

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Influenza A (H1N1) 2009 Monovalent Vaccine safely and effectively. See full prescribing information for Influenza A (H1N1) 2009 Monovalent Vaccine.

### Influenza A (H1N1) 2009 Monovalent Vaccine

Manufactured by ID Biomedical Corporation of Quebec (IDB)

Distributed by GlaxoSmithKline (GSK)

Suspension for Intramuscular Injection

Initial U.S. Approval: 2006

#### RECENT MAJOR CHANGES

Indications and Usage (1) 01/2010

#### INDICATIONS AND USAGE

- Influenza A (H1N1) 2009 Monovalent Vaccine is an inactivated influenza virus vaccine, indicated for active immunization of adults 18 years of age and older against influenza disease caused by pandemic (H1N1) 2009 virus. (1)
- This indication is based on immune response elicited by the seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL). Influenza A (H1N1) 2009 Monovalent Vaccine and FLULAVAL are manufactured by IDB using the same process. There have been no controlled trials demonstrating a decrease in influenza disease after vaccination with FLULAVAL. (14)

#### DOSAGE AND ADMINISTRATION

Based on currently available information, the vaccination regimen is as follows:

Adults 18 years of age and older: A single 0.5-mL intramuscular injection. (2.2)

#### DOSAGE FORMS AND STRENGTHS

- Influenza A (H1N1) 2009 Monovalent Vaccine is a suspension for intramuscular injection available in 10-mL multi-dose vials containing 10 doses (each dose is 0.5 mL). (3)
- Thimerosal, a mercury derivative, is added as a preservative. Each 0.5-mL dose contains 25 mcg mercury. (3, 11)

#### CONTRAINDICATIONS

Known systemic hypersensitivity reactions to egg proteins, or any other component of Influenza A (H1N1) 2009 Monovalent Vaccine, or life-threatening reaction to previous influenza vaccination. (4.1, 11)

#### WARNINGS AND PRECAUTIONS

- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Influenza A (H1N1) 2009 Monovalent Vaccine should be based on careful consideration of the potential benefits and risks. (5.1)
- Immunocompromised persons may have a reduced immune response to Influenza A (H1N1) 2009 Monovalent Vaccine. (5.2)

#### ADVERSE REACTIONS

Adverse reactions information is based on studies conducted with seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL).

- Most common ( $\geq 10\%$ ) local adverse events for FLULAVAL were pain, redness, and/or swelling at the injection site. (6.1)
- Most common ( $\geq 10\%$ ) systemic adverse events for FLULAVAL were headache, fatigue, myalgia, low grade fever, and malaise. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 and [www.vaers.hhs.gov](http://www.vaers.hhs.gov).

#### DRUG INTERACTIONS

- Do not mix with any other vaccine in the same syringe or vial. (7.1)
- Immunosuppressive therapies may reduce immune responses to Influenza A (H1N1) 2009 Monovalent Vaccine. (7.2)

#### USE IN SPECIFIC POPULATIONS

Information is based on studies conducted with seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL).

- Safety and effectiveness of Influenza A (H1N1) 2009 Monovalent Vaccine have not been established in pregnant women, nursing mothers, and children. (8.1, 8.3, 8.4)
- Geriatric Use: Antibody responses to FLULAVAL were lower in geriatric subjects than in younger subjects. (8.5)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: January 2010

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## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

Influenza A (H1N1) 2009 Monovalent Vaccine is an inactivated influenza virus vaccine indicated for active immunization of adults (18 years of age and older) against influenza disease caused by pandemic (H1N1) 2009 virus.

This indication is based on immune response elicited by the seasonal trivalent Influenza Virus Vaccine manufactured by IDB (FLULAVAL<sup>®</sup>). Influenza A (H1N1) 2009 Monovalent Vaccine and FLULAVAL are manufactured by IDB using the same process. There have been no controlled trials demonstrating a decrease in influenza disease after vaccination with FLULAVAL [see *Clinical Studies (14)*].

