Fluzone®

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# Fluzone®
Influenza Vaccine
2024-2025 Formula

## FULL PRESCRIBING INFORMATION

## INDICATIONS AND USAGE
Fluzone® is a vaccine indicated for active immunization for the prevention of disease caused by influenza virus subtypes A and type B contained in the vaccine.

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

## DOSAGE AND ADMINISTRATION
- **For intramuscular use**

**Dose and Schedule**

The dose and schedule for Fluzone is presented in Table 1.

**Table 1: Dose and Schedule for Fluzone**

| 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 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 and national annual recommendations on prevention and control of influenza with vaccines.

"-" Indicates information is not applicable

**Administration**

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

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 Use a separate sterile needle and syringe for each dose withdrawn from the multi-dose vial.

A maximum of ten doses can be withdrawn from the multi-dose vial.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

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

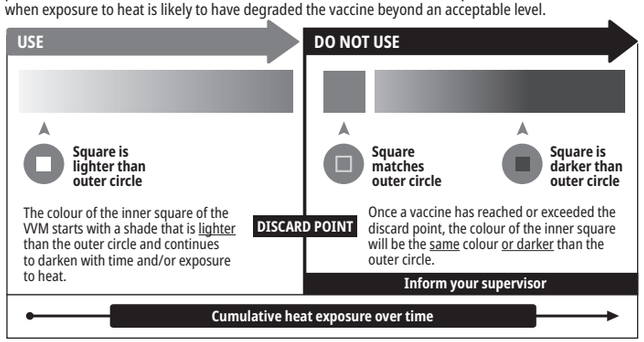
## DOSAGE FORMS AND STRENGTHS
Fluzone is an injectable suspension.

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.

**Use of the Vaccine Vial Monitor (VVM):**

The Vaccine Vial Monitors (VVM) are on the cap of Menactra vaccine supplied through SANOFI PASTEUR. The colour dot which appears on the cap of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.




The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the circle, then the vaccine can be used. As soon as the colour of the central square is the same colour as the circle or of a darker colour than the circle, then the vial should be discarded.

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

## WARNINGS AND PRECAUTIONS
**Guillain-Barré Syndrome**

Recurrence of Guillain-Barré syndrome (GBS) has been temporally associated with administration of the influenza vaccine. 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.

**Preventing and Managing Allergic Reactions**

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

**Altered Immunocompetence**

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

**Limitations of Vaccine Effectiveness**

Vaccination with Fluzone may not protect all recipients.

**Syncope**

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

## ADVERSE REACTIONS
**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 of another vaccine, and may not reflect the rates observed in practice.

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

In a multi-center study conducted in the US, 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 (year 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. The most frequently reported solicited injection site reactions within 7 days following dose 1 and dose 2 vaccination were tenderness (47.3% and 56.3%) and erythema (29.3% and 32.2%) in children 6 months through 35 months; or pain (59.3% and 62.1%) and erythema (27.8% and 27.6%) in children 3 years through 8 years. The most frequently reported solicited systemic adverse events within 7 days following dose 1 and dose 2 vaccination were irritability (42.9% and 34.9%), crying abnormal (31.9% and 18.6%), and drowsiness (26.4% and 26.7%) in children 6 months through 35 months; or myalgia (28.0% and 17.4%), malaise (20.0% and 14.6%), and headache (16.7% and 11.8%) in children 3 years through 8 years.

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.

In a multi-center study conducted in the US, 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.

In children 6 months through 35 months of age, the most common (≥10%) injection-site reactions were pain (57.0%) or tenderness (54.1%) , erythema (37.3%), and swelling (21.6%); the most common solicited systemic adverse reactions were irritability (54.0%), abnormal crying (41.2%), malaise (38.1%), drowsiness (37.7%), appetite loss (32.3%), myalgia (26.7%), vomiting (14.8%), and fever (14.3%). In children 3 years through 8 years of age, the most common (≥10%) injection-site reactions were pain (66.6%), erythema (34.1%), and swelling (24.8%); the most common solicited systemic adverse reactions were myalgia (38.6%), malaise (31.9%), and headache (23.1%).

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; no deaths occurred. 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. One death occurred in the TIV-1 group (a drowning 43 days post-vaccination).

**0.5-mL Dose of Fluzone Quadrivalent in Children 6 Months through 35 Months of Age**

In a randomized, observer-blinded, 2-arm, multi-center safety and immunogenicity study conducted in the US, 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.

