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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use AREPANRIX safely and effectively. See full prescribing information for AREPANRIX.

AREPANRIX (Influenza A [H5] Monovalent Vaccine, Adjuvanted) injectable emulsion, for intramuscular use
Initial U.S. Approval: 2013

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	4/2026
Warnings and Precautions, Febrile Seizures (5.4)	4/2026

---------- INDICATIONS AND USAGE----------

AREPANRIX is indicated for active immunization for the prevention of disease caused by the influenza A virus H5 subtype contained in the vaccine. AREPANRIX is approved for use in individuals 6 months of age and older at increased risk of exposure to the influenza A virus H5 subtype contained in the vaccine. (1)

In individuals 6 months through 17 years of age, this indication is approved under accelerated approval based on immune responses, as measured by hemagglutination-inhibition (HI) titers. Continued approval for this indication in individuals 6 months through 17 years of age may be contingent upon verification and description of clinical benefit in a confirmatory trial. (1)

----------DOSAGE AND ADMINISTRATION----------

For intramuscular use. (2)

Age	Dose	Schedule
6 months through 17 years of age	Two doses 0.25 mL each	Administer 21 days apart
18 years of age and older	Two doses 0.5 mL each	Administer 21 days apart

Add one vial of AS03 Adjuvant Component to one vial of H5 Antigen Component to form AREPANRIX. (2.2)

---------- DOSAGE FORMS AND STRENGTHS----------

- Injectable emulsion. (3)
- The dose for individuals 18 years of age and older is 0.5 mL and the dose for individuals 6 months through 17 years of age is 0.25 mL. (3)

---------- CONTRAINDICATIONS ----------

History of a severe allergic reaction (e.g., anaphylaxis) to any component of AREPANRIX, including egg protein, or after a previous dose of an influenza vaccine. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of AREPANRIX. (5.1)
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give AREPANRIX should be based on careful consideration of potential benefits and risks. (5.2)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including AREPANRIX. Procedures should be in place to avoid injury from fainting. (5.3)
- In two separate postmarketing observational studies, an increased risk of febrile seizures was observed during the first day following vaccination with standard dose trivalent (2024-2025) and quadrivalent (2023-2024) seasonal influenza vaccines in children 6 months through 4 years of age. (5.4)

---------- ADVERSE REACTIONS ----------

- In individuals 18 years of age and older, the most common solicited local and general reactions reported in clinical trials were injection site pain (83%) and muscle aches (45%), respectively. (6.1)
- In individuals 6 months through 17 years of age, the most common solicited local reaction reported in clinical trials was injection site pain: 47% (6 through 35 months of age), 71% (3 through 8 years of age), and 82% (9 through 17 years of age). The most common solicited general reactions were irritability (51% in 6 through 35 months, and 30% in 3 through 5 years of age) and muscle aches (35% in 6 through 8 years of age, and 42% in 9 through 17 years of age). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 4/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dose and Schedule
2.2 Preparation for Administration
2.3 Administration
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Preventing and Managing Allergic Reactions
5.2 Guillain-Barré Syndrome
5.3 Syncope
5.4 Febrile Seizures
5.5 Limitations of Vaccine Effectiveness
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
14.1 Immunogenicity in Adults
14.2 Immunogenicity in Individuals 6 Months through 17 Years of Age
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

AREPANRIX is indicated for active immunization for the prevention of disease caused by the influenza A virus H5 subtype contained in the vaccine. AREPANRIX is approved for use in individuals 6 months of age and older at increased risk of exposure to the influenza A virus H5 subtype contained in the vaccine.

In individuals 6 months through 17 years of age, this indication is approved under accelerated approval based on immune responses, as measured by hemagglutination-inhibition (HI) titers *[see Clinical Studies (14.2)]*. Continued approval for this indication in individuals 6 months through 17 years of age may be contingent upon verification and description of clinical benefit in a confirmatory trial.

2 DOSAGE AND ADMINISTRATION

For intramuscular use.

2.1 Dose and Schedule

The dose and schedule are presented in Table 1.

Table 1. Dose and Schedule for AREPANRIX

Age	Dose	Schedule
6 months through 17 years of age	Two doses 0.25 mL each	Administer 21 days apart
18 years of age and older	Two doses 0.5 mL each	Administer 21 days apart

2.2 Preparation for Administration

AREPANRIX is supplied as two separate vials that must be combined prior to administration: a vial of H5 Antigen Component (liquid) and a vial of AS03 Adjuvant Component (liquid).

1. Place one vial of H5 Antigen Component and one vial of AS03 Adjuvant Component at room temperature for a minimum of 15 minutes and not to exceed 24 hours.
2. Mix each Component thoroughly by inversion. Inspect visually for particulate matter and discoloration. If either of these conditions exist, the vial(s) should not be used.
3. Cleanse both vial stoppers and withdraw the entire contents of the AS03 Adjuvant Component vial using a sterile syringe with a sterile needle (23-gauge is recommended) and add it to the H5 Antigen Component vial to form AREPANRIX. (If a 23-gauge needle is not available, use a 22-gauge or 21-gauge needle.) Once combined, the resulting AREPANRIX volume is 5 mL.
4. Use a permanent marker to label the vial (now containing multiple doses of AREPANRIX) with the date and time combined in the designated area.
5. Mix the vaccine thoroughly by inversion.
6. Withdraw 0.5 mL dose for individuals 18 years of age and older, or 0.25 mL dose for individuals 6 months through 17 years of age.
7. Once combined, AREPANRIX may be stored at room temperature up to 30°C (86°F) or refrigerated between 2° and 8°C (36° and 46°F) for up to 24 hours *[see How Supplied/Storage and Handling (16)]*.

2.3 Administration

Administer AREPANRIX within 24 hours after combining the H5 Antigen Component and AS03 Adjuvant Component.

If AREPANRIX is stored refrigerated after combining, place the vaccine at room temperature for a minimum of 15 minutes prior to administration.

Mix AREPANRIX thoroughly by inversion before each administration. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, AREPANRIX should not be administered.

Use a sterile needle (23-gauge is recommended) and sterile syringe for each dose withdrawal from the multiple-dose vial and for vaccine administration.

The preferred administration sites are the anterolateral thigh and the deltoid muscle of the upper arm (depending on age).

Administer AREPANRIX intramuscularly.

3 DOSAGE FORMS AND STRENGTHS

AREPANRIX is an injectable emulsion. The dose for individuals 18 years of age and older is 0.5 mL and the dose for individuals 6 months through 17 years of age is 0.25 mL.

