Administering Afluria® Influenza Vaccine via PharmaJet® Stratis® Needle-Free Injection System

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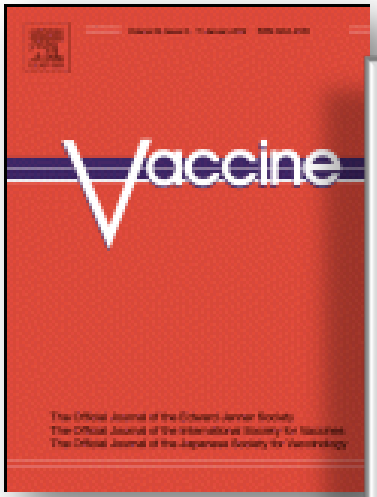
"Survey of the prevalence of immunization non-compliance due to needle fears in children and adults" Taddio et al. 2012 *Vaccine* 30:4807



Survey of children and parents

- **24% of adults (> 18 years; n=883) report a fear of needles**
- **Needle fear was the primary reason for immunization non-compliance for 7% of adults**

Barriers to Immunization

Needle-Stick Injuries

- Needle-stick injuries
  - 800,000 annually in the US
  - 3.5 million annually worldwide
  - $2 billion burden in US alone
  - Cost of needle-stick testing/counseling = $3,000
  - Cost of needle-stick treatment = $3,000-$100,000
- Needle-sticks transmit many blood-borne diseases
- Needle reuse: 40%-70% in the developing world

International Health Care Worker Safety Center
Needlestick and Sharps Injury Prevention Act
American Journal of Industrial Medicine

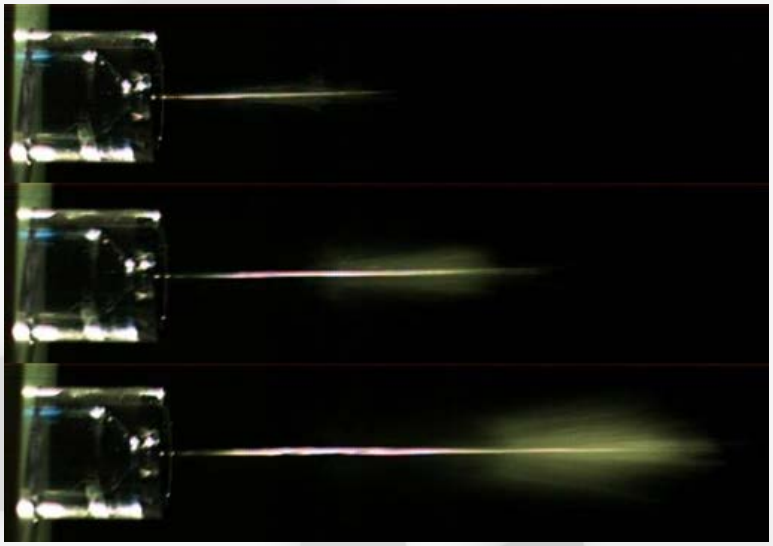
Afluria® Influenza Vaccine

administered via

PharmaJet® Stratis®

Needle-Free Injection System

Delivering Afluria Intramuscularly Via PharmaJet Stratis Needle-Free Injector



exposure times for images ~ 1/100th of a second

Invisible, narrow, precise fluid stream penetrates skin and enters deltoid muscle in ~0.1 second