Solicited reactions within 7 days after vaccination were assessed. Among the 1941 participants who received at least 1 dose of study vaccine, the frequency of solicited injection-site reactions (Group 1 vs. Group 2) were tenderness (47% vs. 50%), erythema (23% vs. 24%), and swelling (13% vs. 15%); the frequency of systemic adverse reactions were irritability (47% vs. 49%), abnormal crying (33% vs. 34%), drowsiness (32% vs. 31%), appetite loss (27% vs. 28%), fever of ≥ 38°C (100.4°F) (11% vs. 12%), and vomiting (10% vs. 10%). 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**

Adults 18 through 64 years of age received Fluzone (year 2008-2009 formulation) in a multi-center trial conducted in the US. The safety analysis set included 1421 Fluzone recipients. The most frequently reported solicited injection-site reaction was pain (53.7%); the most frequently reported solicited systemic adverse events were myalgia (30.8%), headache (30.3%), and malaise (22.2%).

Within 28 days and six 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.

**Geriatric Adults**

Adults 65 years of age and older received Fluzone (year 2006-2007 formulation) in a multi-center, double-blind trial conducted in the US. The safety analysis set included 1260 Fluzone recipients. Onset was usually within the first 3 days after vaccination and a majority of the reactions resolved within 3 days. The most frequently reported solicited injection-site reaction was pain (24.3%); the most frequently reported solicited systemic adverse events were myalgia (18.3%), headache (14.4%), and malaise (14.0%).

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.

***Reporting adverse reactions***

Persons who receive the vaccine and their guardians should be instructed to report any adverse or unusual reaction to their healthcare provider.

**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

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

## USE IN SPECIFIC POPULATIONS
**Pregnancy**

According to WHO, vaccination is especially important for populations who are at a higher risk of serious influenza complications. Therefore, WHO recommends annual vaccination for pregnant women at any stage of pregnancy.

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 and reproductive toxicity study has been performed in female rabbits at a dose approximately 20 times the human dose (on a mg/kg basis) and has revealed no evidence of impaired female fertility or harm to the fetus due to Fluzone Quadrivalent. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Fluzone should be given to a pregnant woman only if clearly needed.

In the developmental and reproductive toxicity study, female rabbits were administered Fluzone Quadrivalent or control saline (each 0.5 mL/dose) by intramuscular injection 24 and 10 days before insemination, and on Days 6, 12, and 27 of gestation. The administration of Fluzone Quadrivalent did not result in systemic maternal toxicity (no adverse clinical signs and no change in body weight or food consumption). In addition, no adverse effects on pregnancy, parturition, lactation, or embryo-fetal or pre-weaning development were observed. There were no vaccine-related fetal malformations or other evidence of teratogenesis noted in this study.

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

**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.

**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 and CLINICAL STUDIES.]

**Geriatric Use**

Safety and immunogenicity of Fluzone was evaluated in adults 65 years of age and older.[See ADVERSE REACTIONS and CLINICAL STUDIES] Antibody responses to Fluzone are lower in persons ≥65 years of age than in younger adults.

## DESCRIPTION

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

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

Antibiotics are not used in the manufacture of Fluzone.

No presentation of Fluzone contains latex.

Fluzone 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 2024-2025 influenza season: A/Victoria/4897/2022 IVR-238 (H1N1), A/California/122/2022 SAN-022 (an A/Thailand/8/2022-like virus) and B/Michigan/01/2021 (a/Austria/1359417/2021-like virus, B Victoria lineage). The amounts of HA and other ingredients per dose of vaccine are listed in Table 2.

**Table 2: 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 |
| **Preservative** | | |
| Multi-Dose Presentation (Thimerosal) | 12.5 mcg mercury | 25 mcg mercury |

a per United States Public Health Service (USPHS) requirement

b Quantity Sufficient

## CLINICAL PHARMACOLOGY

**Mechanism of Action**

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

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

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

## NON-CLINICAL TOXICOLOGY

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

## CLINICAL STUDIES

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

A randomized, double-blind, placebo-controlled study was 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 0.25 mL doses of either Fluzone (N = 525) or a placebo (N = 261). 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.

During the overall study duration of Year 1 (12 months of follow-up), there were 37 culture-confirmed cases of influenza, in 15 participants (5.5%) in the Fluzone group and 22 participants (15.9%) in the Placebo group. During the overall study duration of Year 2 (6 months of follow-up), there were 13 cases of influenza, 9 participants (3.6%) and 4 participants (3.3%), respectively. Efficacy of Fluzone against all cases of influenza during the overall study duration was 66% for Year 1 and -10% for Year 2.