4 CONTRAINDICATIONS

AREPANRIX is contraindicated in individuals with known severe allergic reactions (e.g., anaphylaxis) to any component of AREPANRIX, including egg protein, or after a previous dose of an influenza vaccine *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Preventing and Managing Allergic Reactions

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of AREPANRIX.

5.2 Guillain-Barré Syndrome

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give AREPANRIX should be based on careful consideration of potential benefits and risks.

5.3 Syncope

Syncope (fainting) can occur with administration of injectable vaccines, including AREPANRIX. Procedures should be in place to avoid injury from fainting.

5.4 Febrile Seizures

In two postmarketing observational studies, an increased risk of febrile seizures was observed in the first day following administration of seasonal influenza vaccines among children 6 months through 4 years of age *[see Adverse Reactions (6.2)]*.

5.5 Limitations of Vaccine Effectiveness

Vaccination with AREPANRIX may not protect all susceptible individuals.

Vaccination with AREPANRIX may not be as effective in preventing disease caused by influenza A (H5) virus in immunosuppressed individuals, including individuals receiving immunosuppressive therapy, as in immunocompetent individuals. Immunosuppressive therapies, including irradiation, antimetabolites, alkylating

agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to AREPANRIX.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine and may not reflect the rates observed in practice. It is possible that broad use of AREPANRIX could reveal adverse reactions not observed in clinical trials.

Safety data accrued with AREPANRIX containing hemagglutinin (HA) from influenza virus strain A/Indonesia/05/2005 (H5N1) [referred to as AREPANRIX (Original)] are relevant to AREPANRIX containing HA from influenza virus strain A/Astrakhan/3212/2020-like (H5N8) [referred to as AREPANRIX (H5N8)] because the antigens contained in the vaccines are manufactured according to a similar process.

In individuals 18 years of age and older, the most common solicited local and general reactions with AREPANRIX (Original) were injection site pain (83%) and muscle aches (45%), respectively.

In individuals 6 months through 17 years of age, the most common solicited local reaction with AREPANRIX (Original) was injection site pain: 47% (6 through 35 months of age), 71% (3 through 8 years of age), and 82% (9 through 17 years of age). The most common solicited general reactions were irritability (51% in 6 through 35 months of age, and 30% in 3 through 5 years of age) and muscle aches (35% in 6 through 8 years of age, and 42% in 9 through 17 years of age).

Adults

Study 1

In Study 1, a randomized, placebo-controlled, observer-blind, multicenter study, conducted in the U.S. and Canada, 4,561 subjects 18 years of age and older received AREPANRIX (Original) (n = 3,422) or saline placebo (n = 1,139) as a 2-dose vaccination series. Among adults 18 through 64 years of age, the mean age was 39 years (range: 18 through 64 years) and included 57% female subjects and 86% White subjects. Among adults 65 years of age and older, the mean age was 72 years (range: 65 through 91 years) and included 55% female subjects and 94% White subjects.

Solicited Adverse Reactions: Data on adverse reactions were collected using standardized forms for 7 days following receipt of AREPANRIX (Original) or placebo (i.e., day of vaccination and the next 6 days). The reported frequencies of solicited local and general adverse reactions are presented in Table 2.

Table 2. Percentage of Subjects with Solicited Local and General Adverse Reactions within 7 Days[a] of Any Vaccination in Adults

	AREPANRIX (Original) (n = 3,375-3,376) %			Saline Placebo (n = 1,122-1,123) %		
	Any[b]	Grade 2[c] or 3[d]	Grade 3[d]	Any[b]	Grade 2[c] or 3[d]	Grade 3[d]
Local						
Injection site pain	83	37	5	20	4	1
Injection site swelling	10	3	0.1	1	0.3	0
Injection site erythema	9	2	0.1	1	0.1	0
General						
Muscle aches	45	21	3	21	7	2
Headache	35	15	3	28	10	2
Fatigue	34	16	3	23	9	2
Arthralgia	25	11	2	12	4	1
Shivering	17	7	2	10	5	1
Sweating	11	4	1	7	3	1
Fever	5	2	1	3	1	1

n = Number of subjects who received at least 1 dose and for whom safety data were available.

[a] Within 7 days defined as day of vaccination or placebo injection and the next 6 days.

[b] Any swelling/erythema defined as >20 mm. Any fever defined as ≥100.4ºF (38.0ºC).

[c] Grade 2: Pain defined as pain on moving the limb that interferes with normal activities or requires repeated use of pain relievers. Swelling and erythema defined as >50 mm. Fever defined as ≥101.3ºF (38.5ºC). For all other reactions, defined as some interference with normal everyday activities or requires repeated use of pain relievers (for headache, joint pain, or muscle aches).

[d] Grade 3: Pain defined as significant pain at rest; prevents normal activities as assessed by inability to attend/do work or school. Swelling and erythema defined as >100 mm. Fever defined as ≥102.2ºF (39.0ºC). All other reactions were defined as those that prevented normal everyday activities, as assessed by inability to attend/do work or school, or those that required intervention of a physician/healthcare provider.

Unsolicited Adverse Events: The incidences of unsolicited adverse events reported during the 21-day postvaccination periods for subjects who received AREPANRIX (Original) (n = 3,422) or placebo (n = 1,139) were 38.5% and 35.2%, respectively. Events reported in the AREPANRIX (Original) group at a rate of ≥0.5% of subjects and at a rate at least twice that of the placebo group were injection site pruritus (1.8% vs. 0.4%), dizziness (1.4% vs. 0.7%), injection site warmth (1.3% vs. 0.2%), injection site reaction (0.6% vs. 0.2%), and rash (0.6% vs. 0.3%).

Serious Adverse Events (SAEs): SAEs were reported for 0.5% of recipients of AREPANRIX (Original) (n = 3,422) and for 0.3% of placebo recipients (n = 1,139) through Day 42 (21 days following the second dose

of vaccine or placebo). During the approximately one-year safety follow-up (Day 364), SAEs were reported for 3.3% of recipients of AREPANRIX (Original) and for 4.1% of placebo recipients.

The following SAEs reported through Day 182 in subjects who received AREPANRIX (Original) are noted due to a temporal association with vaccination or because no alternative plausible causes for the event were identified: cerebral vascular accidents on Day 1 and Day 9 following the second vaccine dose (1 subject), pulmonary embolism (1 subject) on Day 21 following the first vaccine dose, and corneal transplant rejection (1 subject) 18 years posttransplant on Day 103 following the second vaccine dose.