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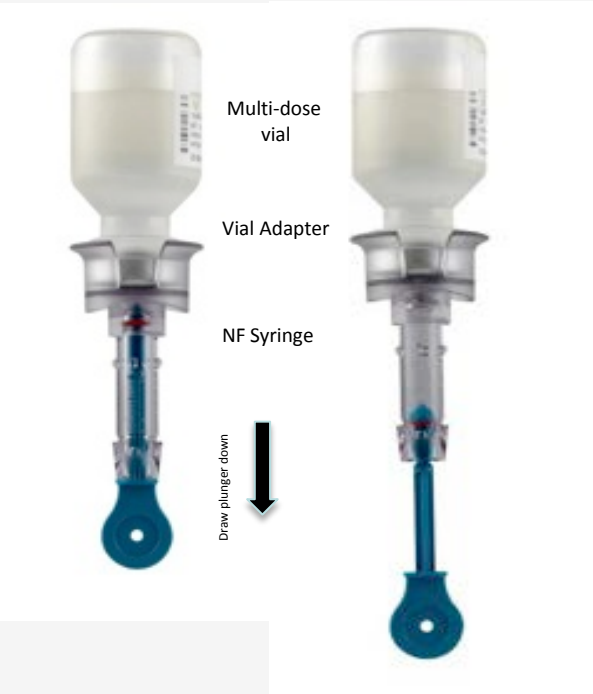
PharmaJet Stratis Workflow

1. Fill syringe – from multi-dose vial



2. Attach needle-free disposable syringe to reusable injector

3. Inject patient

4. Reset injector

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JIFI Study -- Jet Injection for Influenza: a randomized controlled clinical trial to demonstrate non-inferiority of jet injection vs. needle and syringe for administration of Afluria TIV influenza vaccine

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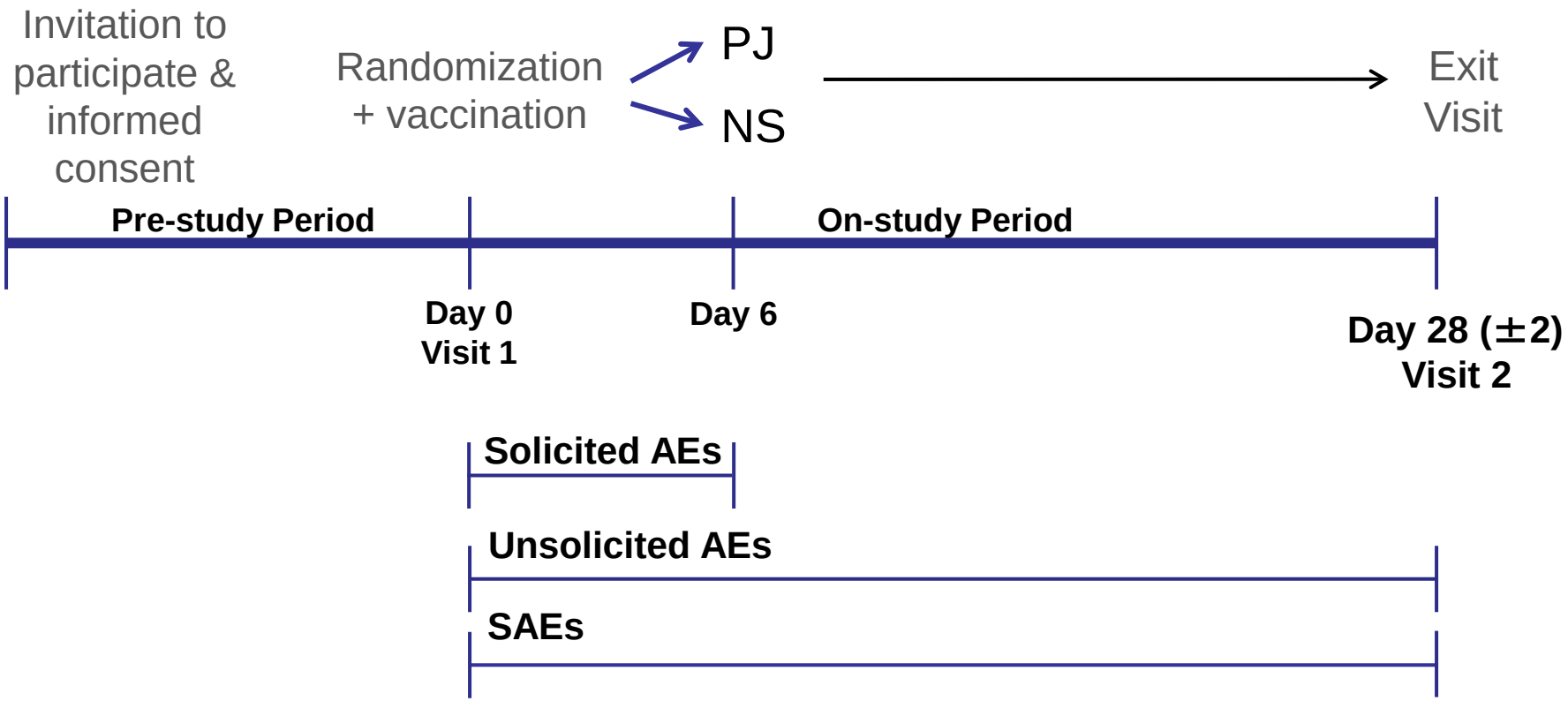
Objectives

