HIGHLIGHTS OF PRESCRIBING INFORMATION

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

Flublok® Quadrivalent (Influenza Vaccine) Sterile Solution for Intramuscular Injection 2018-2019 Formula

Initial U.S. Approval: 2013

INDICATIONS AND USAGE

• Flublok Quadrivalent is a vaccine indicated for active immunization against disease caused by influenza A subtype viruses and influenza type B viruses contained in the vaccine. Flublok Quadrivalent is approved for use in persons 18 years of age and older. (1)

DOSAGE AND ADMINISTRATION

For intramuscular (IM) injection only (0.5 mL). (2)

DOSAGE FORMS AND STRENGTHS

A sterile solution for injection supplied in 0.5mL single dose pre-filled syringes.

CONTRAINDICATIONS

• Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine. (4, 6.2, 11)

WARNINGS AND PRECAUTIONS

• Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of Flublok Quadrivalent. (5.1)

5.2 Guillain Barré Syndrome

The 1976 swine influenza vaccine was associated with an increased frequency 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 one additional case per 1 million persons vaccinated. If GBS has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of the potential benefits and risks. (5.2)

ADVERSE REACTIONS

• In adults 18 through 49 years of age, the most common (≥10%) injection-site reactions were tenderness (48%) and pain (37%); the most common (≥10%) solicited systemic adverse reactions were headache (20%), fatigue (17%), myalgia (13%) and arthralgia (10%). (6.1)

• In adults 50 years of age and older, the most common (≥10%) injection site reactions were tenderness (34%) and pain (19%); the most common (≥10%) solicited systemic adverse reactions were headache (13%) and fatigue (12%). (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 outcomes in women exposed to Flublok Quadrivalent during pregnancy are being monitored. Contact: Sanofi Pasteur Inc. by calling 1-800-822-2463. (6.1)

See 17 for PATIENT COUNSELING INFORMATION

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

For intramuscular injection only.

2.2 Administration

Invert the pre-filled syringe containing Flublok Quadrivalent gently prior to affixing the appropriate size needle for intramuscular administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

The preferred site for injection is the deltoid muscle. Flublok Quadrivalent should not be mixed in the

3 DOSAGE FORMS AND STRENGTHS

Flublok Quadrivalent is a sterile solution supplied in pre-filled, single-dose syringes, 0.5 mL.

4 CONTRAINDICATIONS

Flublok Quadrivalent is contraindicated in individuals with known severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine (see Post-marketing Experience [6.2]; and Description [7]).

5 WARNINGS AND PRECAUTIONS

5.1 Managing Allergic Reactions

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

5.2 Guillain Barré Syndrome

The 1976 swine influenza vaccine was associated with an increased frequency 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 one additional case per 1 million persons vaccinated. If GBS has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Flublok should be based on careful consideration of the potential benefits and risks.

5.3 Altered Immunocompetence

If Flublok Quadrivalent is administered to immunocompromised individuals, including persons receiving immunosuppressive therapy, the immune response may be diminished.

5.4 Limitations of Vaccine Effectiveness

Vaccination with Flublok Quadrivalent may not protect all vaccine recipients.

6 ADVERSE REACTIONS

In adults 18 through 49 years of age, the most common (≥10%) injection-site reactions were tenderness (48%) and pain (37%); the most common (≥10%) solicited systemic adverse reactions were headache (20%), fatigue (17%), myalgia (13%), and arthralgia (10%) (see Clinical Trials Experience [6.1]).

In adults 50 years of age and older, the most common (≥10%) injection site reactions were tenderness (34%) and pain (19%); the most common (≥10%) solicited systemic adverse reactions were headache (13%) and fatigue (12%) (see Clinical Trials Experience [6.1]).

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a vaccine cannot be directly compared to rates in the clinical studies of another vaccine and may not reflect the rates observed in clinical practice.