The following additional SAEs reported through Day 364 are noted because they were reported exclusively in subjects who received AREPANRIX (Original) and because no alternative plausible causes were identified: convulsion (3 subjects) on Days 35, 252, and 346 and thyroid cancer (3 subjects) on Days 21, 29, and 223.

Potential Immune-Mediated Diseases: Based on a prespecified list of events, 14 new onset potential immune-mediated diseases were reported through Day 364, for 13 subjects (0.4%) who received AREPANRIX (Original) (n = 3,422). An additional event was reported for 1 subject (0.09%) who received saline placebo (n = 1,139). Events reported following AREPANRIX (Original) included polymyalgia rheumatica (2 subjects), psoriasis (2 subjects), and 1 of each of the following: autoimmune hepatitis, celiac disease, cranial nerve IV palsy, Crohn's disease, erythema nodosum, facial palsy, radiculitis, rheumatoid arthritis, rheumatoid lung, and temporal arteritis. An additional case of psoriasis was reported following placebo.

Study 2

Study 2 was a Phase 1/2, observer-blind, multicenter trial conducted in the U.S., in which 129 adults received at least 1 dose of AREPANRIX (H5N8). Among 65 adults in the 18 through 64 years of age group, the mean age was 42 years (range: 21 through 63 years), 37% were female, 63% were White, 31% were Black or African American, 2% were Asian, 2% were Native Hawaiian or Other Pacific Islanders, and 34% were Hispanic or Latino. Among 64 adults ages 65 years and older, the mean age was 72 years (range: 65 through 87 years), 50% were female, 78% were White, 20% were Black or African American, 2% were Asian, and 20% were Hispanic or Latino.

Solicited Adverse Reactions: Data on adverse reactions were collected using standardized forms for 7 days following receipt of AREPANRIX (H5N8) (i.e., day of vaccination and the next 6 days). Solicited adverse reactions in Study 2 (AREPANRIX H5N8) were not reported at greater frequencies compared with Study 1 (AREPANRIX Original) The most frequent solicited local and systemic adverse reactions in both studies were injection site pain and muscle ache, respectively.

Serious Adverse Events (SAEs): SAEs were reported for 0.8% of subjects who received AREPANRIX (H5N8) (n = 129) to Day 43 (21 days following the second dose of vaccine). During the approximately 6-month safety follow-up (Day 201), SAEs were reported for 2.3% of subjects who received AREPANRIX (H5N8). None of the reported SAEs were considered related to vaccination.

Potential Immune-Mediated Diseases: No potential immune-mediated diseases were reported during the approximately 6-month safety follow-up (Day 201).

Individuals 6 Months through 17 Years of Age

In Study 3, a randomized, placebo-controlled, observer-blind, multicenter trial, conducted in the U.S., Canada, and Thailand, 838 subjects 6 months through 17 years of age received AREPANRIX (Original) (n = 607) or saline placebo (n = 231) as a 2-dose vaccination series. In the overall population, the mean age was 7 years

(range: 6 months through 17 years); 52% were male; 45% were White, 15% Black, 36% Asian, and 4% other racial groups; 11% were Hispanic or Latino. An uncontrolled crossover study was subsequently conducted in which 155 subjects who initially received placebo, then received AREPANRIX (Original) as a 2-dose series.

Solicited Adverse Reactions: Data on adverse events were collected using standardized forms for 7 days following receipt of AREPANRIX (Original) or placebo (i.e., day of vaccination and the next 6 days). The reported frequencies of solicited local and general adverse reactions are presented in Tables 3 through 5.

Table 3. Percentage of Subjects with Solicited Local and General Adverse Reactions within 7 Days[a] of Any Vaccination in Individuals 6 through 35 Months of Age

	AREPANRIX (Original) %			**Saline Placebo %**		
	Any[b]	**Grade 2[c] or 3[d] or >20 mm**	**Grade 3[d] or >50 mm**	**Any[b]**	**Grade 2[c] or 3[d] or >20 mm**	**Grade 3[d] or >50 mm**
Local	**n = 196**	**n = 196**	**n = 196**	**n = 73**	**n = 73**	**n = 73**
Injection site pain	47.4	15.3	2.6	30.1	4.1	2.7
Injection site erythema	33.7	4.1	0.5	26.0	0	0
Injection site swelling	28.6	3.1	0.5	15.1	0	0
General						
Irritability/fussiness	50.5	16.3	4.1	39.7	15.1	2.7
Drowsiness	37.8	14.8	4.1	30.1	11.0	2.7
Loss of appetite	29.1	10.2	3.1	32.9	15.1	5.5
Fever	22.4	10.7	4.6	16.4	12.3	5.5

n = Number of subjects who received at least 1 dose and for whom safety data were available.

[a] Within 7 days defined as day of vaccination or placebo injection and the next 6 days.

[b] Any swelling/erythema defined as >0 mm. Any fever defined as ≥100.4ºF (38.0ºC).

[c] Grade 2: Pain defined as cries/protests to touch. Fever defined as ≥101.3ºF (38.5ºC). For all other reactions, defined as some interference with normal everyday activities.

[d] Grade 3: Pain defined as cries when limb moved/spontaneously painful. Fever defined as ≥102.2ºF (39.0ºC). Loss of appetite defined as not eating at all. For all other reactions, defined as those that prevented normal everyday activities.

Table 4. Percentage of Subjects with Solicited Local and General Adverse Reactions within 7 Days[a] of Any Vaccination in Individuals 3 through 8 Years of Age

	AREPANRIX (Original) %			Saline Placebo %		
	Any[b]	Grade 2[c] or 3[d] or >20 mm	Grade 3[d] or >50 mm	Any[b]	Grade 2[c] or 3[d] or >20 mm	Grade 3[d] or >50 mm
Local	**n = 197**	**n = 197**	**n = 197**	**n = 76**	**n = 76**	**n = 76**
Injection site pain	71.1	24.4	5.1	38.2	2.6	0
Injection site erythema	31.0	5.6	2.0	13.2	0	0
Injection site swelling	27.9	7.1	2.0	18.4	1.3	1.3
General						
3 Years through 5 Years	**n = 98**	**n = 98**	**n = 98**	**n = 49**	**n = 49**	**n = 49**
Irritability/fussiness	29.6	7.1	2.0	22.4	4.1	0
Drowsiness	27.6	4.1	1.0	14.3	2.0	0
Loss of appetite	22.4	5.1	2.0	10.2	4.1	0
Fever	15.3	9.2	5.1	18.4	8.2	2.0
6 Years through 8 Years	**n = 99**	**n = 99**	**n = 99**	**n = 27**	**n = 27**	**n = 27**
Muscle aches	35.4	8.1	3.0	18.5	0	0
Headache	29.3	10.1	2.0	7.4	0	0
Fatigue	22.2	10.1	0	3.7	0	0
Gastrointestinal[e]	17.2	5.1	1.0	22.2	3.7	0
Joint pain	14.1	4.0	1.0	7.4	0	0
Sweating	6.1	0	0	0	0	0
Shivering	4.0	1.0	1.0	0	0	0
Fever	13.1	6.1	4.0	0	0	0

n = Number of subjects who received at least 1 dose and for whom safety data were available.