**Efficacy of Fluzone (Trivalent Influenza Vaccine) in Adults**

A randomized, double-blind, placebo-controlled study was 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). Influenza virus as identified by cell culture was reported in 2.6% of participants in the Fluzone group and in 9.5% of participants in the combined placebo group and by PCR in 3.4% of participants in the Fluzone group and in 10.8% of participants in the combined placebo group. Virus was identified by one or both methods in 3.4% of participants in the Fluzone group and in 10.8% of participants in the combined placebo group. Efficacy of Fluzone was 73% against culture-confirmed influenza, 68% against PCR confirmed influenza, and 68% against any laboratory-confirmed influenza (by culture, PCR, or both).

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

In 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 (year 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.

Blood samples were obtained before dose one and 28 days post-dose two. The proportion of children 6 months through 35 months of age with HI titers ≥1:40 increased from 11.8% pre-vaccination to 92.6% post-vaccination against A/H1N1, from 29.4% pre-vaccination to 100.0% post-vaccination against A/H3N2, and from 1.5% pre-vaccination to 20.6% post-vaccination against type B.

The proportion of children 3 years through 8 years of age with HI titers ≥1:40 increased from 40.0% pre-vaccination to 99.2% post-vaccination against A/H1N1, from 80.0% pre-vaccination to 100.0% post-vaccination against A/H3N2, and from 3.3% pre-vaccination to 58.3% post-vaccination against type B.

Seroconversion was defined for paired samples with a pre-vaccination HI titer <1:10 and post-vaccination titer ≥1:40 or a minimum 4-fold increase for participants with a pre-vaccination titer ≥1:10. For children 6 months through 35 months of age, seroconversion rates against A/H1N1, A/H3N2, and B were 88.2%, 91.2%, and 20.6%, respectively. For children 3 years through 8 years of age, seroconversion rates were 78.3%, 61.7%, and 53.3%, respectively.

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

In a randomized, observer-blinded, 2-arm, multi-center safety and immunogenicity study conducted in the US, 1027 children, 6 months through 35 months of age, were included in the per-protocol immunogenicity analysis.

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 (GMT0.5-mL dose divided by GMT0.25-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 (SCR0.5-mL dose minus SCR0.25-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%).

**Immunogenicity of Fluzone in Adults**

Adults 18 through 64 years of age received Fluzone (year 2008-2009 formulation) in 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%).

Blood samples were obtained pre-vaccination and 28 days post-vaccination. The proportion of participants with HI titers ≥1:40 increased from 39.1% pre-vaccination to 91.7% post-vaccination against A/H1N1, from 33.6% pre-vaccination to 91.4% post-vaccination against A/H3N2, and from 41.2% pre-vaccination to 89.3% post-vaccination against type B.

Seroconversion was defined for paired samples with a pre-vaccination HI titer <1:10 and post-vaccination titer ≥1:40 or a minimum 4-fold increase for participants with a pre-vaccination titer ≥1:10. Seroconversion rates against A/H1N1, A/H3N2, and B were 60.5%, 74.8%, and 54.2%, respectively.

**Immunogenicity of Fluzone in Geriatric Adults**

Adults 65 years of age and older received Fluzone (year 2006-2007 formulation) in a multi-center trial conducted in the US. For immunogenicity analyses, there were 1,275 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%).

Blood samples were obtained pre-vaccination and 28 days post-vaccination. The proportion of participants with HI titers ≥1:40 increased from 45.9% pre-vaccination to 76.8% post-vaccination against A/H1N1, from 68.6% pre-vaccination to 96.5% post-vaccination against A/H3N2, and from 27.3% pre-vaccination to 67.6% post-vaccination against type B.

Seroconversion was defined for paired samples with a pre-vaccination HI titer <1:10 and post-vaccination titer ≥1:40 or a minimum 4-fold increase for participants with a pre-vaccination titer ≥1:10. Seroconversion rates against A/H1N1, A/H3N2, and B were 23.1%, 50.7%, and 29.9%, respectively.

## HOW SUPPLIED/STORAGE AND HANDLING

**How Supplied**

Multi-dose vial, 5 mL, package of one (does not contain latex). The vial contains ten 0.5 mL doses.

**Storage and Handling**

Store Fluzone multi-dose vials 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.

Fluzone is a registered trademark of **Sanofi Pasteur Inc.**

Manufactured by:
**Sanofi Pasteur Inc.**
Swiftwater PA 18370 USA

sanofi