INDICATIONS AND USAGE

Fluzone 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 Quadrivalent is approved for use in persons 6 months of age and older. (1)

DOSAGE AND ADMINISTRATION

For intramuscular use only (2)

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

*† Indicates information is not applicable

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.

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Fluzone Quadrivalent (Influenza Vaccine)
Suspension for Intramuscular Injection
2023-2024 Formula
Initial U.S. Approval (Fluzone Quadrivalent): 2013

FULL PRESCRIBING INFORMATION: CONTENTS

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Full prescribing information: www.fda.gov/Drugs/InformationOnDrugs/LabelingAndPackaging/ucm2033200.htm

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)

ADVERSE REACTIONS

In children 6 months through 35 months of age, the most common (≥10%) injection-site reactions were pain (57%) and tenderness (47%–54%), erythema (23%–37%), and swelling (13%–22%); the most common solicited systemic adverse reactions were irritability (47%–54%), abnormal crying (33%–41%), malaise (38%), drowsiness (31%–38%), appetite loss (27%–32%), myalgia (27%), vomiting (10%–15%), and fever (11%–14%). (6.1)

In children 3 years through 8 years of age, the most common (≥10%) injection-site reactions were pain (67%), erythema (34%), and swelling (25%); the most common solicited systemic adverse reactions were myalgia (39%), malaise (32%), and headache (23%). (6.1)

In adults 18 years and older, the most common (≥10%) injection-site reaction was pain (47%); the most common solicited systemic adverse reactions were myalgia (24%), headache (16%), and malaise (11%). (6.1)

In adults 65 years of age and older, the most common (≥10%) injection-site reaction was pain (33%); the most common solicited systemic adverse reactions were myalgia (18%), headache (13%), and malaise (11%). (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.

DISCLOSURE

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

Fluzone Quadrivalent (Influenza Vaccine)
Suspension for Intramuscular Injection
2023-2024 Formula
Initial U.S. Approval (Fluzone Quadrivalent): 2013

Fluzone 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 Quadrivalent is approved for use in persons 6 months of age and older. (1)

DOSAGE FORMS AND STRENGTHS

Suspension for injection supplied in 2 presentations: prefilled single-dose syringe (clear plunger rod), 0.5 mL and multi-dose vial, 5 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)

ADVERSE REACTIONS

In children 6 months through 35 months of age, the most common (≥10%) injection-site reactions were pain (57%) and tenderness (47%–54%), erythema (23%–37%), and swelling (13%–22%); the most common solicited systemic adverse reactions were irritability (47%–54%), abnormal crying (33%–41%), malaise (38%), drowsiness (31%–38%), appetite loss (27%–32%), myalgia (27%), vomiting (10%–15%), and fever (11%–14%). (6.1)

In children 3 years through 8 years of age, the most common (≥10%) injection-site reactions were pain (67%), erythema (34%), and swelling (25%); the most common solicited systemic adverse reactions were myalgia (39%), malaise (32%), and headache (23%). (6.1)

In adults 18 years and older, the most common (≥10%) injection-site reaction was pain (47%); the most common solicited systemic adverse reactions were myalgia (24%), headache (16%), and malaise (11%). (6.1)

In adults 65 years of age and older, the most common (≥10%) injection-site reaction was pain (33%); the most common solicited systemic adverse reactions were myalgia (18%), headache (13%), and malaise (11%). (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

- Pregnancy: Pregnancy exposure registry available. Call Sanofi Pasteur Inc. at 1-800-822-2463.
- Antibody responses to Fluzone Quadrivalent 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: 07/2023

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

For intramuscular use only

The dose and schedule for Fluzone Quadrivalent are presented in Table 1. Prior to vaccination, always refer to the current Advisory Committee on Immunization Practices annual recommendations on prevention and control of influenza vaccines.

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

13 NON-CLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

14.1 Efficacy of Fluzone (Trivalent Influenza Vaccine) in Children 6 through 24 Months of Age

14.2 Efficacy of Fluzone (Trivalent Influenza Vaccine) in Adults

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

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

14.5 Immunogenicity of Fluzone Quadrivalent in Adults ≥18 Years of Age

14.6 Immunogenicity of Fluzone Quadrivalent in Geriatric Adults ≥65 Years of Age

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

16.2 Storage and Handling

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed
(≥10%) injection-site reaction was pain (47%); the most common solicited systemic adverse reactions were myalgia (24%), headache (16%), and malaise (11%); in adults 65 years of age and older, the most common (≥10%) injection-site reaction was pain (33%); the most common solicited systemic adverse reactions were myalgia (18%), headache (13%), and malaise (11%).