- **Primary objective:**
  - Evaluate the **noninferiority** of Afluria influenza vaccine administered IM by jet injection using PharmaJet Stratis to Afluria administered IM by NS in healthy adults based on serum hemagglutination inhibition reciprocal titers
    - 2012-13 N. Hemisphere influenza vaccine formulation
      - A/H1N1 (A/California/7/2009)
      - A/H3N2 (A/Victoria/361/2011)
      - B (B/Hubei-Wujiagang)
- **Secondary objectives**
  - Compare the **safety and tolerability** of the vaccine administered by PJ or NS based on specifically solicited local and systemic reactions through 7 days post-vaccination and adverse events spontaneously reported through day 28 post-vaccination

Study Design

1,250 healthy subjects > 17 and < 65 years of age presenting at the Univ. of Colorado health employee influenza clinics during 2012-2013 Northern Hemisphere flu season



AEs = adverse events; PJ = PharmaJet Stratis; NS = needle and syringe; SAEs = serious adverse events.

Endpoints

- **Six co-primary endpoints**
  - **Geometric mean titer (GMT) ratios** (≤ 1.5) for each of the 3 strains
    - ➥[GMT(NS)] / [GMT(JI)]— upper bound of the 95% confidence interval (CI) should not exceed 1.5
  - **Seroconversion rate (SCR) differences** (not to exceed 10%) for each of the 3 strains
    - ➥ SCR(NS)–SCR(JI)—the upper bound of the 95% CI should be ≤ 10%

GMT ratio- geometric mean of post-vaccination (Day **28**) HI titer for NS over the geometric mean of post-vaccination (Day 28) HI titer for JI
Seroconversion- achieving 4-fold increase in postimmunization titer when baseline ≥10 or postimmunization titer of ≥40 when baseline <10

Based on Guidance for Industry Clinical Data Needed to Support Licensure of Seasonal Inactivated Influenza Vaccines 2007

Endpoints (continued)

- **Secondary Safety endpoints**
  - Immediate reactions in 30-minute observation period
  - Solicited local and systemic AEs diary cards
  - Unsolicited AEs & SAEs up to and including 28 days after vaccination
- **Exploratory immunogenicity endpoints**
  - Seroprotection
  - Geometric mean fold rise (GMFR)
- **Exploratory patient experience questions**
  - Patient immunization experience questions

Seroprotection- titer ≥40 at Day 28

Patient Demographics

	ITT Population		Immunogenicity Population*	
	PJ Stratis	NS	PJ Stratis	NS
N	624	623	562	568
Age, median, years	41	42	42	42
Age, range, years	18-64	18-64	18-64	18-64
Sex, female	72%	69%	73%	69%
White non-Hispanic	88%	85%	88%	85%
Hispanic	6%	10%	6%	10%
Asian	2%	1%	1%	2%
Black	1%	1%	1%	1%