Flublok Quadrivalent

Flublok Quadrivalent has been administered to and safety data collected from 998 adults 18-49 years of age (Study 1) and 4328 adults 50 years of age and older (Study 2). In Studies 1 and 2, local (injection site) and systemic adverse reactions were solicited with the use of a memory aid for 7 days following vaccination, unsolicited adverse events were collected for ~28 days post-vaccination, and serious adverse events (SAEs) were collected for 8 months post-vaccination via clinic visit or remote contact.

Study 1 included 1330 subjects 18 through 49 years of age for safety analysis, randomized to receive Flublok Quadrivalent (n=698) or a comparator inactivated influenza vaccine (Fluarix Quadrivalent, manufactured by GlaxoSmithKline) (n=332) (see Clinical Studies [14]). The mean age of participants was 33.5 years. Overall, 65% of subjects were female, 59% white/Caucasian, 37% black/African American, 1.0% Native Hawaiian/Pacific Islander, 0.8% American Indian/Alaskan Native, 0.5% Asian, 1.4% other racial groups, and 16% of Hispanic/Latino ethnicity. Table 1 summarizes the incidence of solicited local and systemic adverse reactions reported within 7 days of vaccination with Flublok Quadrivalent or the comparator vaccine.

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Lactation

8.3 Pediatric Use

8.4 Geriatric Use

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

13 NONCLINICAL TOXICOLOGY

14 CLINICAL STUDIES

14.1 Efficacy Against Laboratory-Confirmed Influenza

14.2 Immunogenicity of Flublok Quadrivalent

16 HOW SUPPLIED/DISTRIBUTION AND HANDLING

16.1 How Supplied

16.2 Storage and Handling

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

Revised: 04/2019

1
Table 1: Frequency of Solicited Local Injection Site Reactions and Systemic Adverse Reactions within 7 Days of Administration of Flublok Quadrivalent or Comparator in Adults 18-49 Years of Age, Study 1 (Reactogenicity Populations) \(^{1, 3}\)

<table>
<thead>
<tr>
<th>Reactogenicity Term</th>
<th>Flublok Quadrivalent</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3</td>
</tr>
</tbody>
</table>

Subjects with ≥1 injection site reaction\( ^{4, 5}\)
- 51
- 1
- 0
- 52
- 2
- 0

Local Tenderness
- 48
- 1
- 0
- 47
- 1
- 0

Local Pain
- 37
- 1
- 0
- 36
- 1
- 0

Firmness / Swelling
- 5
- 0
- 0
- 3
- 0
- 0

Redness
- 4
- 0
- 0
- 1
- 0
- 0

Subjects with ≥1 systemic reaction\( ^{1, 4}\)
- 34
- 2
- <1
- 36
- 3
- <1

Headache
- 20
- 1
- 0
- 21
- 2
- <1

Fatigue
- 17
- 1
- 0
- 17
- 1
- 0

Muscle Pain
- 13
- 1
- 0
- 12
- 0
- 1

Joint Pain
- 10
- 1
- 0
- 10
- 1
- 0

Nausea
- 9
- 1
- <1
- 9
- 1
- 0

Shivering / Chills
- 7
- 1
- 0
- 6
- 1
- 0

Fever\(^{<, 6}\)
- 2
- <1
- <1
- 1
- <1
- 0

NOTE: Data based on the most severe response reported by subjects. Results ≥1% reported to nearest whole percent; results >0 but <1% reported as <1%. Comparator = U.S.-licensed comparator quadrivalent inactivated influenza vaccine manufactured by GlaxoSmithKline.

\( ^{1}\)Study 1 is registered as NCT02395059 under the National Clinical Trials registry.

\( ^{2}\)Denominators for fever: Flublok Quadrivalent n = 990, Comparator n = 327.

\( ^{3}\)Reactogenicity Populations were defined as all randomized subjects who received study vaccine according to the treatment actually received and who had at least one non-missing data point for injection site, systemic or body temperature reactogenicity categories. For local pain, tenderness and systemic reactions: Grade 1 = No interference with activities. Grade 2 = Prevented some activities, and headache may have required non-narcotic pain reliever. Grade 3 = Prevented most or all normal activities or required prescription medications. Grade 4 = Required ER visit or hospitalization. For injection site redness and firmness/swelling: Grade 1=≤ to ≤50 mm (small), Grade 2=≥ to ≤100 mm (medium). Grade 3>≥ to ≥100 mm (large). Grade 4=necrosis or exfoliative dermatitis.