1Assessed in children 24 months through 35 months of age
2Assessed in children 6 months through 23 months of age

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trials 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 (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, 57.6%), 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 2 and Table 3 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 1: Dose and Schedule for Fluzone Quadrivalent

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccination Status</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months through 35 months</td>
<td>Not previously vaccinated with influenza vaccine or unknown vaccination history</td>
<td>Two doses, either 0.25 mL or 0.5 mL</td>
<td>Administer at least 4 weeks apart</td>
</tr>
<tr>
<td>36 months through 8 years</td>
<td>Previously vaccinated with influenza vaccine</td>
<td>One or two doses†, either 0.25 mL or 0.5 mL</td>
<td>If two doses, administer at least 4 weeks apart</td>
</tr>
<tr>
<td>9 years and older</td>
<td>Previously vaccinated with influenza vaccine</td>
<td>One or two 0.5 mL doses†</td>
<td>If two doses, administer at least 4 weeks apart</td>
</tr>
</tbody>
</table>

†Indicates information is not applicable
*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

2.2 Administration
Parenteral drug products should be inspected visually for particulate matter and/or discoloration prior to administration, whenever solution and container permit. If any of these defects or conditions exist, Fluzone Quadrivalent should not be administered. Before administering a dose of vaccine, shake the prefilled syringe or vial. Use a separate sterile needle and syringe for each dose withdrawn from the multi-dose vial. A maximum of ten doses can be withdrawn from the multi-dose vial. The preferred sites for intramuscular injection are the anterolateral aspect of the thigh in infants 6 months through 11 months of age, the anterolateral aspect of the thigh (or the deltoid muscle if muscle mass is adequate) in persons 12 months through 35 months of age, or the deltoid muscle in persons ≥36 months of age. The vaccine should not be injected into the gluteal area or areas where there may be a major nerve trunk. Do not administer this product intravenously, intradermally, or subcutaneously.

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

3 DOSAGE FORMS AND STRENGTHS
Fluzone Quadrivalent is a suspension for injection.
Fluzone Quadrivalent is supplied in 3 presentations:
1) Prefilled single-dose syringe (clear syringe plunger rod), 0.5 mL, for persons 6 months of age and older.
2) Multi-dose vial, 5 mL, for persons 6 months of age and older.

4 CONTRAINDICATIONS
Do not administer Fluzone Quadrivalent to anyone with a history of a severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine (see Description [1]), including egg protein, or to a previous dose of any influenza vaccine.

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. (See ref. 1) If GBS has occurred within 6 weeks following previous influenza vaccination, the decision to give Fluzone Quadrivalent 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 Fluzone Quadrivalent.

5.3 Altered Immunocompetence
If Fluzone 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 Quadrivalent may not protect all recipients.

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

6 ADVERSE REACTIONS
In children 6 months through 35 months of age receiving a 0.25 mL dose of Fluzone Quadrivalent in Study 1 (NCT01240746), the most common (≥10%) injection-site reactions were pain (57%); tenderness (54%), erythema (37%), and swelling (22%); the most common solicited systemic adverse reactions were irritability (54%), abnormal crying (41%), malaise (38%), drowsiness (38%), appetite loss (32%), myalgia (27%), vomiting (15%), and fever (14%). In children 3 years through 8 years of age, the most common (≥10%) injection-site reactions were pain (67%), erythema (34%), and swelling (25%); the most common solicited systemic adverse reactions were myalgia (39%), malaise (32%), and headache (23%). In adults 18 years and older, the most common
Grade 3 - Injection-site pain: incapacitating, unable to perform usual activities; injection-site erythema, injection-site swelling: ≥5 cm; fever: >103.1°F to ≤104°F (≥39.5°C to ≤40°C); malaise; myalgia; headache: significant; fever: ≥5 days post-vaccination via diary cards for the 0.25 mL and 0.5 mL volumes of Fluzone Quadrivalent.