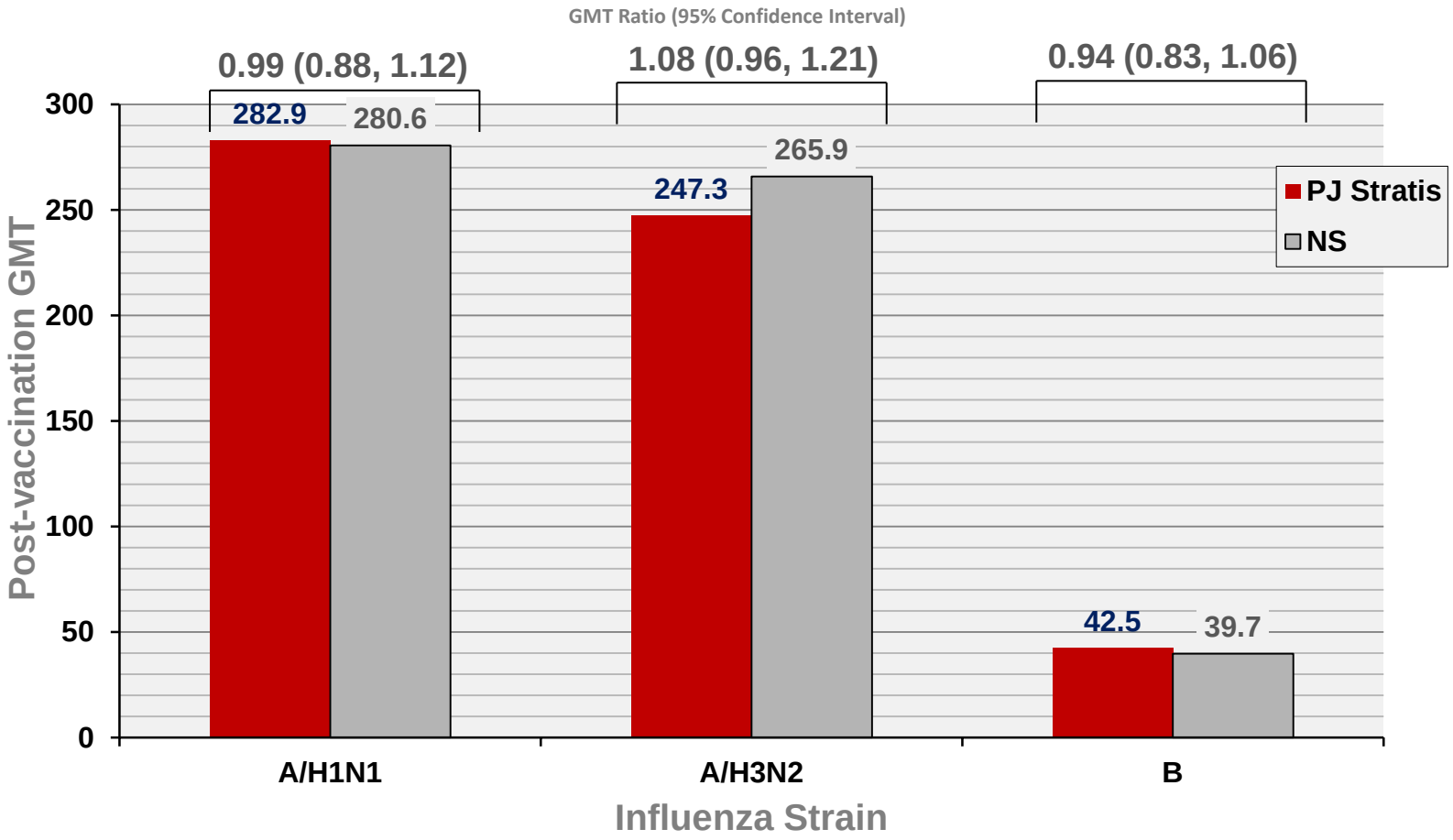
*Completed the study with no major protocol violations.