[a] Within 7 days defined as day of vaccination or placebo injection and the next 6 days.

[b] Any swelling/erythema defined as >0 mm. Any fever defined as ≥100.4ºF (38.0ºC).

[c] Grade 2: Pain defined as cries/protests to touch (for those younger than 6 years) or pain on moving the limb that interferes with normal activities or requires repeated use of pain relievers. Fever defined as ≥101.3ºF (38.5ºC). For all other reactions, defined as some interference with normal everyday activities or requires repeated use of pain relievers (for headache, joint pain, or muscle aches).

[d] Grade 3: Pain defined as cries when limb moved/spontaneously painful (for those younger than 6 years) or significant pain at rest; prevents normal activities as assessed by inability to attend/do work or school. Fever defined as ≥102.2ºF (39.0ºC). Loss of appetite defined as not eating at all. For all other reactions, defined as those that prevented normal everyday activities, as assessed by inability to attend/do work or school for those 6 years and older, or those that required intervention of a healthcare provider.

[e] Nausea, vomiting, diarrhea, and/or abdominal pain.

Table 5. Percentage of Subjects with Solicited Local and General Adverse Reactions within 7 Days[a] of Any Vaccination in Individuals 9 through 17 Years of Age

	AREPANRIX (Original) %			Saline Placebo %		
	Any[b]	Grade 2[c] or 3[d] or >20 mm	Grade 3[d] or >50 mm	Any[b]	Grade 2[c] or 3[d] or >20 mm	Grade 3[d] or >50 mm
Local	**n = 210**	**n = 210**	**n = 210**	**n = 80**	**n = 80**	**n = 80**
Injection site pain	81.9	24.8	4.8	22.5	5.0	2.5
Injection site erythema	25.7	3.3	0.5	12.5	0	0
Injection site swelling	28.6	8.6	1.9	8.8	0	0
General						
Muscle aches	41.9	14.3	1.9	15.0	3.8	1.3
Headache	33.8	10.5	2.9	20.0	6.3	3.8
Fatigue	31.9	10.0	1.9	22.5	5.0	2.5
Joint pain	17.1	5.7	0.5	8.8	1.3	0
Gastrointestinal[e]	12.4	6.2	1.4	15.0	3.8	2.5
Shivering	10.0	3.3	0.5	8.8	3.8	1.3
Sweating	9.0	3.3	1.0	5.0	1.3	0
Fever	2.9	0.5	0.5	3.8	1.3	1.3

n = Number of subjects who received at least 1 dose and for whom safety data were available.

[a] Within 7 days defined as day of vaccination or placebo injection and the next 6 days.

[b] Any swelling/erythema defined as >0 mm. Any fever defined as ≥100.4ºF (38.0ºC).

[c] Grade 2: Pain defined as pain on moving the limb that interferes with normal activities or requires repeated use of pain relievers. Fever defined as ≥101.3ºF (38.5ºC). For all other reactions, defined as some interference with normal everyday activities or requires repeated use of pain relievers (for headache, joint pain, or muscle aches).

[d] Grade 3: Pain defined as significant pain at rest; prevents normal activities as assessed by inability to attend/do work or school. Fever defined as ≥102.2ºF (39.0ºC). For all other reactions, defined as those that prevented normal everyday activities, as assessed by inability to attend/do work or school, or those that required intervention of a healthcare provider.

[e] Nausea, vomiting, diarrhea, and/or abdominal pain.

Unsolicited Adverse Events: The incidences of unsolicited adverse events reported during the 21-day postvaccination periods for subjects who received AREPANRIX (Original) (n = 607) or placebo (n = 231) were 39.4% and 42.0%, respectively. Events reported in the AREPANRIX (Original) group at a rate of ≥0.5% of subjects and at a rate at least twice that of the placebo group were all injection site reactions combined (1.6% vs. 0.4%), gastroenteritis (1.2% vs. 0.4%), eye infections (1.0% vs. 0.4%), varicella (0.7% vs. 0%), and fatigue (0.5% vs. 0%).

Serious Adverse Events (SAEs): SAEs were reported for 2 (0.3%) subjects who received AREPANRIX (Original) (n = 607) and for 0 subjects who received placebo (n = 231) through Day 42 (21 days following the second dose of vaccine or placebo). During the approximately one-year safety follow-up (Day 385), SAEs were reported for 8 (1.3%) subjects who received AREPANRIX (Original), and for 4 (1.7%) subjects who received placebo. One SAE of febrile convulsion was reported on Day 11 following the first vaccine dose in a

30-month-old subject who received AREPANRIX (Original); although no fever occurred during the first 7 days postvaccination, febrile convulsion is noted due to the temporal association with vaccination and because no alternative plausible cause for the event is identified.

Potential Immune-Mediated Diseases: Based on a prespecified list of events, 1 potential immune-mediated disease (alopecia) was reported through Day 385 in a subject who received AREPANRIX (Original) (n = 607). One event (Type 1 diabetes) was reported for 1 subject who received placebo (n = 231).

Uncontrolled Crossover Study: One hundred fifty-five subjects who initially received placebo, received a 2-dose series of AREPANRIX (Original) in the crossover study. Two (1.3%) subjects reported SAEs, which were not related to vaccination, through the one-year safety follow-up (Day 385). No potential immune-mediated diseases were reported.

Additional Safety Experience with AS03-Adjuvanted Influenza Vaccine (H1N1) in Individuals 6 Months through 9 Years of Age

In a randomized, controlled, observer-blind, multicenter trial, conducted in 8 countries outside of the U.S., a total of 6,145 subjects 6 months through 9 years of age were randomized 1:1:1 to receive: 1 dose of a non-U.S. licensed influenza A (H1N1) virus vaccine adjuvanted with AS03 (manufactured by GlaxoSmithKline); 2 doses of the same vaccine administered 21 days apart; or 2 doses of a non-U.S. licensed, unadjuvanted influenza A (H1N1) virus vaccine (manufactured by GlaxoSmithKline) administered 21 days apart.

