Please see Important Safety Information on page 13 and accompanying US full Prescribing Information.

FLUAD™
influenza vaccine, adjuvanted

Power to the people 65+

INFLUENZA: A SIGNIFICANT BURDEN IN ADULTS AGED 65 AND OLDER

Adults aged 65+ are most at risk for severe illness, hospitalization, and death as a result of flu

- The flu can make certain comorbid conditions worse. It can also increase the risk of death in people with certain chronic comorbid conditions (eg, heart disease, stroke, pneumonia)[1]
- Impacts of the flu can include diminished quality of life, loss of independence in activities of daily living, and functional decline[2]
- With advancing age (85+), the risks of influenza-associated deaths are even greater[3]

In the United States, the 65+ population accounts for most seasonal influenza-related hospitalizations and deaths[3,4]

90% OF **DEATHS** FROM INFLUENZA OCCUR IN ADULTS AGED **65+**[4]

ADULTS AGED **65+**
MORTALITY RATE

22.1 per 100,000 person-years[3]

50%–60%
of seasonal flu-related hospitalizations[4]

ADULTS AGED **85+ OR OLDER**

32x MORE LIKELY TO **DIE** OF UNDERLYING **PNEUMONIA** AND **INFLUENZA DEATH** VS 65-69 YEAR OLDS[3]

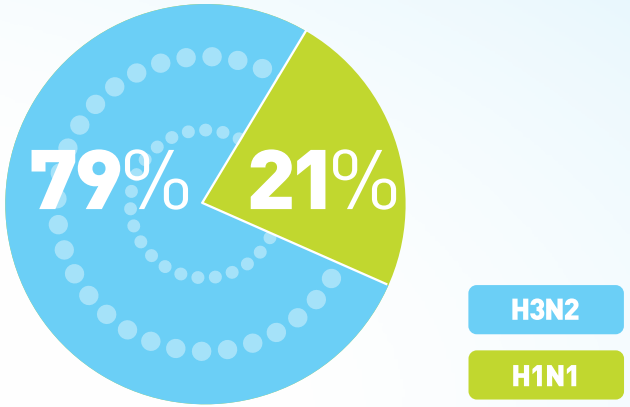
INFLUENZA A STRAINS HAVE THE GREATEST IMPACT ON THOSE AGED 65+

A strains:

- Have been the predominant circulating influenza strains in the United States (70%-99% from 2009 to 2013)[5-8]
- Have accounted for the majority of infections[a] and are the most common cause of hospitalization and death in those aged 65+[2,3,5-8]

[a] Except for the 2009-2010 season, when the pandemic H1N1 strain predominated.

In an analysis of the 2010-2013 flu seasons, **A/H3N2 strains caused the majority of infections**[8-10]



IN THE UNITED STATES, **INFLUENZA A STRAINS** HAVE BEEN ESTIMATED TO CAUSE

85% OF **RESPIRATORY** AND **CIRCULATORY DEATHS** IN ADULTS 65+[3]

A/H3N2 STRAINS IN PARTICULAR HAVE BEEN **RESPONSIBLE FOR**

80.5% OF **DEATHS** IN ADULTS 65+[3]

FLUAD™
influenza vaccine, adjuvanted

Power to the people 65+

FLUAD™: Next-Generation flu shot for the 65+ generation

What is FLUAD?

Indications and Usage

FLUAD is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUAD is approved for use in persons 65 years of age and older. Approval is based on the immune response elicited by FLUAD. Data demonstrating a decrease in influenza disease after vaccination with FLUAD are not available.[9]

Contraindications

Do not administer FLUAD to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine, including egg protein, or to a previous influenza vaccine.[9]

What makes FLUAD different?

FLUAD contains[9]:

- At least 15 mcg of hemagglutinin (HA) of each influenza strain recommended for the current influenza season
- The proprietary adjuvant MF59®

What is MF59®?