\( ^{4}\)Denominators for injection site reactions: Flublok Quadrivalent n = 996, Comparator n = 332.

\( ^{5}\)Denominators for systemic reactions: Flublok Quadrivalent n = 994, Comparator n = 332.

\( ^{6}\)Fever defined as ≥100.4°F (38°C). Grade 1 (<100.4°F); Grade 2 (101.2°F to <102.2°F); Grade 3 (102.1°F to <104°F); Grade 4 ≥104°F.

Table 2: Frequency of Solicited Local Injection Site Reactions and Systemic Adverse Reactions within 7 Days of Administration of Flublok Quadrivalent or Comparator in Adults 50 Years of Age and Older, Study 2 (Reactogenicity Populations) \(^{1, 4}\)

<table>
<thead>
<tr>
<th>Reactogenicity Term</th>
<th>Flublok Quadrivalent</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3</td>
</tr>
</tbody>
</table>

Subjects with ≥1 injection site reaction\( ^{4, 5}\)
- 38
- <1
- <1
- 40
- <1
- <1

Local Tenderness
- 34
- <1
- <1
- 37
- <1
- <1

Local Pain
- 19
- <1
- <1
- 22
- <1
- <1

Firmness / Swelling
- 3
- 0
- 0
- 3
- <1
- 0

Redness
- 3
- 0
- 0
- 2
- <1
- 0

Subjects with ≥1 systemic reaction\( ^{1, 4}\)
- 25
- 1
- <1
- 26
- 1
- <1

NOTE: Data based on the most severe response reported by subjects. Results ≥1% reported to nearest whole percent; results >0 but <1% reported as <1%.

\( ^{1}\)Comparator = U.S.-licensed comparator quadrivalent inactivated influenza vaccine, Fluarix Quadrivalent, manufactured by GlaxoSmithKline.

\( ^{2}\)Study 2 is registered as NCT02285998 under the National Clinical Trials registry.

\( ^{4}\)Reactogenicity Populations were defined as all randomized subjects who received study vaccine according to the treatment actually received and who had at least one non-missing data point for injection site, systemic or body temperature reactogenicity categories. For local pain, tenderness, and systemic reactions: Grade 1 = No interference with activity. Grade 2 = Some interference with activity. Grade 3 = Prevents daily activity. Grade 4 = Required ER visit or hospitalization. For injection site redness and firmness/swelling: Grade 1 = ≤ to ≤50 mm (small), Grade 2 = ≥ to ≤100 mm (medium). Grade 3 = >≥ to ≥100 mm (large). Grade 4 = Necrosis or exfoliative dermatitis.

\( ^{4}\)Denominators for injection site reactions: Flublok Quadrivalent n = 4307, Comparator n = 4319.

\( ^{5}\)Denominators for systemic reactions: Flublok Quadrivalent n = 4306, Comparator n = 4318.

\( ^{6}\)Fever defined as ≥100.4°F (38°C). Grade 1 (<100.4°F) to ≤<101.1°F); Grade 2 (101.2°F to ≤102.2°F); Grade 3 (102.1°F to <104°F); Grade 4 ≥104°F.

Among adults 18-49 years of age (Study 1), through 6 months post-vaccination, no deaths were reported. SAEs were reported by 145 (3.4%) Flublok Quadrivalent recipients and 2 (0.6%) Comparator recipients. No SAEs were considered related to study vaccine. Among adults 50 years of age and older (Study 2), 20 deaths occurred in the 6 months post-vaccination, including 8 Flublok Quadrivalent and 12 Comparator recipients. No deaths were considered related to study vaccine. SAEs were reported by 145 (3.4%) Flublok Quadrivalent recipients and 132 (3%) Comparator recipients. No SAEs were considered related to study vaccine.