### **2 DOSAGE AND ADMINISTRATION**

#### **2.1 Preparation for Administration**

Before withdrawing a dose of vaccine, shake the multi-dose vial vigorously each time to obtain a homogeneous translucent to whitish opalescent suspension. Do not use if resuspension does not occur with vigorous shaking. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Inspect visually for cracks in the vial prior to administration. If any of these conditions exist, the vaccine should not be administered.

Between uses, return the multi-dose vial to the recommended storage conditions, between 2° and 8°C (36° and 46°F). Do not freeze. Discard if the vaccine has been frozen. Once entered, a multi-dose vial, and any residual contents, should be discarded after 28 days.

It is recommended that small syringes (0.5-mL or 1-mL) be used to minimize any product loss.

#### **2.2 Recommended Dose and Schedule**

Clinical studies are ongoing with Influenza A (H1N1) 2009 Monovalent Vaccine to determine the optimal dosage, number of doses, and schedule.

Adults 18 years of age and older should receive a single 0.5-mL intramuscular dose.

The preferred site for intramuscular injection is the deltoid muscle of the upper arm.

The vaccine should not be injected in the gluteal area or areas where there may be a major nerve trunk. A needle length of  $\geq 1$  inch is preferred because needles  $< 1$  inch might be of insufficient length to penetrate muscle tissue in certain adults.

Do not administer this product intravenously, intradermally, or subcutaneously.

### **3 DOSAGE FORMS AND STRENGTHS**

Influenza A (H1N1) 2009 Monovalent Vaccine is a suspension for intramuscular injection available in 10-mL multi-dose vials containing 10 doses (each dose is 0.5 mL).

Thimerosal, a mercury derivative, is added as a preservative. Each 0.5-mL dose contains 25 micrograms (mcg) mercury [see Description (11)].

## **4 CONTRAINDICATIONS**

### **4.1 Hypersensitivity**

Influenza A (H1N1) 2009 Monovalent Vaccine should not be administered to anyone with known systemic hypersensitivity reactions to egg proteins (eggs or egg products), to chicken proteins, or to any component of the vaccine, or who has had a life-threatening reaction to previous influenza vaccination [see Description (11)].

## **5 WARNINGS AND PRECAUTIONS**

### **5.1 Guillain-Barré Syndrome**

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Influenza A (H1N1) 2009 Monovalent Vaccine should be based on careful consideration of the potential benefits and risks.

### **5.2 Altered Immunocompetence**

If Influenza A (H1N1) 2009 Monovalent Vaccine is administered to immunocompromised persons, including individuals receiving immunosuppressive therapy, the expected immune response may not be obtained.

### **5.3 Preventing and Managing Allergic Vaccine Reactions**

Prior to administration, the healthcare provider should review the patient's immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions. Appropriate medical treatment, including epinephrine, and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.

### **5.4 Limitations of Vaccine Effectiveness**

Vaccination with Influenza A (H1N1) 2009 Monovalent Vaccine may not protect all susceptible individuals.

### **5.5 Persons at Risk of Bleeding**

Influenza A (H1N1) 2009 Monovalent Vaccine should be given with caution in individuals with bleeding disorders such as hemophilia or on anticoagulant therapy to avoid the risk of hematoma following the injection.

## **6 ADVERSE REACTIONS**

Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (FLULAVAL) are manufactured by IDB using the same process. The following sections summarize data obtained from clinical studies and postmarketing experience with FLULAVAL.

### **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 trials of another vaccine, and may not reflect the rates observed in practice. As with any vaccine,

there is the possibility that broad use could reveal adverse events not observed in clinical trials.

In clinical trials for FLULAVAL, the most common ( $\geq 10\%$ ) local and systemic adverse events were pain, redness, and/or swelling at the injection site, headache, fatigue, myalgia, low grade fever, and malaise.