- MF59 is derived from squalene, an oil naturally occurring in the body.[10,11]
- Though the mechanism of action is not fully understood, studies in animals and humans suggest that MF59 recruits immune cells to the site of injection and enhances their activity.[12]

How might FLUAD help your patients?

- In clinical trials, FLUAD induced a strong immune response to the vaccine in adults 65+.[9]

FLUAD may not be 100% effective in all who receive it.[9]

IMMUNOGENICITY OF FLUAD WAS DEMONSTRATED IN A PIVOTAL STUDY IN SUBJECTS AGED 65 YEARS AND OLDER

In a clinical trial of adults aged 65+, FLUAD was shown to elicit a

against 3 strains of influenza that cause the flu[9]

A phase 3, pivotal, randomized controlled, observer-blinded, multicenter trial studied the immunogenicity and safety of FLUAD vs AGRIFLU (influenza vaccine)[9,a]

- A total of 7082 subjects aged 65 years and older were randomized and vaccinated with FLUAD (N = 3541) or AGRIFLU (N = 3541).
- The primary immunogenicity analysis was performed on all subjects with a blood sample collected at day 22 (N = 3225-3227 [91%] and 3256-3259 [92%] in the FLUAD and AGRIFLU groups, respectively).
- A determination of noninferiority was made on the basis of predefined thresholds for seroconversion rate differences and GMT ratios.
- The safety analysis included subjects (N = 3545 FLUAD, 3537 AGRIFLU) from Study 1 who completed a symptom diary card for 7 days following vaccination.
- Additional safety data were derived from 15 randomized controlled studies involving 10,952 adults aged 65 years and older who received FLUAD (N = 5754) or other US-licensed vaccines (N = 5198).

[a] AGRIFLU (influenza vaccine), a US-licensed nonadjuvanted trivalent influenza vaccine.

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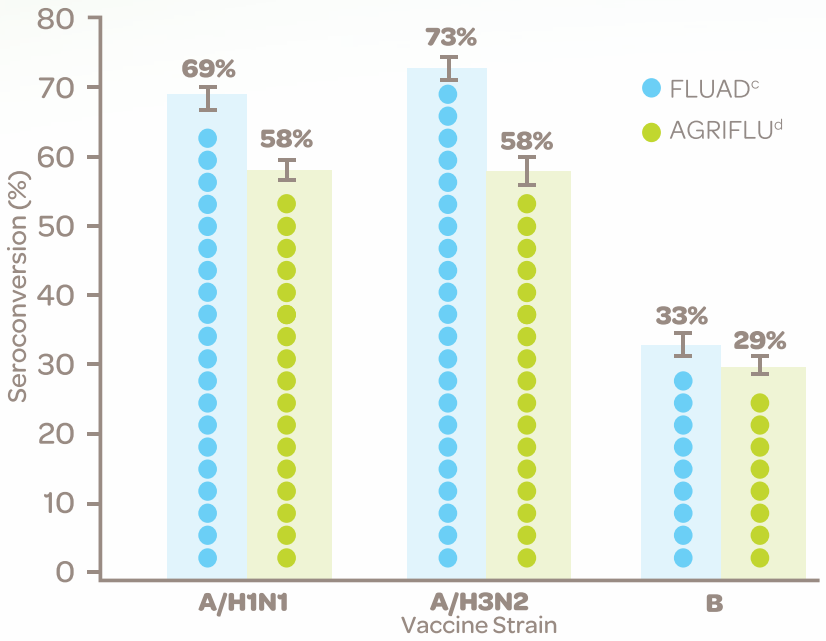
IMMUNOGENICITY AGAINST 3 INFLUENZA STRAINS[a]

Takeaway: At day 22, FLUAD demonstrated noninferiority to AGRIFLU on the basis of seroconversion rates.[9]

Seroconversion[b] rates: FLUAD established noninferiority vs AGRIFLU at day 22[9]



	A/H1N1	A/H3N2	B
Differences in Seroconversion rate[e] **(95% CI)**	**9.8%** (7.5%-12.1%)	**13.9%** (11.7%-16.1%)	**3.2%** (1.1%-5.3%)

