and 28
2 days following vaccination.

3

4 **Table 9: Percentage (%) with Pre and Post-Vaccination HI Titers $\geq 1:40$ and Seroconversion**
5 **in Adult Fluzone Recipients 65 Years of Age and Older**

Antigen	Pre-Vaccination HI Titer $\geq 1:40$ %(95% CI) N ^c =1267-1268	Post-Vaccination ^a Titer $\geq 1:40$ %(95% CI) N ^c =1252	Seroconversion ^b %(95% CI) N ^c =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)

6 ^a Post-vaccination HI titers drawn at 28 days post-dose

7 ^b Seroconversion: Paired samples with pre-vaccination HI titer $< 1:10$ and post-vaccination (28 days post-dose) titer
8 $\geq 1:40$ or a minimum 4-fold increase for participants with pre-vaccination titer $\geq 1:10$

9 ^c N is the number of vaccinated subjects with available data for the immunologic endpoint listed

10 .

1 **15 REFERENCES**

2

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5 2 Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza
6 vaccination. *Virus Res* 2004;103:133-138.

7 3 Hobson D, Curry RL, Beare AS, Ward-Gardner A. The role of serum haemagglutination-
8 inhibiting antibody in protection against challenge infection with influenza A2 and B
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10

11

12

1 **16 HOW SUPPLIED/STORAGE AND HANDLING**

2 **16.1 How Supplied**

3 Single-dose, prefilled syringe, without needle, 0.25 mL, package of 10 (does not contain latex) –
4 NDC 49281-112-25.

5
6 Single-dose, prefilled syringe, without needle, 0.5 mL, package of 10 (does not contain latex) –
7 NDC 49281-012-50.

8
9 Single-dose vial, 0.5 mL, package of 10 (does not contain latex) – NDC 49281-012-10.

10
11 Multi-dose vial, 5 mL, package of one (does not contain latex). The vial contains ten 0.5 mL
12 doses – NDC 49281-390-15.

13
14 **16.2 Storage and Handling**

15 Store all Fluzone presentations refrigerated at 2° to 8°C (35° to 46°F). DO NOT FREEZE.

16 Discard if vaccine has been frozen.

17
18 Between uses, return the multi-dose vial to the recommended storage conditions at 2° to 8°C (35°
19 to 46°F).

20
21 Do not use after the expiration date shown on the label.

22
23 **17 PATIENT COUNSELING INFORMATION**

1 See FDA-approved patient labeling (Patient Information).

- 2 • Inform the patient or guardian that Fluzone contains killed viruses and cannot cause influenza.
- 3 • Fluzone stimulates the immune system to produce antibodies that help protect against
- 4 influenza, but does not prevent other respiratory infections.
- 5 • Annual influenza vaccination is recommended.
- 6 • Instruct vaccine recipients and guardians to report adverse reactions to their healthcare
- 7 provider and/or to the Vaccine Adverse Event Reporting System (VAERS).

8

9 Fluzone is a registered trademark of Sanofi Pasteur Inc.

10

11 Manufactured by:

12 **Sanofi Pasteur Inc.**

13 Swiftwater PA 18370 USA

14

1 **Patient Information Sheet**

2 **Fluzone®**

3 **Influenza Virus Vaccine**

4

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

8

9 **What is Fluzone vaccine?**

10 Fluzone is a vaccine that helps protect against influenza illness (flu).

11 Fluzone vaccine is for people who are 6 months of age and older.

12 Vaccination with Fluzone vaccine may not protect all people who receive the vaccine.

13

14 **Who should not get Fluzone vaccine?**

15 You should not get Fluzone vaccine if you:

- 16 • ever had a severe allergic reaction to eggs or egg products.
- 17 • ever had a severe allergic reaction after getting any flu shot.
- 18 • are younger than 6 months of age.

19

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

- 21 • Guillain-Barré syndrome (severe muscle weakness) after getting a flu shot.
- 22 • problems with your immune system as the immune response may be diminished.

23

24 **How is the Fluzone vaccine given?**

25 Fluzone vaccine is a shot given into the muscle of the arm.

26 For infants, Fluzone vaccine is a shot given into the muscle of the thigh.

1 **What are the possible side effects of Fluzone vaccine?**

2 The most common side effects of Fluzone vaccine are:

- 3 • pain, redness, swelling, bruising and hardness where you got the shot
- 4 • muscle aches
- 5 • tiredness
- 6 • headache
- 7 • fever

8

9 These are not all of the possible side effects of Fluzone vaccine. You can ask your healthcare
10 provider for a list of other side effects that is available to healthcare professionals.

11

12 Call your healthcare provider for advice about any side effects that concern you. You may report
13 side effects to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or
14 <http://vaers.hhs.gov>.

15

16 **What are the ingredients in Fluzone vaccine?**

17 Fluzone vaccine contains 3 killed flu virus strains.

18 Inactive ingredients include formaldehyde, octylphenol ethoxylate, and gelatin. The preservative
19 thimerosal is only in the 10 dose (multi-dose) vial of Fluzone vaccine.

20

21 Manufactured by: Sanofi Pasteur Inc.

22 Swiftwater, PA 18370 USA