Participants received 1 or 2 doses according to ACIP recommendations.

The safety analysis set included all persons who received at least one dose of the study vaccine.

Fluzone Quadrivalent (0.25 mL) containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria lineage), licensed

Fluzone Quadrivalent (0.25 mL) containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

Participants received 1 or 2 doses according to ACIP recommendations.

The safety analysis set included all persons who received at least one dose of the 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)

Participants received 1 or 2 doses according to ACIP recommendations.

The safety analysis set included all persons who received at least one dose of the study vaccine.

Fluzone Quadrivalent containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria lineage), licensed

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

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 (≥38.5°C to ≤39.5°C) 6 months through 23 months; >102.1°F to ≤102.2°F (≥39°C to ≤39.1°C) 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

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

Assessed in children 24 months through 35 months of age

Assessed in children 6 months through 23 months of age

Fever measured by any route

Table 2: Study 1: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Safety Analysis Set) (continued)

Table 3: Study 1: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Safety Analysis Set) (continued)

Table 4: Study 1: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 3 Years Through 8 Years of Age (Safety Analysis Set)

Table 5: Study 2: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Children 6 Months Through 35 Months of Age (Safety Analysis Set)

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

In Study 3 (NCT00988143), a multi-centered randomized, open-label trial conducted in the US, adults 18 years of age and older received one dose of either Fluzone Quadrivalent or one of two formulations of comparator trivalent influenza vaccine (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). The safety analysis set included 570 recipients, half aged 18-60 years and half aged 61 years or older. Among participants in the three vaccine groups combined, 67.2% were female (Fluzone Quadrivalent, 68.4%; TIV-1, 66.9%; TIV-2, 65.3%), 88.4% Caucasian (Fluzone Quadrivalent, 91.1%; TIV-1, 86.8%; TIV-2, 87.4%), 9.6% Black (Fluzone Quadrivalent, 6.8%; TIV-1, 12.1%; TIV-2, 10.0%), 0.4% Hispanic (Fluzone Quadrivalent, 0.0%; TIV-1, 0.5%; TIV-2, 0.5%), and 1.7% were of other racial/ethnic groups (Fluzone Quadrivalent, 2.1%; TIV-1, 0.5%; TIV-2, 2.2%). Table 5 summarizes solicited injection-site and systemic adverse reactions reported within 3 days post-vaccination via diary cards. Participants were monitored for unsolicited adverse events and SAEs during the 21 days following vaccination.

Unsolicited non-serious adverse events were reported in 33 (17.4%) recipients in the Fluzone Quadrivalent group, 45 (23.7%) recipients in the TIV-1 group, and 45 (23.7%) recipients in the TIV-2 group. The most commonly reported unsolicited non-serious adverse events were headache, cough, and oropharyngeal pain. In the follow-up period, there were two SAEs, 1 (0.5%) in the Fluzone Quadrivalent group and 1 (0.5%) in the TIV-2 group.

For Geriatric Adults
In Study 4 (NCT01218646), a multi-center, randomized, double-blind trial conducted in the US, adults 65 years of age and older received one dose of either Fluzone Quadrivalent, or one of two formulations of comparator trivalent influenza vaccine (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). The safety analysis set included 675 recipients. Among participants in the three vaccine groups combined, 55.7% were female (Fluzone Quadrivalent, 57.3%; TIV-1, 56.0%; TIV-2, 53.8%), 89.5% Caucasian (Fluzone Quadrivalent, 92.1%; TIV-1, 89.8%; TIV-2, 91.1%), 22.6% Black (Fluzone Quadrivalent, 4.0%; TIV-1, 1.6%; TIV-2, 0.9%), 7.4% Hispanic (Fluzone Quadrivalent, 8.4%; TIV-1, 7.6%; TIV-2, 6.2%) and 0.9% were of other racial/ethnic groups (Fluzone Quadrivalent, 0.0%; TIV-1, 0.9%; TIV-2, 1.8%). Table 6 summarizes solicited injection-site and systemic adverse reactions reported within 7 days post-vaccination via diary cards. Participants were monitored for unsolicited adverse events and SAEs during the 21 days following vaccination.