CI = confidence interval

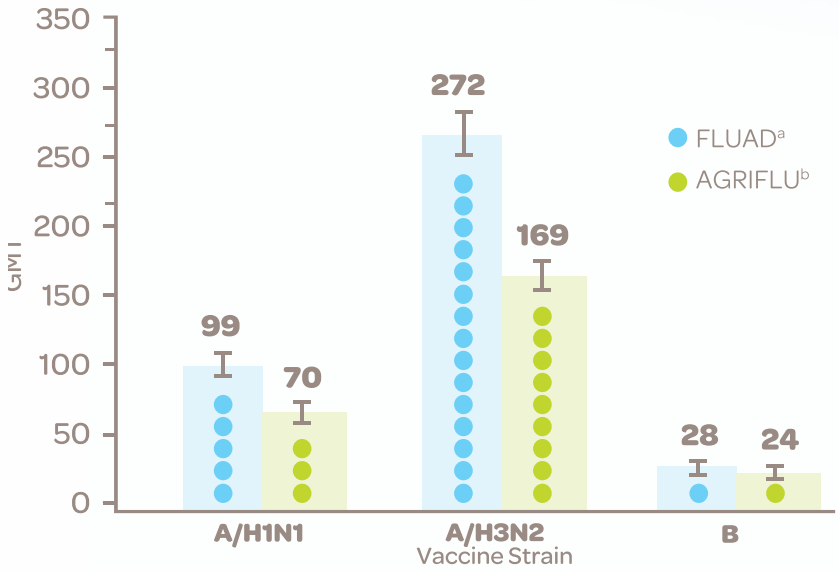
[a] Results obtained following vaccination with influenza vaccine formulated for the 2010-2011 season. [b] Seroconversion was defined as prevaccination HI titer <10 and postvaccination HI titer ≥ 40 or at least a 4-fold increase in HI from prevaccination HI titer ≥ 10. [c] N = 3225-3227, the number of vaccinated participants with available data for the immunologic endpoint listed. [d] N = 3256-3259, the number of vaccinated participants with available data for the immunologic endpoint listed. [e] FLUAD met noninferiority criteria based on seroconversion rate differences if the lower limit of the 95% CI [FLUAD – AGRIFLU] for each strain was >-10%.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- If Guillain-Barré Syndrome (GBS) has occurred within six weeks of previous influenza vaccination, the decision to give FLUAD should be based on careful consideration of the potential benefits and risks.

GMTs and GMT ratios: FLUAD established noninferiority vs AGRIFLU at day 22[9]



	A/H1N1	A/H3N2	B
GMT ratio[f] (95% CI)	**1.4** (1.32-1.49)	**1.61** (1.52-1.7)	**1.15** (1.08-1.21)

GMT = geometric mean antibody titer

[a]N = 3225-3227; this is the number of vaccinated participants with available data for the immunologic endpoint listed. [b]N = 3256-3259; this is the number of vaccinated participants with available data for the immunologic endpoint listed. [c]FLUAD met noninferiority criteria based on GMT ratios if the lower limit of the 95% CI [FLUAD: AGRIFLU] for each strain was >0.67.

Takeaway:
Noninferiority was established for all 3 influenza vaccine strains on the basis of GMTs and GMT ratios.[9]

Power to the people 65+

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FLUAD: SAFETY RESULTS FROM THE PIVOTAL TRIAL

The most common (≥10%) solicited local adverse reactions observed were injection site pain and tenderness.[9]

The most common (≥10%) solicited systemic adverse reactions observed were myalgia, headache, and fatigue.[9]

FLUAD: Solicited local adverse reactions[9]