Safety information for FLULAVAL was collected in 2 randomized, controlled clinical trials, one in the United States (IDB707-105) and the second in Canada (SPD707-104). The safety population from these trials includes 1,049 adults 18 years of age and older vaccinated with products representative of the licensed formulation of FLULAVAL. The US study included subjects 18 to 64 years of age who were randomized to receive FLULAVAL (N = 721) or a US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE) (N = 279). The Canadian study compared 4 vaccine groups: FLULAVAL, a similar investigational formulation of FLULAVAL with reduced thimerosal, and 2 Canadian-licensed trivalent influenza vaccines.

Among recipients of FLULAVAL, 56.6% were women; 92.4% of subjects were white, 6.5% black, 2.7% Native American, and 1.0% Asian. In the US study, 74.8% of the recipients of FLULAVAL were Hispanic/Latino. The mean age of subjects in the US study was 38 years (range 18 to 64 years) and 19% of subjects were 50 to 64 years of age. In the Canadian study, the mean age was 63 years (range 50 to 92 years), and 46.6% were 65 years of age and older.

A series of symptoms and/or findings were specifically solicited by a diary/memory aid used by subjects for at least the day of vaccination and 3 days post-treatment (Table 1). Subjects were actively queried about changes in their health status through 42 days post-vaccination in the US trial, and 6 months post-vaccination in the Canadian study. In addition, spontaneous reports of adverse events were also collected (Table 2).

**Table 1. Solicited Adverse Events in the First 4 Days After Administration of FLULAVAL or Comparator Influenza Vaccine**

Adverse Events	US Trial Adults 18 to 64 years of age (80% <50 years of age)		Canadian Trial Adults 50 years of age and older
	FLULAVAL N = 721	Comparator Influenza Vaccine <sup>a</sup> N = 279	FLULAVAL <sup>b</sup> N = 328
<b>Local</b>			
Pain	174 (24%)	85 (31%)	70 (21%)
Redness	76 (11%)	28 (10%)	48 (14%)
Swelling	71 (10%)	29 (10%)	21 (6%)
<b>Systemic</b>			
Headache	127 (18%)	48 (17%)	34 (10%)
Fatigue	123 (17%)	43 (15%)	33 (10%)
Myalgia	93 (13%)	44 (16%)	35 (11%)
Fever <sup>c</sup>	79 (11%)	28 (10%)	1 (1%)
Malaise	73 (10%)	28 (10%)	13 (4%)
Sore throat	64 (9%)	26 (9%)	17 (5%)
Reddened eyes	44 (6%)	15 (5%)	10 (3%)
Cough	44 (6%)	19 (7%)	11 (3%)
Chills	38 (5%)	6 (2%)	10 (3%)
Chest tightness	24 (3%)	4 (1%)	6 (2%)
Facial swelling	7 (1%)	1 (1%)	1 (1%)

Results >1% reported to nearest whole percent; results >0 but ≤1 reported as 1%.

<sup>a</sup> US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE).

<sup>b</sup> Includes subjects who received FLULAVAL and a similar investigational formulation of FLULAVAL with reduced thimerosal.

<sup>c</sup> Fever defined as ≥37.5°C in the US study, and ≥38.0°C in the Canadian study.

Local adverse events occurred with similar frequency in the 2 trials. In the US study, the only significant difference between FLULAVAL and a US-licensed trivalent, inactivated influenza virus vaccine was an increased frequency of chills in subjects receiving FLULAVAL.

Table 2 summarizes the most common adverse events in the 2 clinical trials; adverse events were reported, either spontaneously or in response to queries about changes in health status. The most common events were headache and cough in both studies. These, as well as throat pain, were the only adverse events reported by >1% of subjects in the US trial. The Canadian trial featured a longer safety follow-up (6 months versus 42 days) and enrolled a population exclusively 50 years of age and older. Therefore, spontaneous adverse event reports were more frequent in this trial. As indicated in Table 2, upper respiratory infection, arthralgia,

myalgia, nasopharyngitis, back pain, injection site erythema, diarrhea, fatigue, nausea, and nasal congestion were each reported by  $\geq 5\%$  of the recipients of FLULAVAL in the Canadian study.