In the 28 days following vaccination, one or more unsolicited treatment emergent adverse events occurred in 10.3% of Flublok Quadrivalent and 10.5% of Comparator recipients in Study 1 (adults 18-49 years of age) and in 13.8% of Flublok Quadrivalent and 14.1% of Comparator recipients in Study 2 (adults ≥50 years of age). In both studies, rates of individual events were similar between treatment groups, and most events were mild to moderate in severity.

Flublok (Trivalent Formulation)

The safety experience with Flublok is relevant to Flublok Quadrivalent because both vaccines are manufactured by GlaxoSmithKline as an active control (n=3434) (see Clinical Studies [14]). The mean age of participants was 62.7 years. Overall, 58% of subjects were female, 40% white/Caucasian, 16% black/African American, 9% American Indian/Alaskan Native, 0.4% Asian, 0.2% Native Hawaiian/Pacific Islander, 0.7% other racial groups, and 5% of Hispanic/Latino ethnicity. Table 3 summarizes the incidence of solicited local and systemic adverse reactions reported within seven days of vaccination with Flublok Quadrivalent or Comparator.

Table 3: Frequency of Solicited Local Injection Site Reactions and Systemic Adverse Reactions within 7 Days of Administration of Flublok Quadrivalent or Comparator in Adults 648 received Afluria. Flublok and 665 received Afluria. Among subjects aged 65 years and older, 642 received Flublok and 665 received Afluria. Fatigue was reported by 10 subjects, 6 Flublok recipients and 4 Comparator recipients. One of the SAEs, vasovagal syncope following injection of Flublok, was considered related to administration of study vaccine.

Among adults 18-49 years of age (Study 1), through 6 months post-vaccination, no deaths were reported. SAEs were reported by 145 (3.4%) Flublok Quadrivalent recipients and 2 (0.6%) Comparator recipients. No SAEs were considered related to study vaccine. Among adults 50 years of age and older (Study 2), 20 deaths occurred in the 6 months post-vaccination, including 8 Flublok Quadrivalent and 12 Comparator recipients. No deaths were considered related to study vaccine. SAEs were reported by 145 (3.4%) Flublok Quadrivalent recipients and 132 (3%) Comparator recipients. No SAEs were considered related to study vaccine.

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Flublok Quadrivalent is standardized according to United States Public Health Service (USPHS) requirements. For the 2019-2020 influenza season it is formulated to contain 180 mcg HA per 0.5 mL dose, with 45 mcg HA of each of the following 4 influenza virus strains: A/Michigan/45/2015 (H1N1), A/Singapore/INFIMH-16-0019/2016 (H3N2), B/Indiana/15/2016 (a B/Colorado/62/2017-like virus), and B/Phuket/3073/2013. A single 0.5 mL dose of Flublok Quadrivalent contains sodium chloride (4.4 mg), monobasic sodium phosphate (0.195 mg), dibasic sodium phosphate (1.3 mg), and polysorbate 20 (Tween® 20) (27.5 mcg). Each 0.5 mL dose of Flublok Quadrivalent may also contain residual amounts of baculovirus and Spodoptera frugiperda cell proteins (< 19 mcg), baculovirus and cellular DNA (< 10 ng), and Triton X-100 (≤ 100 mcg).

Flublok Quadrivalent contains no egg proteins, antibiotics, or preservatives. The single-dose, pre-filled syringes contain no natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Flublok Quadrivalent contains recombinant HA proteins of the four strains of influenza virus specified by the A/Aichi/2/2005 and B/Florida/4/2012 inactivated seasonal vaccine. These proteins function as antigens which induce a humoral immune response, measured by hemagglutination inhibition (HI) antibody. 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 (usually annual) development of antigenic variants through antigen drift is the virologic basis for seasonal epidemics and the reason for the usual replacement of one or more influenza virus strains in each year’s influenza vaccine. Therefore, influenza vaccines are standardized to contain the hemagglutinins of influenza virus strains (i.e., typically type A H1N1, and in quadrivalent formulations, type B), representing the influenza viruses likely to be circulating in the U.S. in the upcoming winter.