		FLUAD N[b] = 3418-3496 %	AGRIFLU[a] N[b] = 3420-3488 %
Injection site pain	Any	25.0	12.2
	Moderate[c]	3.9	1.9
	Severe[d]	0.3	0.2
Tenderness	Any	21.1	11.2
	Moderate	3.0	1.0
	Severe	0.1	0.2
Erythema	Any	1.2	0.5
	25 to ≤50 mm	1.1	0.5
	51 to ≤100 mm	0.2	<0.1
	>100 mm	0.0	0.0
Induration	Any	1.3	0.5
	25 to ≤50 mm	1.0	0.5
	51 to ≤100 mm	0.3	0.0
	>100 mm	0.0	0.0
Swelling	Any	1.2	0.4
	25 to ≤50 mm	1.0	0.4
	51 to ≤100 mm	0.2	<0.1
	>100 mm	<0.1	0.0

[a]AGRIFLU (influenza vaccine) is a US-licensed nonadjuvanted influenza vaccine. [b]N = number of subjects with safety data. [c]Moderate: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "some limitation in normal daily activity," diarrhea defined as "4 to 5 stools a day." [d]Severe: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "unable to perform normal daily activity," diarrhea defined as "6 or more watery stools a day."

Takeaway:
While higher rates of solicited adverse reactions were noted, they were typically mild to moderate.[9]

FLUAD: Solicited systemic adverse reactions[9]

		FLUAD N[b] = 3418-3496 %	AGRIFLU[a] N[b] = 3420-3488 %
Myalgia	Any	14.7	9.7
	Moderate[c]	2.6	1.8
	Severe[d]	0.3	0.7
Fatigue	Any	13.3	10.4
	Moderate	3.1	2.4
	Severe	0.4	0.6
	PLT[e]	0.0	<0.1
Headache	Any	13.2	11.2
	Moderate	3.0	2.6
	Severe	0.4	0.6
	PLT	0.0	<0.1
Arthralgia	Any	8.5	7.8
	Moderate	1.6	1.6
	Severe	0.2	0.6
Chills	Any	6.7	4.7
	Moderate	1.5	1.2
	Severe	0.3	0.3
	PLT	<0.1	0.0
Diarrhea	Any	4.8	4.5
	Moderate	1.3	0.9
	Severe	0.3	0.2
	PLT	<0.1	<0.1
Fever	Any	3.6	3.4
	≥38.0°C to ≤38.4°C	1.8	1.7
	≥38.5°C to ≤38.9°C	1.3	1.3
	39.0°C to ≤40.0°C	0.4	0.4
	≥40.0°C	0.1	0.0
Nausea	Any	2.9	2.8
	Moderate	0.4	0.6
	Severe	0.1	0.1
	PLT	<0.1	0.0
Vomiting	Any	1.4	1.7
	Moderate	0.4	0.5
	Severe	<0.1	0.1
	PLT	<0.1	0.0

[a]AGRIFLU (influenza vaccine) is a US-licensed nonadjuvanted influenza vaccine. [b]N = number of subjects with safety data. [c]Moderate: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "some limitation in normal daily activity," diarrhea defined as "4 to 5 stools a day." [d]Severe: pain, tenderness, myalgia, fatigue, headache, arthralgia, chills, nausea, vomiting defined as "unable to perform normal daily activity," diarrhea defined as "6 or more watery stools a day." [e]Potentially life-threatening (PLT) reaction defined as requiring emergency room visit or hospitalization.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions in latex sensitive individuals.

FLUAD: ADDITIONAL SAFETY STUDIES CONDUCTED IN MORE THAN 10,000 ADULTS[9]

Unsolicited Adverse Events (AEs) and AEs of Special Interest (AESIs)[9]

FLUAD was assessed in 15 randomized controlled studies (N = 10,952) in adults aged 65 years and older; 5754 subjects received FLUAD and 5198 received other US-licensed influenza vaccines.

The percentage of subjects with AEs or AESIs following vaccination was similar between vaccine groups. There were no notable imbalances for specific AESIs.

Unsolicited AEs and AESIs[9]

	FLUAD N = 5754 %	Comparator[a] N = 5198 %
Unsolicited AE	16.9	18.0
AESI[b]	0.9	0.9

[a] Other US-licensed influenza vaccines. [b] Rates of new onset neuroinflammatory and immune mediated diseases were assessed in a post hoc analysis of the 15 randomized controlled trials for 1 year following vaccination.