Immunogenicity

Geometric Mean Titer (GMT) Ratio

28 days post-vaccination

Influenza strain–specific GMT ratio met criteria for noninferiority



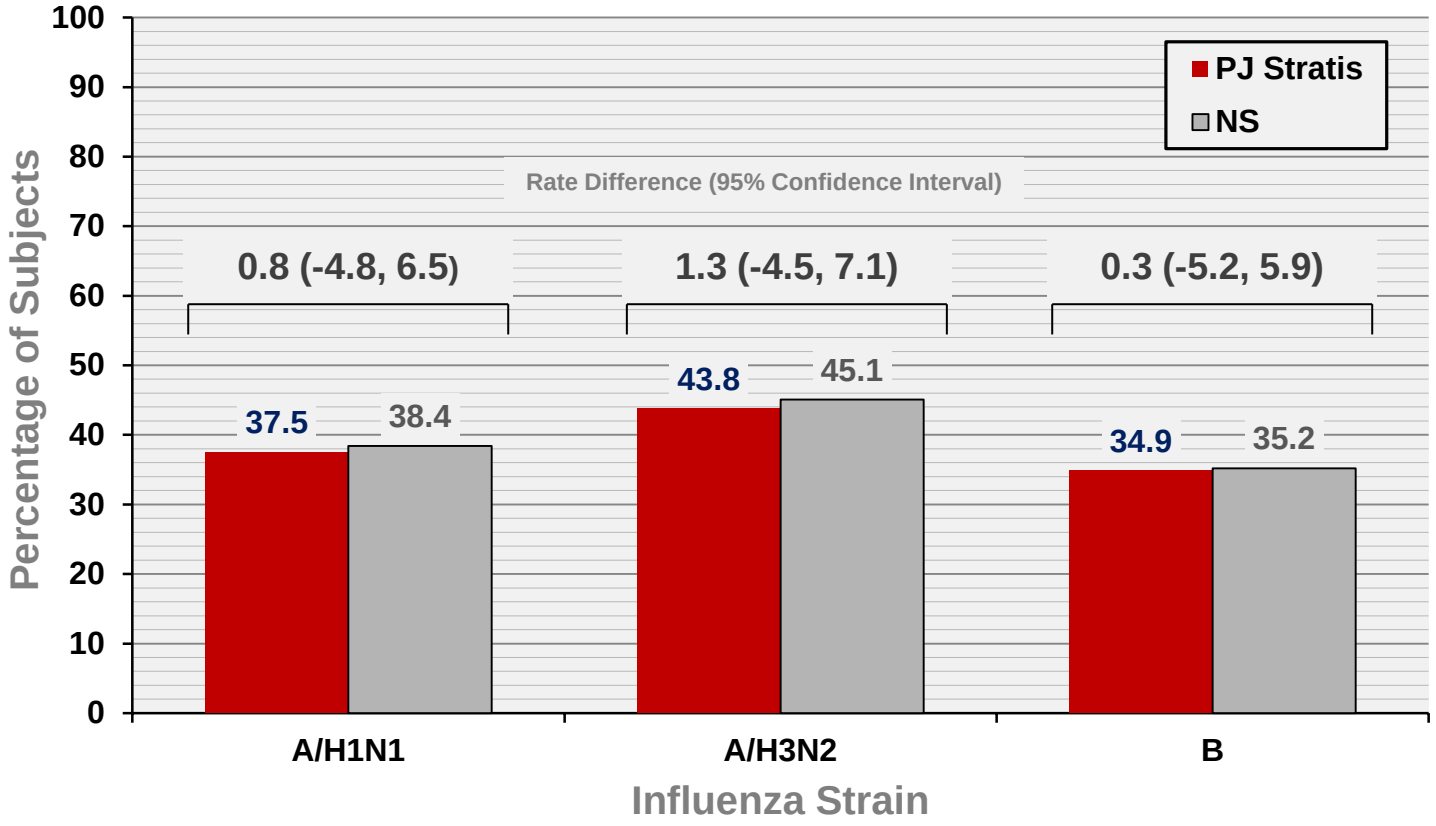
CSR September 15, 2013.