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

<table>
<thead>
<tr>
<th></th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
</tr>
<tr>
<td><strong>Fever</strong> (<em>≥100.4°F)</em></td>
<td>11.3</td>
<td>0.6</td>
<td>12.2</td>
<td>1.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Vomiting</strong></td>
<td>10.0</td>
<td>0.4</td>
<td>10.2</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

### Table 5: Study 3: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 3 Days After Vaccination in Adults 18 Years of Age and Older (Safety Analysis Set) (continued)

<table>
<thead>
<tr>
<th></th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
</tr>
<tr>
<td><strong>Injection-site adverse reactions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>47.4</td>
<td>6.8</td>
<td>0.5</td>
<td>52.1</td>
<td>7.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Erythema</td>
<td>1.1</td>
<td>0.0</td>
<td>0.0</td>
<td>1.6</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Swelling</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
<td>3.2</td>
<td>0.5</td>
<td>0.0</td>
</tr>
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<td>Induration</td>
<td>0.5</td>
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<td>0.0</td>
<td>1.6</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Ecchymosis</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

### Table 6: Study 4: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Adults 65 Years of Age and Older (Safety Analysis Set) (continued)

<table>
<thead>
<tr>
<th></th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
<th>Fluzone Quadrivalent</th>
<th>Fluzone Quadrivalent</th>
<th>TIV-1 TIV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
<td>Any (%)</td>
<td>Grade 2 (%)</td>
<td>Grade 3 (%)</td>
</tr>
<tr>
<td><strong>Injection-site adverse reactions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>32.6</td>
<td>1.3</td>
<td>0.9</td>
<td>28.6</td>
<td>2.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Erythema</td>
<td>2.7</td>
<td>0.9</td>
<td>0.0</td>
<td>1.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Swelling</td>
<td>1.8</td>
<td>0.4</td>
<td>0.0</td>
<td>1.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>Systemic adverse reactions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>18.3</td>
<td>4.0</td>
<td>0.4</td>
<td>18.3</td>
<td>4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Headache</td>
<td>13.4</td>
<td>1.3</td>
<td>0.4</td>
<td>11.6</td>
<td>1.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Malaise</td>
<td>10.7</td>
<td>4.5</td>
<td>0.4</td>
<td>6.3</td>
<td>0.4</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Table 6: Study 4: Percentage of Solicited Injection-site and Systemic Adverse Reactions Within 7 Days After Vaccination in Adults 65 Years of Age and Older (Safety Analysis Set) (continued)

<table>
<thead>
<tr>
<th></th>
<th>Fluzone Quadrivalent† (N=225)</th>
<th>TIV-1† (B Victoria) (N=225)</th>
<th>TIV-2† (B Yamagata) (N=225)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (≥100.4°F)</td>
<td>1.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*The safety analysis set includes all persons who received 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)
§N is the number of participants in the safety analysis set
‡To 2010-2011 Fluze IV 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
¶Grade 2 - Injection-site pain: some interference with activity; Injection-site erythema and Injection-site swelling: ≥5.1 to ≥10 cm; Fever: ≥101.2°F to ≤102.0°F; Myalgia, Headache, and Malaise: some interference with activity
ßGrade 3 - Injection-site pain: Significant; prevents daily activity; Injection-site erythema and Injection-site swelling: >10 cm; Fever: ≥102.1°F; Myalgia, Headache, and Malaise: Significant; prevents daily activity
aFever measured by any route

Unsolicited non-serious adverse events were reported in 28 (12.4%) recipients in the Fluzone Quadrivalent group, 22 (9.8%) recipients in the TIV-1 group, and 22 (9.8%) recipients in the TIV-2 group. The most commonly reported adverse events were oropharyngeal pain, rhinorrhea, injection-site induration, and headache. Three SAEs were reported during the follow-up period, 2 (0.9%) in the TIV-1 group and 1 (0.4%) in the TIV-2 group.

6.2 Post-Marketing Experience

The following events have been spontaneously reported during the post-approval use of Fluzone (trivalent) 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 Flu (trivalent) or Flu Quadrivalent.