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Serious Adverse Events (SAEs) and Deaths in Study 1 and Pooled Data From 14 Randomized Controlled Trials[9]

Study 1[9]

- Subjects were followed for SAEs and deaths for one year following vaccination.
- The percentages of subjects with an SAE were similar between vaccine groups.
- Four SAEs (1 FLUAD and 3 AGRIFLU) were assessed as related to study vaccination over one year of observation
  - 2 of these (1 FLUAD and 1 AGRIFLU) occurred within 21 days following study vaccination
- There were 98 deaths over one year (none occurred within the first 21 days following vaccination).

SAEs and Deaths in Study 1

	FLUAD N = 3545	AGRIFLU N = 3537
SAE, %	7	7
Deaths, n	52	46

14 Randomized Controlled Trials[9]

- SAEs were collected over a 3- to 4-week period in 4 studies, over an 8-week period in 1 study, and over a 6-month period in 9 studies.
- The percentages of subjects with an SAE within 30 days or within 6 months were similar between vaccine groups.
- The percentages of deaths within 30 days or within 6 months were also similar.

Percentage of SAEs and Deaths in 14 Randomized Controlled Studies of FLUAD vs Other US-licensed Vaccines

	FLUAD N = 2209	Comparator[a] N = 1661
Percentage of subjects with SAEs		
Within 30 days	1.1	1.8
Within 6 months	4.3	5.9
Percentage of deaths		
Within 30 days	0.3	0.6
Within 6 months	1.0	1.5

[a]The comparator for SAEs was AGRIFLU; the comparator for deaths was other US-licensed vaccines.

IMPORTANT SAFETY INFORMATION

Adverse Reactions

- The most common (≥ 10%) local (injection site) adverse reactions observed in clinical studies were injection site pain (25%) and tenderness (21%).
- The most common (≥ 10%) systemic adverse reactions observed in clinical studies were myalgia (15%), headache (13%) and fatigue (13%).

Safety of Annual Revaccination[9]

- Subjects in 5 of the randomized controlled trials were followed for 6 months after revaccination to assess SAEs and deaths.
- After the second annual vaccination, the percentages of subjects with an SAE were similar between vaccine groups; 23 deaths were reported.
- Causes of death included cardiovascular events, malignancy, trauma, gastrointestinal disorders, and respiratory failure
- Clinical characteristics of the deaths did not provide evidence for a causal relationship with FLUAD

SAEs and Deaths Reported After Second Annual Vaccination With FLUAD or Comparator Influenza Vaccines

	FLUAD N = 492	Comparator[a] N = 330
SAE, %	6.1	5.5
Deaths, n	17	6

[a] US-licensed and non-US-licensed influenza vaccines.

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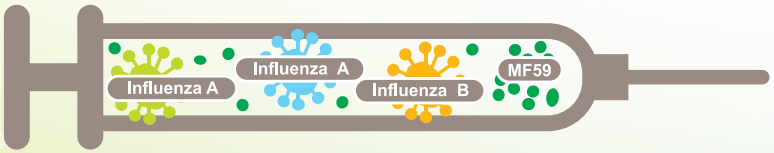
ADDITIONAL INFORMATION ABOUT FLUAD

- FLUAD does not contain latex. Please note: the tip caps of the prefilled syringes contain latex.[9]
- FLUAD does not contain a preservative.[9]

Dosing and Administration of FLUAD[9]

- **For intramuscular injection only**
- Administer FLUAD as a single 0.5-mL intramuscular injection in adults aged 65 years and older.
- Gently shake each syringe. FLUAD has a milky white appearance. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.
  - If either condition exists, FLUAD should not be administered.
- The vaccine should be administered by intramuscular injection, preferably in the region of the deltoid muscle of the upper arm. Do not inject the vaccine in the gluteal region or areas where there may be a major nerve trunk.