Serious Adverse Events (SAEs): SAE rates in subjects who received the adjuvanted vaccine (one or two doses) and the unadjuvanted vaccine were similar (0.4% in these groups through Day 42, and 3.5% and 3.3% in these groups, respectively, through Day 385). The following SAEs reported through Day 385 in subjects who received the adjuvanted vaccine are noted because no alternative plausible causes for the event were identified or due to the temporal association with vaccination. One death was reported within 42 days of any vaccination: a 6-month-old with a prior episode of pneumonia developed symptoms described as pneumonia and asthma exacerbation beginning on Day 7 following the first dose of the adjuvanted vaccine and died of sepsis on Day 19. The following nonfatal SAEs were reported through Day 385: hepatitis and nasopharyngitis on Day 5 following vaccination (1 subject), appendicitis on Days 8 or 9 following vaccination (3 subjects), and papillary thyroid cancer on Day 84 following vaccination (1 subject).

Potential Immune-Mediated Diseases: Based on a prespecified list of events, 7 subjects (0.2%) in the adjuvanted arms (n = 4,096) reported new-onset potential immune-mediated diseases through Day 385; four subjects (0.2%) in the unadjuvanted arms (n = 2,049) reported such events. Events reported following administration of the adjuvanted vaccine were alopecia areata (2 subjects), glomerulonephritis (2 subjects), hypothyroidism (2 subjects), and idiopathic thrombocytopenic purpura (1 subject). Events reported following administration of the unadjuvanted vaccine were glomerulonephritis (2 subjects), Guillain-Barré syndrome (1 subject), and erythema multiforme (1 subject).

6.2 Postmarketing Experience

There is no postmarketing experience following administration of AREPANRIX.

Spontaneously Reported Events

Because spontaneously reported events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their incidence or to establish a causal relationship to AREPANRIX.

Other influenza vaccines containing AS03 adjuvant, Influenza vaccine (A/California/7/2009 H1N1), manufactured by GlaxoSmithKline in Quebec, Canada, and Influenza vaccine (A/California/7/2009 H1N1), manufactured by GlaxoSmithKline in Dresden, Germany, were administered outside the U.S. during the Influenza A 2009 (H1N1) pandemic.

The following events were reported spontaneously following vaccination with AS03 adjuvanted H1N1 influenza vaccines administered outside the U.S.:

Immune System Disorders: Anaphylaxis, allergic reactions.

Nervous System Disorders: Febrile convulsions, Guillain-Barré syndrome, narcolepsy, somnolence, paresthesia.

Skin and Subcutaneous Tissue Disorders: Angioedema, generalized skin reactions, urticaria.

General Disorders and Administration Site Conditions: Injection site reactions (including inflammation, mass, necrosis, and ulcer).

Narcolepsy

Epidemiological studies[1-7] in several European countries evaluated a potential association between an influenza vaccine containing AS03 adjuvant, Influenza vaccine (A/California/7/2009 H1N1), manufactured by GlaxoSmithKline in Dresden, Germany, and narcolepsy. Some published studies reported a 2.9- to 14.2-fold increase in the risk of narcolepsy, with or without cataplexy, among vaccinated children and adolescents (younger than 20 years), and a 2.2- to 5.5-fold increase among vaccinated adults 20 years of age and older, compared with individuals of the same age group who did not receive this H1N1 vaccine.[1-7] Approximately 3 to 8 additional cases of narcolepsy per 100,000 vaccinated children/adolescents and approximately 1 additional case per 100,000 vaccinated adults were estimated to occur based on data from some of these studies.[2,3,6,7] No increase in the risk of narcolepsy was reported in some studies.[1] The relevance of these findings on narcolepsy to the U.S. population or to AREPANRIX is unknown.

Febrile Seizures

Postmarketing Observational Study of the Risk of Febrile Seizures following Vaccination with Trivalent/Quadrivalent Seasonal Influenza Vaccines

The association between seasonal influenza vaccine and febrile seizures was evaluated in children ages 6 months through 4 years during the 2023-2024[8] and 2024-2025 respiratory seasons using three commercial health insurance claims data sources.

A self-controlled case series (SCCS) analyses compared the risk of febrile seizures within a risk window of 0 to 1 day postvaccination to a control window of 8 to 63 days postvaccination. The 2023-2024 and 2024-2025 season SCCS analyses found significantly increased risks of febrile seizures in the first day following influenza standard dose quadrivalent and trivalent vaccinations, respectively. The estimated attributable risk from one data partner was 21.2 per million excess febrile seizure episodes or a 97% increase in relative risk (IRR: 1.97 [95% CI: 1.09, 3.54]) after the standard dose quadrivalent vaccine and a 44.2 per million excess febrile seizure episodes or a 194% increase in relative risk (IRR: 2.94 [95% CI: 1.72, 5.01]) following the standard dose trivalent vaccine. The results of this type of observational study suggest a causal relationship between standard dose influenza quadrivalent and trivalent vaccines and febrile seizures in children 6 months through 4 years of age.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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.

There are no data on AREPANRIX administered to pregnant women to inform the vaccine-associated risks.

A developmental toxicity study was performed in female rats administered AREPANRIX (Original) prior to mating, during gestation, and during lactation. The dose was 0.2 mL at each occasion (a single adult human dose is 0.5 mL). This study revealed no evidence of harm to the fetus or offspring (until weaning) due to AREPANRIX (Original) in rats *[see Data]*.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk: There is limited information on the risk of H5 infection in pregnant women. However, pregnant women infected with pandemic H1N1 or with seasonal influenza are at increased risk of severe illness associated with influenza infection compared with non-pregnant women. Pregnant women with influenza may be at increased risk for adverse pregnancy outcomes, including preterm labor and delivery.

Data

Animal Data: A developmental toxicity study was performed in female rats. Animals were administered AREPANRIX (Original) by intramuscular injection once prior to gestation, and on gestation Days 7, 9, 12, and 16. Some rats were administered an additional dose on lactation Day 7. The dose was 0.2 mL at each occasion (a single adult human dose is 0.5 mL). No adverse effects on pre-weaning development up to postnatal Day 25 were observed. There were no fetal malformations or variations observed due to AREPANRIX (Original).

8.2 Lactation

Risk Summary

It is not known whether AREPANRIX is excreted in human milk. Data are not available to assess the effects of AREPANRIX 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 AREPANRIX and any potential adverse effects on the breastfed child from AREPANRIX or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of AREPANRIX in infants younger than 6 months have not been established.