- Blood and Lymphatic System Disorders: Thrombocytopenia, lymphopenopathy
- 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, syncope
- Vascular Disorders: Vasculitis, vasodilatation/flushing
- Respiratory, Thoracic and Mediastinal Disorders: Dyspnea, cough, wheezing, throat tightness, oropharyngeal pain, rhinorrhea
- Skin and Subcutaneous Tissue Disorders: Rash, pruritus, and Stevens-Johnson syndrome
- General Disorders and Administration Site Conditions: Asthenia/fatigue, pain in extremities, chest pain
- Gastrointestinal Disorders: Vomiting

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

Pregnancy Exposure Registry

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

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 Quadrivalent use in pregnant women are insufficient to inform vaccine-associated risk of adverse developmental outcomes.

A developmental and reproductive toxicity study was performed in female rabbits given a 0.5 mL/dose of Fluzone Quadrivalent prior to mating and during gestation (a single human dose is 0.5 mL). This study revealed no adverse effects to the fetus or pre-weaning development due to Fluzone Quadrivalent [see Animal Data (8.1)].

Data

Animal Data: In a developmental and reproductive toxicity study female rabbits were administered a 0.5 mL/dose of Fluzone Quadrivalent by intramuscular injection 24 and 10 days before conception, and on Days 6, 12, and 27 of gestation (a single human dose is 0.5 mL). There were no adverse effects on pre-weaning development or vaccine-related fetal malformations noted in this study.

Clinical Considerations

Disease-associated Maternal and/or Embryofetal 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 premie labor and delivery.

8.2 Lactation

Risk Summary

It is not known whether Fluzone Quadrivalent is excreted in human milk. Data are not available to assess the effects of Fluzone Quadrivalent 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 Quadrivalent and any potential adverse effects on the breastfed child from Fluzone Quadrivalent or from the underlying maternal condition.

For preventive vaccines, the underlying maternal condition is susceptible to the disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of Fluzone Quadrivalent in children below the age of 6 months have not been established.

8.5 Geriatric Use

Safety and immunogenicity of Fluzone Quadrivalent were evaluated in adults 65 years of age and older. [See Clinical Studies (14.6)] Antibody responses to Fluzone Quadrivalent are lower in persons ≥65 years of age than in younger adults.

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

Table 7: Fluzone Quadrivalent Ingredients

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Quantity (per dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluzone Quadrivalent 0.5 mL Dose</td>
<td>Fluzone Quadrivalent 0.5 mL Dose</td>
</tr>
<tr>
<td>Active Substance: Split influenza virus, inactivated strains:</td>
<td></td>
</tr>
<tr>
<td>A (H1N1)</td>
<td>30 mcg HA total</td>
</tr>
<tr>
<td>B (H3N2)</td>
<td>7.5 mcg HA</td>
</tr>
<tr>
<td>B (Victoria lineage)</td>
<td>7.5 mcg HA</td>
</tr>
<tr>
<td>B(Yamagata lineage)</td>
<td>7.5 mcg HA</td>
</tr>
<tr>
<td>Other:</td>
<td></td>
</tr>
<tr>
<td>Sodium phosphate-buffered isotonic sodium chloride solution</td>
<td>QS* to appropriate volume</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>≤50 mcg</td>
</tr>
<tr>
<td>Octylphenol ethoxylate</td>
<td>≤125 mcg</td>
</tr>
<tr>
<td>Preservative</td>
<td>25 mcg</td>
</tr>
<tr>
<td>Single-dose presentations</td>
<td>-</td>
</tr>
<tr>
<td>Multi-dose presentation (thimerosal)</td>
<td>12.5 mcg mercury</td>
</tr>
</tbody>
</table>

*\"Indicates information is not applicable
†per United States Public Health Service (USPHS) requirement
‡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

5
Vaccine efficacy against all influenza viral types and subtypes was a secondary endpoint. Illness was defined as fever with signs or symptoms of an upper respiratory infection. 52.5% were male, 50.8% were Caucasian, 42.0% were Black, and 7.2% 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 9.