13 NONCLINICAL TOXICOLOGY

Flublok Quadrivalent has not been evaluated for carcinogenic or mutagenic potential, or for impairment of male fertility in animals. A developmental toxicity study conducted in rats vaccinated with Flublok Quadrivalent formulation revealed no evidence of impaired female fertility (see Pregnancy [8.1]).

14 CLINICAL STUDIES

14.1 Efficacy Against Laboratory-Confirmed Influenza

14.1.1 Efficacy Against Influenza-like Illness—CDC-ILI

The efficacy of Flublok (trivalent formulation) is relevant to Flublok Quadrivalent because both vaccines are manufactured using the same process and have overlapping compositions (see Description [11]). The efficacy of Flublok (trivalent formulation) in protecting against influenza illness was evaluated in a randomized, observer-blind, placebo-controlled multicenter trial conducted in the U.S. during the 2007-2008 influenza season in adults 18-49 years of age (Study 3). Study 3 enrolled and vaccinated 4648 healthy adults (mean age 32.5 years) randomized in a 1:1 ratio to receive a single dose of Flublok (n=2344) or saline placebo (n=2304). Among enrolled subjects, 59% were female, 67% were white, 15% African-American, 2% Asian, < 1% other races, and 11% of Latino/Hispanic ethnicity. Culture-confirmed influenza was assessed by active and passive surveillance for influenza-like illness (ILI) beginning at least 7 days after vaccination and continuing for 8 weeks post-vaccination. ILI cases were assigned to one of 7 categories: fluid 100°F; 2) respiratory symptoms (cough, sore throat, or runny nose/stuffy nose); or 3) systemic symptoms (myalgias, arthralgias, headache, chills/sweats, or tiredness/malaise). For subjects with an episode of ILI, nasal and throat swab samples were collected for viral culture.

The primary efficacy endpoint of Study 3 was Centers for Disease Control-defined influenza-like illness (CDC-ILI) with a positive culture for an influenza virus strain antigenically resembling a strain represented in Flublok. CDC-ILI is defined as fever of ≥100°F oral accompanied by cough, sore throat, or both on the same day or on consecutive days. Attack rates and vaccine efficacy (VE), defined as the reduction in the influenza rate for Flublok relative to placebo, were calculated for the total vaccinated cohort (n=4648). The pre-defined success criterion for the primary efficacy analysis was that the lower bound of the 95% confidence interval (CI) of VE should be at least 45%. Vaccine efficacy against antigenically matched culture-confirmed CDC-ILI could not be determined reliably because 96% of the influenza isolates obtained from subjects in Study 3 were not antigenically matched to the strains represented in the vaccine. An exploratory analysis of VE of Flublok against all strains, regardless of antigenic match, isolated from any subject with an ILI not necessarily meeting CDC-ILI criteria, demonstrated an efficacy estimate of 44.8% (95% CI 24.4, 60.0). See Table 3 for a presentation of VE by case definition and antigenic similarity.

Table 3: Vaccine Efficacy Against Culture-Confirmed Influenza in Healthy Adults 18-49 Years of Age, Study 3*

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Flublok (trivalent) (N=2344)</th>
<th>Saline Placebo (N=2304)</th>
<th>Flublok Vaccine Efficacy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive culture with a strain represented in the vaccine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDC-ILI, all matched strains‡§</td>
<td>64</td>
<td>2.7</td>
<td>114</td>
</tr>
<tr>
<td>Any ILI, all matched strains‡**</td>
<td>41</td>
<td>1.7</td>
<td>79</td>
</tr>
</tbody>
</table>

*CDC-ILI, all strains‡‡,§§ |
Sub-Type A | 26 | 1.1 | 56 | 2.4 | 54.4 |
Sub-Type B | 18 | 0.8 | 23 | 1.0 | 33.1 |

** Any ILI, all strains‡‡,§§ |
Sub-Type A | 41 | 1.7 | 79 | 3.4 | 49.0 |

†,§,‡§,‡‡,§§,**
Table 3: Vaccine Efficacy Against Culture-Confirmed Influenza in Healthy Adults 18-49 Years of Age. Study 3 (continued)