8.5 Geriatric Use

Study 1 included 1,489 subjects 65 years of age and older who received AREPANRIX (Original). Of the total number of subjects in the clinical study, 32.6% were 65 years of age and older, while 9.8% were 75 years of age and older. Study 2 included 64 individuals, 65 years of age and older, including 22 individuals 75 years of age and older, who received AREPANRIX (H5N8).

Although subjects 65 years of age and older had a lower immune response to AREPANRIX than subjects 18 through 64 years of age, the pre-specified targets for the immunogenicity endpoints were met in the geriatric subjects in both Study 1 and Study 2 *[see Clinical Studies (14.1)]*. No clinically relevant differences in safety between subjects 65 years of age and older and younger subjects were observed *[see Adverse Reactions (6.1)]*.

11 DESCRIPTION

AREPANRIX (Influenza A [H5] Monovalent Vaccine, Adjuvanted) is a sterile injectable emulsion administered intramuscularly. The vaccine is supplied as 2 components: a vial of inactivated, split-virion, H5 Antigen Component and a vial of AS03 Adjuvant Component that must be combined prior to administration to form AREPANRIX.

The H5 Antigen Component is manufactured according to a similar process as that used to produce the antigens contained in FLULAVAL (Influenza Vaccine) and FLULAVAL QUADRIVALENT (Influenza Vaccine), which are unadjuvanted seasonal influenza vaccines licensed in the U.S. The H5 Antigen Component is a sterile, translucent to whitish opalescent suspension in a phosphate-buffered, thimerosal-containing saline solution that may sediment slightly. The sediment resuspends upon mixing by inversion to form a homogeneous suspension. The H5 Antigen Component is prepared from virus propagated in the allantoic cavity of embryonated hen's eggs. The virus is inactivated with ultraviolet light treatment followed by formaldehyde treatment, purified by centrifugation, and disrupted with sodium deoxycholate. The AS03 Adjuvant Component is a homogenized, sterile, whitish to yellowish milky emulsion composed of squalene, DL-α-tocopherol, and polysorbate 80.

AREPANRIX is prepared by combining the H5 Antigen Component with the AS03 Adjuvant Component. After combining, AREPANRIX is a whitish to yellowish homogenous milky emulsion.

Each 0.5-mL dose of AREPANRIX (H5N8) for individuals 18 years of age and older contains 3.75 mcg hemagglutinin (HA) of the influenza virus strain A/Astrakhan/3212/2020-like (H5N8, clade 2.3.4.4b); 5 mcg thimerosal, a mercury derivative, as a preservative (2.5 mcg mercury); and AS03 adjuvant (10.69 mg squalene, 11.86 mg DL-α-tocopherol, and 4.86 mg polysorbate 80). Each 0.5-mL dose may also contain residual amounts of ovalbumin (≤0.083 mcg), formaldehyde (≤12.5 mcg), and sodium deoxycholate (≤3.75 mcg) from the manufacturing process.

Each 0.25-mL dose of AREPANRIX (H5N8) for individuals 6 months through 17 years contains 1.9 mcg hemagglutinin (HA) of the influenza virus strain A/Astrakhan/3212/2020-like (H5N8, clade 2.3.4.4b); 2.5 mcg thimerosal, a mercury derivative, as a preservative (1.25 mcg mercury); and AS03 adjuvant (5.35 mg squalene, 5.93 mg DL-α-tocopherol, and 2.43 mg polysorbate 80). Each 0.25-mL dose may also contain residual amounts of ovalbumin (≤0.042 mcg), formaldehyde (≤6.25 mcg), and sodium deoxycholate (≤1.88 mcg) from the manufacturing process.

The vial stoppers are not made with natural rubber latex.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

A specific postvaccination hemagglutination-inhibition (HI) antibody titer has not been correlated with protection from H5 influenza illness; however, HI titers have been used as a measure of influenza vaccine

activity. In some human challenge studies with other influenza viruses, antibody titers of ≥1:40 have been associated with protection from influenza illness in up to 50% of subjects.[9,10]

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

AREPANRIX has not been evaluated for carcinogenic or mutagenic potential, or male infertility in animals. Vaccination of female rats with AREPANRIX (Original) had no effect on fertility *[see Use in Specific Populations (8.1)]*.

14 CLINICAL STUDIES

The H5 Antigen Component of AREPANRIX is manufactured according to a similar process as that used to produce the antigens contained in FLULAVAL and FLULAVAL QUADRIVALENT, unadjuvanted seasonal influenza vaccines licensed in the U.S. Effectiveness of AREPANRIX was demonstrated based on serum HI antibody responses to AREPANRIX, and effectiveness of FLULAVAL and FLULAVAL QUADRIVALENT, including a demonstration of efficacy of FLULAVAL QUADRIVALENT in the prevention of influenza disease.

AREPANRIX containing HA from influenza virus strain A/Indonesia/05/2005 (H5N1) is referred to as AREPANRIX (Original); and AREPANRIX containing HA from influenza virus strain A/Astrakhan/3212/2020-like (H5N8) is referred to as AREPANRIX (H5N8).

14.1 Immunogenicity in Adults

Study 1

In Study 1, a randomized, placebo-controlled, observer-blind, multicenter study, conducted in the U.S. and Canada, 4,561 adult subjects were randomized 3:1, stratified by age (18 through 49 years of age, 50 through 64 years of age, and 65 years of age and older) to AREPANRIX (Original) (n = 3,422) or a saline placebo (n = 1,139). Each group received a 2-dose series administered approximately 21 days apart (range: 19 to 25 days). In the overall population, 56% of subjects were female and 88% were White; analyses of age groups 18 through 64 years (mean: 39 years) and 65 years of age and older (mean: 72 years) were conducted. In a subset of subjects, HI antibody titers to the A/Indonesia/05/2005 (H5N1) strain were evaluated in sera obtained 21 days after the second dose with AREPANRIX (Original) or placebo.

Analyses of the following co-primary endpoints were performed for the HA antigen: endpoint 1) assessment of the rates of seroconversion (defined as a 4-fold increase in postvaccination HI antibody titer from pre-vaccination titer ≥1:10, or an increase in titer from <1:10 to ≥1:40), and endpoint 2) assessment of the percentage of subjects with HI antibody titers of ≥1:40 after vaccination. The pre-specified targets for the endpoints varied by age of subjects enrolled. For the rates of seroconversion, the pre-specified target was a lower bound for the 2-sided 95% confidence interval ≥40% for the age group 18 through 64 years and ≥30% for the age group 65 years and older. For the percentage of subjects with HI antibody titers of ≥1:40 after vaccination, the pre-specified target was a lower bound for the 2-sided 95% confidence interval ≥70% for the age group 18 through 64 years and ≥60% for the age group 65 years and older.