### Table 9: Estimated Efficacy of Fluzone (Trivalent Influenza Vaccine) Against Influenza in Adults Aged 18 through 49 Years during the 2007-2008 Influenza Season – Intent-to-Treat Analysis Set†‡

<table>
<thead>
<tr>
<th>Laboratory-Confirmed Symptomatic Influenza</th>
<th>Fluzone† (N=813)</th>
<th>Placebo† (N=325)</th>
<th>Fluzone vs. Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative Risk (95% CI)</td>
<td>0.64 (0.46; 0.84)</td>
<td>1.00 (0.82; 0.64)</td>
<td>36.1% (28.0; 45.0)</td>
</tr>
<tr>
<td>Percent Relative Reduction (95% CI)</td>
<td>36.1% (28.0; 45.0)</td>
<td>0.00 (0.00; 0.00)</td>
<td>63.9% (55.0; 72.8)</td>
</tr>
</tbody>
</table>

### 14.3 Immunogenicity of Fluzone Quadrivalent in Children 6 Months Through 8 Years of Age

In Study 1 (NCT01240746) [see Adverse Reactions (6.1)], 1419 children 6 months through 35 months of age and 2101 children 3 years through 8 years of age were included in the per-protocol immunogenicity analysis. Participants 6 months through 35 months of age received one or two 0.25 mL doses and participants 3 years through 8 years of age received one or two 0.5 mL doses of Fluzone Quadrivalent, TIV-1, or TIV-2. For participants who received two doses, the doses were administered approximately 4 weeks apart. The distribution of demographic characteristics was similar to that of the safety analysis set [see Adverse Reactions (6.1)]. Antibody geometric mean titers (GMTs) and seroconversion rates 28 days following vaccination with Fluzone Quadrivalent were non-inferior to those following each TIV for all four strains, based on pre-specified criteria (see Table 10 and Table 11).

### Table 10: Study 1: Non-inferiority of Fluzone Quadrivalent Relative to TIV for Each Strain by HI Antibody GMts at 28 Days Post-Vaccination, Persons 6 Months Through 8 Years of Age* (Per-protocol Analysis Set)

<table>
<thead>
<tr>
<th>Antigen Strain</th>
<th>Fluzone Quadrivalent* (N=2339)</th>
<th>Pooled TIV* (N=1181)</th>
<th>GMT Ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1N1</td>
<td>1124</td>
<td>1096</td>
<td>1.03 (0.93; 1.14)</td>
</tr>
<tr>
<td>H3N2</td>
<td>822</td>
<td>828</td>
<td>0.99 (0.91; 1.08)</td>
</tr>
</tbody>
</table>

---

1. The intent-to-treat analysis includes all enrolled participants who were randomly assigned to receive Fluzone or placebo and vaccinated.
3. §n is the number of participants randomly assigned to receive Fluzone or placebo.
4. †Rate (%): n/N * 100
5. Relative reduction in vaccine efficacy was defined as (1 - relative risk) * 100
6. Includes all culture-confirmed influenza cases throughout the study duration for Year 1 (12 months of follow-up) and includes all culture-confirmed influenza cases throughout the study duration for Year 2 (6 months of follow-up).
In this study, children 6 months through 35 months of age received one or two doses of 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 (GMTs.5 mL dose divided by GMTs.25 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.5 mL dose minus SCR.25 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%).

14.5 Immunogenicity of Fluzone Quadrivalent in Adults ≥18 Years of Age

In Study 3 (NCT00988143) [see Adverse Reactions (6.1)], 565 adults 18 years of age and older who had received one dose of Fluzone Quadrivalent, TIV-1, or TIV-2 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)]. HI antibody GMTs 21 days following vaccination with Fluzone Quadrivalent were non-inferior to those following each TIV for all four strains, based on pre-specified criteria (see Table 12).

Table 12: Study 3: Non-inferiority of Fluzone Quadrivalent Relative to TIV for Each Strain by HI Antibody GMTs at 21 Days Post-Vaccination, Adults 18 Years of Age and Older (Per-protocol Analysis Set)

<table>
<thead>
<tr>
<th>Antigen Strain</th>
<th>Fluzone Quadrivalent&lt;sup&gt;‡&lt;/sup&gt;</th>
<th>Pooled TIV&lt;sup&gt;§&lt;/sup&gt;</th>
<th>GMT Ratio (95% CI)&lt;sup&gt;§&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H1N1)</td>
<td>161</td>
<td>151</td>
<td>1.06 (0.87; 1.31)</td>
</tr>
<tr>
<td>A (H3N2)</td>
<td>304</td>
<td>339</td>
<td>0.90 (0.70; 1.15)</td>
</tr>
<tr>
<td>B (Victoria)</td>
<td>114</td>
<td>135</td>
<td>0.89 (0.70; 1.12)</td>
</tr>
<tr>
<td>B (Yamagata)</td>
<td>155</td>
<td>135</td>
<td>1.15 (0.93; 1.42)</td>
</tr>
</tbody>
</table>