<table>
<thead>
<tr>
<th>Case definition</th>
<th>Flublok Quadrivalent (N=2344)</th>
<th>Saline Placebo (N=2304)</th>
<th>Flublok Vaccine Efficacy*</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, n</td>
<td>Rate, %</td>
<td>Cases, n</td>
<td>Rate, %</td>
<td></td>
</tr>
<tr>
<td>Type B</td>
<td>23</td>
<td>1.0</td>
<td>36</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*In Study 3 (NCT00639891), vaccine efficacy analyses were conducted on the Total Vaccinated Cohort (all randomized subjects who received study vaccine according to the treatment actually received and who provided data). Vaccine efficacy (VE) = 1 minus the ratio of Flublok/placebo infection rates.
†Determined under the assumption of Poisson event rates, according to Breslow and Day, 1987.
‡Meets CDC influenza-like illness (CDCl-ILI) defined as fever of ≥100.4°F oral accompanied by cough and/or sore throat, on the same day or on consecutive days.
¶Primary endpoint of trial.
#All culture-confirmed cases are considered, regardless of whether they qualified as CDC-ILI.
§Secondary endpoint of trial.

Table 4: Relative Vaccine Efficacy (rVE) of Flublok Quadrivalent versus Comparator against Laboratory-Confirmed Influenza. Regardless of Antigenic Similarity to Vaccine Antigens, Adults 50 Years of Age and Older, Study 2 (Efficacy Population)

<table>
<thead>
<tr>
<th>Flublok Quadrivalent (N=4303)</th>
<th>Comparator (N=4301)</th>
<th>n</th>
<th>Attack Rate (%/n)</th>
<th>RR</th>
<th>VEE (% 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All rPCR-positive Influenza†</td>
<td>96</td>
<td>2.2</td>
<td>96</td>
<td>2.2</td>
<td>0.70</td>
</tr>
<tr>
<td>All rPCR-positive Influenza‡</td>
<td>73</td>
<td>1.7</td>
<td>73</td>
<td>1.7</td>
<td>0.64</td>
</tr>
<tr>
<td>All rPCR-positive Influenza§</td>
<td>23</td>
<td>0.5</td>
<td>24</td>
<td>0.6</td>
<td>0.96</td>
</tr>
<tr>
<td>All Culture-confirmed Protocol-defined ILI ¶</td>
<td>58</td>
<td>1.3</td>
<td>101</td>
<td>2.3</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Table 5: Comparison of Day 28 Post-Vaccination Geometric Mean Titers (GMT) for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population)

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Post-vaccination GMT Flublok Quadrivalent</th>
<th>Post-vaccination Comparator GMT</th>
<th>Flublok Quadrivalent Comparator Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>493</td>
<td>397</td>
<td>0.81</td>
<td>(0.71, 0.92)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>748</td>
<td>577</td>
<td>0.50</td>
<td>(0.44, 0.57)</td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>156</td>
<td>134</td>
<td>0.86</td>
<td>(0.74, 0.89)</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>43</td>
<td>64</td>
<td>1.49</td>
<td>(1.29, 1.71)</td>
</tr>
</tbody>
</table>

Table 6: Comparison of Day 28 Serum Conversion Rates for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population)

<table>
<thead>
<tr>
<th>Antigen</th>
<th>SCR (%)</th>
<th>95% CI</th>
<th>Flublok Quadrivalent N=999</th>
<th>Comparator N=323</th>
<th>SCR Difference</th>
<th>Comparator - Flublok Quadrivalent [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>66.7 (63.8, 69.6)</td>
<td>63.5 (58.0, 68.7)</td>
<td>-3.2 (-9.2, 2.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>57.0 (51.4, 62.4)</td>
<td>-15.2 (-21.3, -9.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>56.9 (55.6, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>0.7 (5.4, 6.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/Victoria</td>
<td>40.6 (37.4, 43.7)</td>
<td>58.2 (52.6, 63.6)</td>
<td>17.6 (11.4, 23.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Comparison of Day 28 Serum Conversion Rates for Flublok Quadrivalent and Comparator in Adults 18-49 Years of Age, Study 1 (Immunogenicity Population)