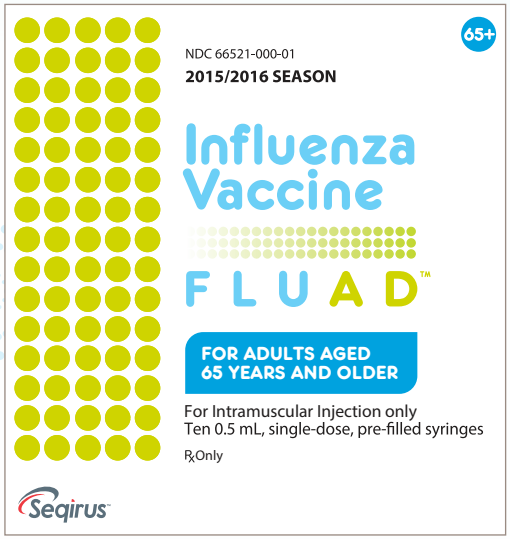


Storage and Handling of FLUAD

- **FLUAD is supplied as a 0.5-mL prefilled, needleless syringe in the following format[9]:**
  - Package of 10 prefilled syringes per carton (NDC number: 66521-000-01)
- Store FLUAD refrigerated at 2°C to 8°C (36°F-46°F). Protect from light. Do not freeze. Discard if the vaccine has been frozen. Do not use after expiration date.

FLUAD: GLOBAL USE

- More than **81 MILLION DOSES** distributed worldwide since 1997[11]
- Approved in more than **30 COUNTRIES** worldwide[11]



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IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

FLUAD is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUAD is approved for use in persons 65 years of age and older.[9]

CONTRAINDICATIONS

Severe allergic reaction to any component of the vaccine, including egg protein, or after a previous dose of any influenza vaccine.[9]

WARNINGS AND PRECAUTIONS[9]

- If Guillain-Barré Syndrome (GBS) has occurred within six weeks of previous influenza vaccination, the decision to give FLUAD should be based on careful consideration of the potential benefits and risks.
- The tip caps of the prefilled syringes contain natural rubber latex, which may cause allergic reactions in latex sensitive individuals.

ADVERSE REACTIONS[9]

- The most common (≥ 10%) local (injection-site) adverse reactions observed in clinical studies were injection site pain (25%) and tenderness (21%).
- The most common (≥ 10%) systemic adverse reactions observed in clinical studies were myalgia (15%), headache (13%) and fatigue (13%).

Please see accompanying US full Prescribing Information.

Introducing a flu shot for people 65+

CONSIDER FLUAD FOR YOUR PATIENTS AGED 65+[9]

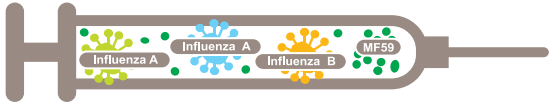
FLUAD PROVIDES A STRONG IMMUNE RESPONSE IN ADULTS AGED 65 YEARS AND OLDER TO HELP PROTECT THEM FROM THE FLU[9]

In a clinical trial of adults aged 65+, FLUAD was shown to elicit a

STRONG IMMUNE RESPONSE

against 3 strains of influenza that cause the flu[9]

- Though the mechanism of action is not fully understood, studies in animals and humans suggest that MF59® recruits immune cells to the site of injection and enhances their activity.[12]
- Demonstrated safety profile[9]
- Do not administer FLUAD to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine, including egg protein, or to a previous influenza vaccine.[9]
- Each 0.5-mL prefilled syringe provides 15 mcg of recommended viral strains for the current influenza season.[9]
- FLUAD was first approved in 1997 and is currently approved in more than 30 countries.[11]
- More than 81 million doses of FLUAD have been distributed worldwide.[11]
- In clinical trials, FLUAD was noninferior to AGRIFLU for all 3 vaccine strains on the basis of both seroconversion rates and GMTs.[9]



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For more information, visit **www.fluad.com**.

Seqirus

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Holly Springs, North Carolina 27540

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