* NCT00988143
† Per-protocol analysis set included all persons who had no study protocol deviations
‡ Fluzone Quadrivalent containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), B/Brisbane/80/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)
§ N is the number of participants in the per-protocol analysis set
¶ Pooled TIV group includes participants vaccinated with either TIV-1 or TIV-2
* N is the number of participants in the per-protocol analysis set
† Per-protocol analysis set included all persons who had no study protocol deviations
‡ Fluzone Quadrivalent containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)
¶ N is the number of participants in the per-protocol analysis set
§ Pooled TIV group includes participants vaccinated with either TIV-1 or TIV-2
* N is the number of participants in the per-protocol analysis set
† Per-protocol analysis set included all persons who had no study protocol deviations
‡ Fluzone Quadrivalent containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)
¶ N is the number of participants in the per-protocol analysis set
§ Pooled TIV group includes participants vaccinated with either TIV-1 or TIV-2
* N is the number of participants in the per-protocol analysis set
† Per-protocol analysis set included all persons who had no study protocol deviations
‡ Fluzone Quadrivalent containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)
¶ N is the number of participants in the per-protocol analysis set
§ Pooled TIV group includes participants vaccinated with either TIV-1 or TIV-2
* N is the number of participants in the per-protocol analysis set
† Per-protocol analysis set included all persons who had no study protocol deviations
‡ Fluzone Quadrivalent containing A/Brisbane/59/2007 (H1N1), A/Uruguay/716/2007 (H3N2), B/Brisbane/60/2008 (Victoria lineage), and B/Florida/04/2006 (Yamagata lineage)

14.6 Immunogenicity of Fluzone Quadrivalent in Geriatric Adults ≥65 Years of Age

In Study 4 (NCT01218646) [see Adverse Reactions (6.1)], 660 adults 65 years of age and older 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)]. HI antibody GMTs 21 days following vaccination with Fluzone Quadrivalent were non-inferior to those following TIV for all four strains, based on pre-specified criteria (see Table 13). Seroconversion rates 21 days following Fluzone Quadrivalent were higher than those following TIV for the B strain not contained in each respective TIV, based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of GMTs (Fluzone Quadrivalent divided by pooled TIV for the A strains, or the TIV containing the corresponding B strain) was > 1.5 for each B strain in Fluzone Quadrivalent

Non-inferiority immunogenicity criteria based on HI antibody GMTs and seroconversion rates were also met when age subgroups (6 months to < 36 months and 3 years to < 9 years) were examined. In addition, HI antibody GMTs and seroconversion rates following Fluzone Quadrivalent were higher than those following TIV for the B strain not contained in each respective TIV based on pre-specified criteria (the lower limit of the 2-sided 95% CI of the ratio of the GMTs (Fluzone Quadrivalent divided by TIV) > 1.5 for each B strain in Fluzone Quadrivalent compared with the corresponding B strain not contained in each TIV and the lower limit of the two-sided 95% CI of the difference of the seroconversion rates (Fluzone Quadrivalent minus TIV) > 10% for each B strain in Fluzone Quadrivalent compared with the corresponding B strain not contained in each TIV).

14.4 Immunogenicity of the 0.5 mL Dose of Fluzone Quadrivalent in Children 6 Months Through 35 Months of Age

In Study 2 (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)].
### Table 13: Study 4: Non-inferiority of Fluzone Quadrivalent relative to TIV for Each Strain by HI Antibody GMTs at 21 Days Post-Vaccination, Adults 65 Years of Age and Older (Per-protocol Analysis Set)\(^1\)