<table>
<thead>
<tr>
<th>Antigen</th>
<th>SCR (%)</th>
<th>95% CI</th>
<th>Flublok Quadrivalent N=999</th>
<th>Comparator N=323</th>
<th>SCR Difference</th>
<th>Comparator - Flublok Quadrivalent [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>66.7 (63.8, 69.6)</td>
<td>63.5 (58.0, 68.7)</td>
<td>-3.2 (-9.2, 2.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>72.1 (69.2, 74.9)</td>
<td>57.0 (51.4, 62.4)</td>
<td>-15.2 (-21.3, -9.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/Yamagata</td>
<td>56.9 (55.6, 62.8)</td>
<td>60.4 (54.8, 65.7)</td>
<td>0.7 (5.4, 6.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/Victoria</td>
<td>40.6 (37.4, 43.7)</td>
<td>58.2 (52.6, 63.6)</td>
<td>17.6 (11.4, 23.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; GMT, geometric mean titer.
†Study 1 is registered as NCT02205509.
§The Immunogenicity Population included all randomized subjects who received a dose of study vaccine, provided serum samples for Day 0 and Day 28 within specified windows, and had no major protocol deviations that might adversely affect the immune response. The pre-defined success criterion for the GMT ratio of Comparator to Flublok Quadrivalent was that the upper bound of the 2-sided 95% CI of the GMT ratio, Comparator / Flublok Quadrivalent at 28 days post-vaccination, must not exceed 1.5.
¶HI titers were assayed using egg-derived antigens.
§Comparator: U.S.-licensed quadrivalent inactivated influenza vaccine, Flurix Quadrivalent, manufactured by GlaxoSmithKline.

Success in meeting the seroconversion rate (SCR) endpoint was pre-defined as an upper bound (UB) of the two-sided 95% CI of SCR Comparator – SCR Flublok Quadrivalent ≤10%. Flublok Quadrivalent met the success criterion for SCRs for three of the four antigens but not for the B/Victoria lineage antigen (Table 6). Sub-population analyses of immunogenicity did not reveal significant differences between genders. Sub-analyses according to race and ethnicity were not informative because the sizes of the subsets were insufficient to reach meaningful conclusions. The HI response to the B/Victoria lineage antigen was low in both vaccine groups.
16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied
Flublok Quadrivalent is supplied as a single-dose, 0.5 mL syringe in a 5 or 10 syringe carton:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components and NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-Dose Pre-filled Syringe</td>
<td>49281-718-10</td>
<td>Ten 0.5 mL single-dose pre-filled syringes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[NDC 49281-718-88]</td>
</tr>
</tbody>
</table>

16.2 Storage and Handling
- Store refrigerated between 2° and 8°C (36° and 46°F).
- Do not freeze. Discard if product has been frozen.
- Protect syringes from light.
- Do not use after expiration date shown on the label.

17 PATIENT COUNSELING INFORMATION
Inform the vaccine recipient of the potential benefits and risks of vaccination with Flublok Quadrivalent.
Inform the vaccine recipient that:
- Flublok Quadrivalent contains non-infectious proteins that cannot cause influenza.
- Flublok Quadrivalent stimulates the immune system to produce antibodies that help protect against the influenza viruses carrying the proteins contained in the vaccine, but does not prevent other respiratory infections.
Instruct the vaccine recipient to report any adverse events to their healthcare provider and/or to the Vaccine Adverse Event Reporting System (VAERS).
Provide the vaccine recipient with the Vaccine Information Statements which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to vaccination. These materials are available free of charge at the Centers for Disease Control (CDC) website (www.cdc.gov/vaccines).
Encourage women who receive Flublok or Flublok Quadrivalent while pregnant to notify Sanofi Pasteur Inc., by calling 1-800-822-2463.
Instruct the vaccine recipient that annual vaccination to prevent influenza is recommended.

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Rx Only