**Table 2. Adverse Events Reported Spontaneously<sup>a</sup> by  $\geq 5\%$  of Subjects in Either Clinical Trial of FLULAVAL**

Adverse Events	US Trial (safety follow-up 42 days) Adults 18 to 64 years of age (80% <50 years of age)		Canadian Trial (safety follow-up 6 months) Adults 50 years of age and older
	FLULAVAL N = 721	Comparator Influenza Vaccine <sup>b</sup> N = 279	FLULAVAL <sup>c</sup> N = 328
Headache	49 (7%)	18 (7%)	63 (19%)
Cough	16 (2%)	5 (2%)	48 (15%)
Pharyngolaryngeal pain	17 (2%)	9 (3%)	38 (12%)
Upper respiratory infection	3 (1%)	2 (1%)	30 (9%)
Arthralgia	5 (1%)	3 (1%)	27 (8%)
Myalgia	4 (1%)	2 (1%)	23 (7%)
Nasopharyngitis	1 (1%)	1 (1%)	23 (7%)
Back pain	5 (1%)	3 (1%)	19 (6%)
Injection site erythema	2 (1%)	1 (1%)	18 (5%)
Diarrhea	5 (1%)	0	18 (5%)
Fatigue	6 (1%)	2 (1%)	17 (5%)
Nausea	5 (1%)	1 (1%)	17 (5%)
Nasal congestion	7 (1%)	2 (1%)	16 (5%)

Results  $>1\%$  reported to nearest whole percent; results  $>0$  but  $\leq 1\%$  reported as 1%.

<sup>a</sup> Adverse events reported spontaneously or in response to queries about changes in health status.

<sup>b</sup> US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE).

<sup>c</sup> Includes subjects who received FLULAVAL and a similar investigational formulation of FLULAVAL with reduced thimerosal.

## 6.2 Postmarketing Experience

The following additional adverse events have been identified during postapproval use of FLULAVAL. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their incidence rate or establish a causal relationship to the vaccine. Adverse events described here are included because: a) they represent reactions which are known to occur following immunizations generally or influenza immunizations specifically; b) they are potentially serious; or c) the frequency of reporting.

Blood and Lymphatic System Disorders: Lymphadenopathy.

Eye Disorders: Conjunctivitis, eye pain, photophobia.

Gastrointestinal Disorders: Dysphagia, vomiting.

General Disorders and Administration Site Conditions: Chest pain, injection site inflammation, rigors, asthenia, injection site rash, influenza-like symptoms, abnormal gait, injection site bruising, injection site sterile abscess.

Immune System Disorders: Allergic edema of the face, allergic edema of the mouth, anaphylaxis, allergic edema of the throat.

Infections and Infestations: Pharyngitis, rhinitis, laryngitis, cellulitis.

Musculoskeletal and Connective Tissue Disorders: Muscle weakness, back pain, arthritis.

Nervous System Disorders: Dizziness, paresthesia, hypoesthesia, hypokinesia, tremor, somnolence, syncope, Guillain-Barré syndrome, convulsions/seizures, facial or cranial nerve paralysis, encephalopathy, limb paralysis.

Psychiatric Disorders: Insomnia.

Respiratory, Thoracic, and Mediastinal Disorders: Dyspnea, dysphonia, bronchospasm, throat tightness.

Skin and Subcutaneous Tissue Disorders: Urticaria, localized or generalized rash, pruritus, periorbital edema, sweating.

Vascular Disorders: Flushing, pallor.

### **6.3 Adverse Events Associated With Influenza Vaccines**

Anaphylaxis has been reported after administration of FLULAVAL. Although FLULAVAL and Influenza A (H1N1) 2009 Monovalent Vaccine contain only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Allergic reactions include hives, angioedema, allergic asthma, and systemic anaphylaxis [*see Contraindications (4.1)*].