<table>
<thead>
<tr>
<th>Antigen Strain</th>
<th>Fluzone Quadrivalent(^1) N(^2)=220</th>
<th>Pooled TIV(^1) N(^4)=440</th>
<th>GMT Ratio (95% CI)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (H1N1)</td>
<td>231</td>
<td>270</td>
<td>0.85 (0.67; 1.09)</td>
</tr>
<tr>
<td>A (H3N2)</td>
<td>501</td>
<td>324</td>
<td>1.55 (1.25; 1.92)</td>
</tr>
</tbody>
</table>

\(^1\)Per-protocol analysis set included all persons who had no study protocol deviations
\(^2\)Fluzone Quadrivalent containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Fluored/04/2009 (Yamagata lineage), licensed for investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

### Table 14: Study 4: Non-inferiority of Fluzone Quadrivalent Relative to TIV for Each Strain by Seroconversion Rates at 21 Days Post-Vaccination, Adults 65 Years of Age and Older (Per-protocol Analysis Set)\(^1\)

<table>
<thead>
<tr>
<th>Antigen Strain</th>
<th>Fluzone Quadrivalent(^1) N(^2)=220</th>
<th>Pooled TIV(^1) N(^4)=440</th>
<th>Difference of Seroconversion Rates (95% CI)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Brisbane/60/2008 (B Victoria)</td>
<td>73.8</td>
<td>57.9</td>
<td>1.27 (1.05; 1.55)</td>
</tr>
<tr>
<td>B/Florida/04/2006 (B Yamagata)</td>
<td>61.1</td>
<td>(26.5)(^3)</td>
<td>1.11 (0.90; 1.37)</td>
</tr>
</tbody>
</table>

\(^1\)Per-protocol analysis set included all persons who had no study protocol deviations
\(^2\)Fluzone Quadrivalent containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Fluored/04/2009 (Yamagata lineage), licensed for investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

\(^3\)Seroconversion: Paired samples with pre-vaccination HI titer <1:10 and post-vaccination titer ≥1:20

### 15 REFERENCES


### 16 HOW SUPPLIED/STORAGE AND HANDLING

1. How Supplied:
   - Single-dose, prefilled syringe (clear plunger rod), without needle, 0.5 mL (NDC 49281-423-88) (not made with natural rubber latex).
   - Supplied as package of 10 (NDC 49281-423-50).
   - Multi-dose vial, 5 mL (NDC 49281-639-78) (not made with natural rubber latex).
   - Supplied as package of 1 (NDC 49281-639-15).

2. Storage and Handling:
   - Store all Fluzone Quadrivalent presentations refrigerated at 2° to 8°C (35° to 46°F).
   - DO NOT FREEZE. Discard if vaccine has been frozen.

3. 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 Quadrivalent contains killed viruses and cannot cause influenza.
- Fluzone Quadrivalent stimulates the immune system to protect against influenza, but does not prevent other respiratory infections.
- Annual influenza vaccination is recommended.
- 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 Quadrivalent during pregnancy. Women who receive Fluzone 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.

### Table 14: Study 4: Non-inferiority of Fluzone Quadrivalent Relative to TIV for Each Strain by Seroconversion Rates at 21 Days Post-Vaccination, Adults 65 Years of Age and Older (Per-protocol Analysis Set)\(^1\)

1. Per-protocol analysis set included all persons who had no study protocol deviations
2. Fluzone Quadrivalent containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), licensed for investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed
3. *Seroconversion:* Paired samples with pre-vaccination HI titer <1:10 and post-vaccination titer ≥1:20

4. Fluzone Quadrivalent contains A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), licensed for investigational TIV containing A/California/07/2009 (H1N1), A/Victoria/210/2009 (H3N2), and B/Florida/04/2006 (Yamagata lineage), non-licensed

5. TIV-2 did not contain B/Florida/04/2006 (B Yamagata)
- headache
- fever

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

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 Quadrivalent during pregnancy. Women who receive Fluzone 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.

**What are the ingredients in Fluzone Quadrivalent?**

Fluzone Quadrivalent contains 4 killed flu virus strains. Inactive ingredients include formaldehyde and octylphenol ethoxylate. The preservative thimerosal is only in the multi-dose vial of Fluzone Quadrivalent.

Manufactured by:

**Sanofi Pasteur Inc.**

Swiftwater, PA 18370 USA

INFZ4-FPLR-SL-JUL23 Rx Only