In the subset of subjects evaluated, serum HI antibody responses to AREPANRIX (Original) met the pre-specified seroconversion criteria, and also the pre-specified criteria for the percentage of subjects with HI titers ≥1:40 (Table 6).

Table 6. Seroconversion Rates and Percentage of Subjects with HI Titers ≥1:40 following AREPANRIX (Original) or Placebo (21 Days after Dose 2) (ATP Cohort for Immunogenicity)

	AREPANRIX (Original) % (95% CI)	Placebo % (95% CI)
Subjects 18 through 64 Years of Age	**n = 1,571**	**n = 76**
Seroconversion[a]	90.8[b] (89.3, 92.2)	1.3 (0.0, 7.1)
% with HI titers ≥1:40	90.8[c] (89.3, 92.2)	1.3 (0.0, 7.1)
Subjects 65 Years of Age and Older	**n = 396**	**n = 40**
Seroconversion[a]	74.0[b] (69.4, 78.2)	2.5 (0.1, 13.2)
% with HI titers ≥1:40	74.5[c] (69.9, 78.7)	2.5 (0.1, 13.2)

HI = Hemagglutination-inhibition; ATP = According to protocol; CI = Confidence Interval.
ATP cohort for immunogenicity included a subset of subjects who received 2 doses of vaccine and had serum collections according to the protocol.

[a] Seroconversion defined as at least a 4-fold increase in postvaccination HI antibody titer from pre-vaccination titer ≥1:10, or an increase in titer from <1:10 to ≥1:40.

[b] For the rates of seroconversion, the prespecified target was met based on a lower bound for the 2-sided 95% confidence interval ≥40% for the age group 18 through 64 years and ≥30% for the age group 65 years and older.

[c] For the percentage of subjects with HI antibody titers of ≥1:40 after vaccination, the prespecified target was met based on a lower bound for the 2-sided 95% confidence interval ≥70% for the age group 18 through 64 years and ≥60% for the age group 65 years and older.

Study 2

In Study 2, a Phase 1/2, randomized, observer-blind, multicenter trial conducted in the U.S., adults 18 through 64 years of age (n = 65) and adults 65 years of age and older (n = 64) received at least 1 dose of AREPANRIX (H5N8). Two doses were administered 21 days apart. HI antibody titers against the A/Astrakhan/3212-like (H5N8) strain were evaluated in sera obtained 21 days after the second dose. Among 46 adults 18 through 64 years of age in the per protocol set, the mean age was 44 years (range: 21 through 63 years), 37% were female, 70% were White, 22% were Black or African American, 2% were Asian, 2% were Native Hawaiian or Other Pacific Islanders, and 33% were Hispanic or Latino. Among 40 adults 65 years of age and older in the per protocol set, the mean age was 72 years (range: 65 through 84 years), 50% were female, 83% were White, 15% were Black or African American, 3% were Asian, and 25% were Hispanic or Latino.

Analyses included the following co-primary endpoints for the HA antigen: HI titers (geometric mean titer, GMT) and the percentage of subjects with HI antibody titers of ≥1:40 after vaccination. For the percentage of subjects with HI antibody titers of ≥1:40 after vaccination, the prespecified target was a lower bound for the 95% confidence interval ≥70% for the age group 18 through 64 years of age and ≥60% for the age group 65 years of age and older.

In the per protocol set of subjects evaluated, serum HI antibody responses to AREPANRIX (H5N8) met the prespecified criteria for the percentage of subjects with HI titers ≥1:40 in both age groups (Table 7).

Table 7. Geometric Mean Titers and Percentage of Subjects with HI Titers ≥1:40 against A/Astrakhan/3212/2020-like virus following Administration of AREPANRIX (H5N8) in Study 2 (21 Days after Dose 2) (Per Protocol Set for Immunogenicity)

	AREPANRIX (H5N8) (95% CI)[a]
Subjects 18 through 64 Years of Age	**n = 46**
H5N8 GMT	175.2 (138.0, 222.5)
% with HI titers ≥1:40	97.8 (88.5, 99.9)
Subjects 65 Years of Age and Older	**n = 40**
H5N8 GMT	110.2 (85.7, 141.8)
% with HI titers ≥1:40	92.5 (79.6, 98.4)

HI = Hemagglutination-inhibition; CI = Confidence Interval; GMT = Geometric Mean Titer.
Per protocol set for immunogenicity included subjects who received 2 doses of vaccine, complied with the protocol, and had serum collections at the time intervals specified in the protocol.

[a] For the percentage of subjects with HI antibody titers of ≥1:40 after vaccination, the prespecified target was met based on a lower bound for the 2-sided 95% confidence interval (CI) ≥70% for the age group 18 through 64 years and ≥60% for the age group 65 years and older. 95% CIs for the percentage of subjects with HI antibody titers of ≥1:40 calculated using Clopper-Pearson method; 95% CIs for the GMTs were computed by exponentiating the 95% CIs (based on Student's t distribution) of the mean log-transformed titer.

Additional analysis

After completion of Study 1 and Study 2, additional *post hoc* analyses were performed to support a strain change to A/Astrakhan/3212/2020-like (H5N8).

Stored serum samples from Study 2 (conducted in 2024) and Study 1 (completed in 2008) were evaluated in HI assays against A/Astrakhan/3212/2020-like (H5N8) strain. HI GMTs and percentage of subjects with HI titers ≥1:40 21 days after the second dose were calculated. Subjects were propensity score-matched based on age group, sex, race, and ethnicity.

Across age groups, AREPANRIX (H5N8) subjects showed higher adjusted GMTs (183.3, 95% CI: 126.9, 264.7) than AREPANRIX (Original) subjects (16.3, 95% CI: 11.6, 22.9) against A/Astrakhan/3212/2020-like (H5N8) strain. The adjusted H5N8 HI GMT ratio was 11.2 (90% CI: 9.3, 13.6). GMTs and percentage of subjects with HI titers ≥1:40 in each age group are presented in Table 8.