The 1976 swine influenza vaccine was associated with an increased frequency of Guillain-Barré syndrome (GBS). Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. If influenza vaccine does pose a risk, it is probably slightly more than 1 additional case/1 million persons vaccinated.

Neurological disorders temporally associated with influenza vaccination such as encephalopathy, optic neuritis/neuropathy, partial facial paralysis, and brachial plexus neuropathy have been reported.

Microscopic polyangiitis (vasculitis) has been reported temporally associated with influenza vaccination.

## **7 DRUG INTERACTIONS**

### **7.1 Concomitant Administration With Other Vaccines**

There are no data to assess the concomitant administration of Influenza A (H1N1) 2009 Monovalent Vaccine with other vaccines, including trivalent seasonal influenza vaccines. If

Influenza A (H1N1) 2009 Monovalent Vaccine is to be given at the same time as another injectable vaccine(s), the vaccines should always be administered at different injection sites. Influenza A (H1N1) 2009 Monovalent Vaccine should not be mixed with any other vaccine in the same syringe or vial.

## **7.2 Immunosuppressive Therapies**

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to Influenza A (H1N1) 2009 Monovalent Vaccine.

## **8 USE IN SPECIFIC POPULATIONS**

Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (FLULAVAL) are manufactured by IDB using the same process. Available information for FLULAVAL is provided in this section.

### **8.1 Pregnancy**

Pregnancy Category C

Animal reproduction studies have not been conducted with Influenza A (H1N1) 2009 Monovalent Vaccine or FLULAVAL. It is also not known whether these vaccines can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Influenza A (H1N1) 2009 Monovalent Vaccine should be given to a pregnant woman only if clearly needed.

### **8.3 Nursing Mothers**

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated in nursing mothers. It is not known whether Influenza A (H1N1) 2009 Monovalent Vaccine or FLULAVAL is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Influenza A (H1N1) 2009 Monovalent Vaccine is administered to a nursing woman.

### **8.4 Pediatric Use**

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated in children. Safety and effectiveness in the pediatric population have not been established.

### **8.5 Geriatric Use**

In the 2 clinical trials, there were 157 subjects who were  $\geq 65$  years of age and received FLULAVAL; 21 of these subjects were  $\geq 75$  years of age. Hemagglutination-inhibiting (HI) antibody responses were lower in geriatric subjects than younger subjects after administration of FLULAVAL. Solicited adverse events were similar in frequency to those reported in younger subjects [*see Adverse Reactions (6.1) and Clinical Studies (14)*].

## **11 DESCRIPTION**

Influenza A (H1N1) 2009 Monovalent Vaccine is a monovalent, split-virion, inactivated influenza virus subtype A vaccine prepared from virus propagated in the allantoic cavity of embryonated hens' eggs. The virus is inactivated with ultraviolet light treatment followed by formaldehyde treatment, purified by centrifugation, and disrupted with sodium deoxycholate.

Influenza A (H1N1) 2009 Monovalent Vaccine, for intramuscular injection, is a sterile, translucent to whitish opalescent suspension in a phosphate-buffered saline solution that may sediment slightly. The sediment resuspends upon shaking to form a homogeneous suspension. Influenza A (H1N1) 2009 Monovalent Vaccine is formulated to contain 15 mcg hemagglutinin per 0.5-mL dose of the influenza A/California/7/2009 (H1N1)v-like virus. Thimerosal, a mercury derivative, is added as a preservative. Each dose contains 25 mcg mercury. Each dose may also contain residual amounts of egg proteins ( $\leq 1$  mcg ovalbumin), formaldehyde ( $\leq 25$  mcg), and sodium deoxycholate ( $\leq 50$  mcg). Antibiotics are not used in the manufacture of this vaccine.