Immunogenicity

Seroconversion rate

28 days post-vaccination

Overall rate of seroconversion met criteria for noninferiority

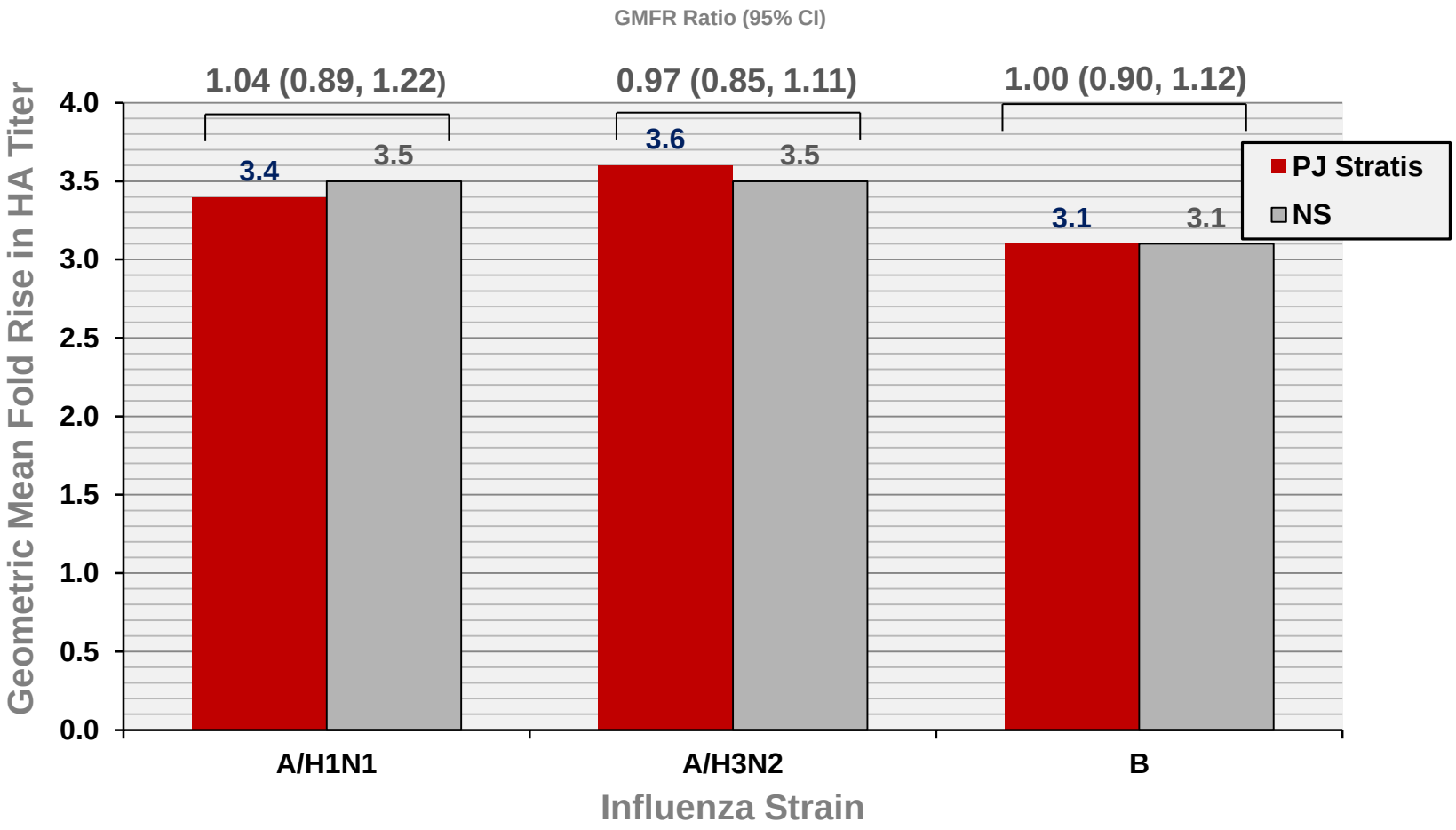


Immunogenicity

Geometric Mean Fold Rise (GMFR)