Table 8. Geometric Mean Titers and Percentage of Subjects with HI Titers ≥1:40 against A/Astrakhan/3212/2020-like strain following Administration of AREPANRIX (H5N8) in Study 2 and Administration of AREPANRIX (Original) in Study 1 (21 Days after Dose 2) (Immunogenicity Set)

	AREPANRIX (H5N8) (95% CI)[a]	**AREPANRIX (Original) (95% CI)[a]**
Subjects 18 through 64 Years of Age	**n = 36**	**n = 111**
H5N8 GMT	194.0 (148.3, 253.6)	13.6 (11.5, 16.0)
% with HI titers ≥1:40 (95% CI)	100.0 (90.3, 100)	14.4 (8.5, 22.4)
Subjects 65 Years of Age and Older	**n = 30**	**n = 74**
H5N8 GMT	98.4 (70.6, 137.3)	11.8 (9.7, 14.3)
% with HI titers ≥1:40	86.7 (69.3, 96.2)	12.2 (5.7, 21.8)

HI = Hemagglutination-inhibition; CI = Confidence Interval; GMT = Geometric Mean Titer.
Immunogenicity set included subjects who belonged to the per protocol set for immunogenicity (Study 2) or the ATP cohort for immunogenicity (Study 1), had samples available, and had consented to use of their samples in further research related to the original study. Subjects were matched based on age group, sex, race and ethnicity using propensity score matching method. Samples were tested for HI titers against A/Astrakhan/3212/2020-like (H5N8) strain with the same assay concurrently (Study 2 samples were retested).

[a] 95% CIs for the percentage of subjects with HI titers ≥ 1:40 calculated using Clopper-Pearson method; 95% CIs for the GMTs were computed by exponentiating the 95% CIs (based on Student's t distribution) of the mean log-transformed titer.

The additional immunogenicity analysis is subject to several limitations. The *post hoc* analysis was not prespecified in either the Study 1 or Study 2 protocols and was subject to unmeasured confounders. The time interval between studies may have introduced differences in influenza virus or seasonal influenza vaccine exposure among subjects, which may result in varying degrees of preexisting immunity. AREPANRIX (Original) samples were retained for over 15 years. Despite an approximately 2-fold reduction in titers against A/Indonesia /5/2005-like (H5N1) when Study 1 samples (collected 21 days after the second dose) were retested, acceptable sample stability was supported by agreement in serostatus (92.4%) and correlation (0.82) between initial and re-test results. The study population was also limited, with small subgroup sample sizes and wide confidence intervals.

14.2 Immunogenicity in Individuals 6 Months through 17 Years of Age

In Study 3, a randomized, placebo-controlled, observer-blind, multicenter trial conducted in the United States, Canada, and Thailand, 838 subjects were randomized in an 8:3 ratio, stratified by age (6 through 35 months of age, 3 through 8 years of age, and 9 through 17 years of age) to receive either AREPANRIX (Original) (1.9 mcg/AS03B: half of adult dose) (n = 607) or a saline placebo (n = 231). Each group received a 2-dose series administered 21 days apart. Analyses of age groups 6 through 35 months of age (mean: 22 months), 3 through 8 years of age (mean: 6 years), and 9 through 17 years of age (mean: 13 years) were conducted. HI antibody titers to the A/Indonesia/05/2005 (H5N1) strain were evaluated in sera obtained 21 days after the second dose with AREPANRIX (Original) or placebo.

The primary endpoint was the percentage of subjects with HI antibody titers of ≥1:40 after vaccination for the HA antigen. The pre-specified criterion for success was a lower bound for the 98.3% confidence interval ≥70% for any age stratum. Each age stratum was evaluated independently. Serum HI antibody responses to AREPANRIX (Original) met the pre-specified criteria for all age strata (Table 9).

Table 9. Percentage of Subjects with HI Titers ≥1:40 following AREPANRIX (Original) or Placebo (21 Days after Dose 2) (ATP Cohort for Immunogenicity at Day 42)

	AREPANRIX (Original)		Placebo	
Age Group	n	% (98.3% CI)	n	% (98.3% CI)
Subjects 6 through 35 months of age	175	100.0[a] (97.3, 100.0)	64	0 (0, 7.2)
Subjects 3 through 8 years of age	184	99.5[a] (96.3, 100)	71	0 (0, 6.5)
Subjects 9 through 17 years of age	203	99.0[a] (95.8, 99.9)	76	1.3 (0, 8.6)

HI = Hemagglutination-inhibition; ATP = According-to-protocol; CI = Confidence Interval.
n = Number of subjects with available results.
ATP cohort for immunogenicity included a subset of subjects who received 2 doses of vaccine and had serum collections according to the protocol.
[a] For the percentage of subjects with HI antibody titers of ≥1:40 after vaccination, the pre-specified target was met based on a lower bound for the 2-sided 98.3% confidence interval ≥70% for all 3 age strata.

The immune responses to AREPANRIX (H5N8) in individuals 18 years of age and older and the immune responses in individuals 6 months through 17 years of age to AREPANRIX (Original), as measured by HI titers, form the basis of accelerated approval of AREPANRIX (H5N8) in individuals 6 months through 17 years of age.

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16 HOW SUPPLIED/STORAGE AND HANDLING

AREPANRIX is supplied as two separate vials: a larger vial of H5 Antigen Component (2.5 mL liquid) and a smaller vial of AS03 Adjuvant Component (2.5 mL liquid). Once combined, the resulting volume is 5 mL in a multiple-dose vial.

Table 10. Product Presentation for AREPANRIX

Presentation	Carton NDC Number	Components	
		H5 Antigen Component	AS03 Adjuvant Component
Outer carton	58160-742-25	10 vials (NDC 58160-753-01) in carton (NDC 58160-753-19)	10 vials (NDC 58160-855-01) in carton (NDC 58160-855-19)

Storage before Combining

Store both H5 Antigen Component and AS03 Adjuvant Component vials refrigerated between 2° and 8°C (36° and 46°F). Do not freeze. Discard if the vials have been frozen. Protect from light.

Storage after Combining

Administer AREPANRIX within 24 hours of combining. Once combined, store AREPANRIX refrigerated between 2° and 8°C (36° and 46°F) or at room temperature up to 30°C (86°F) for up to 24 hours. Do not freeze. Discard if AREPANRIX has been frozen. Protect from light.

17 PATIENT COUNSELING INFORMATION

Vaccine Information Statements are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization to the vaccine recipient, parent, or guardian. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Inform vaccine recipients, parents, or guardians that/to:

- AREPANRIX contains a non-infectious killed virus and cannot cause influenza.
- AREPANRIX is only intended to prevent illness due to the influenza virus contained in the vaccine.
- it is important to complete the immunization series.
- the potential for adverse reactions that have been temporally associated with administration of AREPANRIX or other vaccines containing similar components exists.
- report any adverse events to their healthcare provider and/or VAERS.

Updated information about this product may be available by scanning the QR code on the outer carton with a camera-enabled mobile phone/tablet, or by visiting https://epi-pla.org.

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