The vial stopper does not contain latex.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

Influenza illness and its complications follow infection with influenza viruses. Specific levels of HI antibody titer post-vaccination with inactivated influenza virus vaccines have not been correlated with protection from influenza illness but the antibody titers have been used as a measure of vaccine activity. In some human challenge studies, antibody titers of  $\geq 1:40$  have been associated with protection from influenza illness in up to 50% of subjects.<sup>1,2</sup> Antibody against one influenza virus type or subtype confers little or no protection against another virus. Furthermore, antibody 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 virological basis for seasonal epidemics and the reason for the usual change of one or more new strains in each year's influenza vaccine.

## **13 NONCLINICAL TOXICOLOGY**

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

Neither Influenza A (H1N1) 2009 Monovalent Vaccine nor FLULAVAL has been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

## **14 CLINICAL STUDIES**

Influenza A (H1N1) 2009 Monovalent Vaccine and seasonal trivalent Influenza Virus Vaccine (FLULAVAL) are manufactured by IDB using the same process. Data in this section were obtained in clinical studies conducted with FLULAVAL.

In 2 randomized, active-controlled trials of FLULAVAL, the immune responses, specifically HI antibody titers to each virus strain in the vaccine, were evaluated in sera obtained 21 days after administration of FLULAVAL. No controlled trials demonstrating a decrease in influenza disease after vaccination with FLULAVAL have been performed.

A 1,000-subject randomized, blinded, and controlled study was performed in the United States in 18- to 64-year-old healthy adults. A total of 721 subjects received FLULAVAL, and 279 received a US-licensed trivalent, inactivated influenza virus vaccine (FLUZONE); 959 subjects had complete serological data and no major protocol deviations. Among recipients of FLULAVAL, 57.4% were women. The mean age of recipients of FLULAVAL was 37.9 years;

80.4% were 18 to 49 years of age and 19.6% were 50 to 64 years of age.

A second, randomized, blinded, and controlled study which enrolled 658 subjects 50 years of age and older (stratified by age <65 and ≥65 years) was conducted in Canada. This study included elderly persons with medically controlled chronic high-risk diagnoses who were clinically stable. This study compared 4 vaccine groups: FLULAVAL, a similar investigational formulation of FLULAVAL with reduced thimerosal, and 2 Canadian-licensed trivalent influenza vaccines. Results from the 2 groups that received FLULAVAL were submitted in support of the US licensure of FLULAVAL. Among these 2 groups, 54.9% of subjects were women. The mean age of recipients of FLULAVAL was 63 years; 53.4% were 50 to 64 years of age and 46.6% were 65 years of age and older.

For both studies, analysis of the following co-primary endpoints (Table 3) were performed for each HA antigen contained in the vaccine: 1) assessment of the lower bounds of 2-sided 95% confidence intervals for the proportion of subjects with HI antibody titers of ≥1:40 after vaccination, and 2) assessment of the lower bounds of 2-sided 95% confidence intervals for rates of seroconversion (defined as a 4-fold increase in post-vaccination HI antibody titer from pre-vaccination titer ≥1:10, or an increase in titer from <1:10 to ≥1:40). The pre-specified targets for the 2 endpoints varied by study because of age of subjects enrolled. The pre-specified target for endpoint 1) was 70% in the US study and 60% in the Canadian study. For endpoint 2) the pre-specified target was 40% in the US study and 30% in the Canadian study. For the Canadian study, the primary endpoints, as originally designed, were descriptive comparisons of immune response; therefore, a post-hoc analysis of the endpoints, as described above, was performed.

**Table 3. Serum Hemagglutination-Inhibiting (HI) Antibody Responses to FLULAVAL in 2 Clinical Trials<sup>a</sup> (Per Protocol Cohort)<sup>b</sup>**

US Trial in Adults 18 to 64 years of age	% of Subjects (lower bound of 2-sided 95% confidence interval) <sup>c</sup>		
	FLULAVAL N = 692		Primary endpoint met post-vaccination
HI titers $\geq$ 1:40 against:	Pre-vaccination	Post-vaccination	
A/New Caledonia/20/99 (H1N1)	24.6	96.5 (94.9)	Yes
A/Wyoming/03/03 (H3N2)	58.7	98.7 (97.6)	Yes
B/Jiangsu/10/03	5.4	62.9 (59.1)	No
Seroconversion <sup>d</sup> to:			
A/New Caledonia/20/99 (H1N1)	85.6 (82.7)		Yes
A/Wyoming/03/03 (H3N2)	79.3 (76.1)		Yes
B/Jiangsu/10/03	58.4 (54.6)		Yes
Canadian Trial in Adults $\geq$ 50 years of age	% of Subjects (lower bound of 2-sided 95% confidence interval) <sup>c</sup>		
	FLULAVAL <sup>e</sup> N = 324		Primary endpoint met post-vaccination
HI titers $\geq$ 1:40 against:	Pre-vaccination	Post-vaccination	
A/New Caledonia/20/99 (H1N1)	39.5	86.4 (82.2)	Yes
A/Wyoming/03/03 (H3N2)	67.9	99.1 (97.3)	Yes
B/Jiangsu/10/03	10.2	57.1 (51.5)	No
Seroconversion <sup>d</sup> to:			
A/New Caledonia/20/99 (H1N1)	44.8 (39.3)		Yes
A/Wyoming/03/03 (H3N2)	69.1 (63.8)		Yes
B/Jiangsu/10/03	49.1 (43.5)		Yes

<sup>a</sup> Results obtained following vaccination with FLULAVAL manufactured for the 2004–2005 season.

<sup>b</sup> Per Protocol Cohort for immunogenicity included subjects with complete pre- and post-dose HI titer data and no major protocol deviations.

<sup>c</sup> Lower bounds were calculated using Clopper-Pearson method.

<sup>d</sup> Seroconversion = a 4-fold increase post-vaccination in HI antibody titer from pre-vaccination titer  $\geq$ 1:10, or an increase in titer from  $<$ 1:10 to  $\geq$ 1:40.

<sup>e</sup> Includes subjects who received FLULAVAL and a similar investigational formulation of FLULAVAL with reduced thimerosal.

Across both studies, serum HI antibody responses to FLULAVAL met the pre-specified seroconversion criteria for all 3 virus strains, and also the pre-specified criterion for the proportion of subjects with HI titers  $\geq$ 1:40 for both influenza A viruses. In both trials, both FLULAVAL and the comparator vaccine did not meet the pre-specified criterion for the proportion of subjects with HI titers  $\geq$ 1:40 for the influenza B virus. The clinical relevance of

this finding on vaccine-induced protection against illness caused by influenza type B strains is unknown.

## 15 REFERENCES

1. Hannoun C, Megas F, Piercy J. Immunogenicity and protective efficacy of influenza vaccination. *Virus Res.* 2004;103:133-138.
2. Hobson D, Curry RL, Beare AS, et al. The role of serum haemagglutination-inhibiting antibody in protection against challenge infection with influenza A2 and B viruses. *J Hyg Camb.* 1972;70:767-777.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Influenza A (H1N1) 2009 Monovalent Vaccine is supplied in a 10-mL multi-dose vial containing ten 0.5-mL doses. Once entered, the multi-dose vial should be discarded after 28 days.

Store refrigerated between 2° and 8°C (36° and 46°F). Do not freeze. Discard if the vaccine has been frozen. Store in the original package to protect from light.

NDC 19515-801-10 (package of 6 multi-dose vials, with each vial containing ten 0.5-mL doses)

## 17 PATIENT COUNSELING INFORMATION

The vaccine recipient or guardian should be:

- informed of the potential benefits and risks of immunization with Influenza A (H1N1) 2009 Monovalent Vaccine.
- educated regarding potential side effects, emphasizing that Influenza A (H1N1) 2009 Monovalent Vaccine contains non-infectious killed viruses and cannot cause influenza.
- instructed to report any adverse events to their healthcare provider.
- informed that there are 2 influenza vaccine formulations for this influenza season, the monovalent vaccine against influenza disease caused by pandemic (H1N1) 2009 influenza virus and seasonal trivalent influenza vaccine.

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