28 days post-vaccination

GMFR comparable in both groups

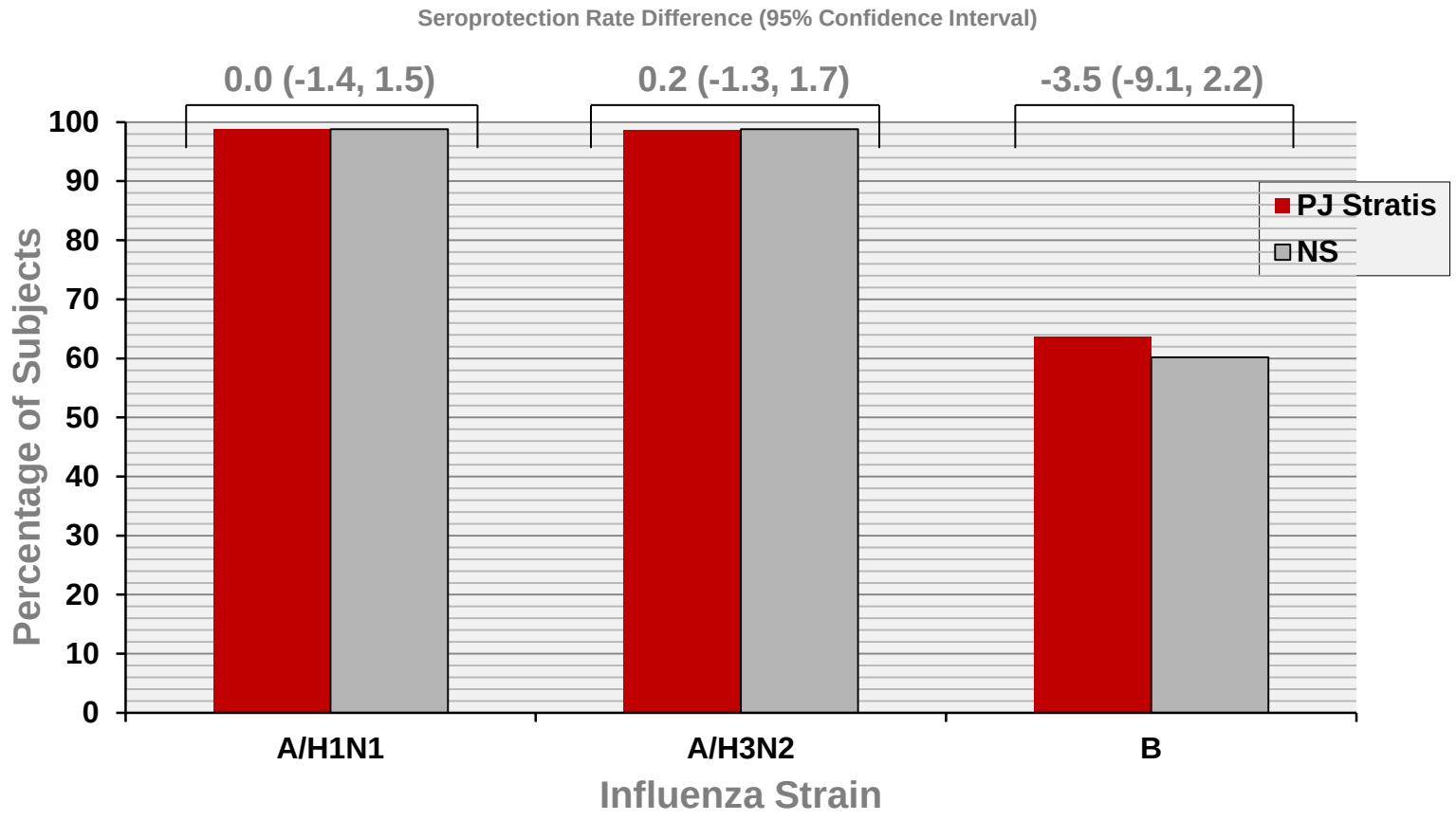


Immunogenicity

Seroprotection Rate

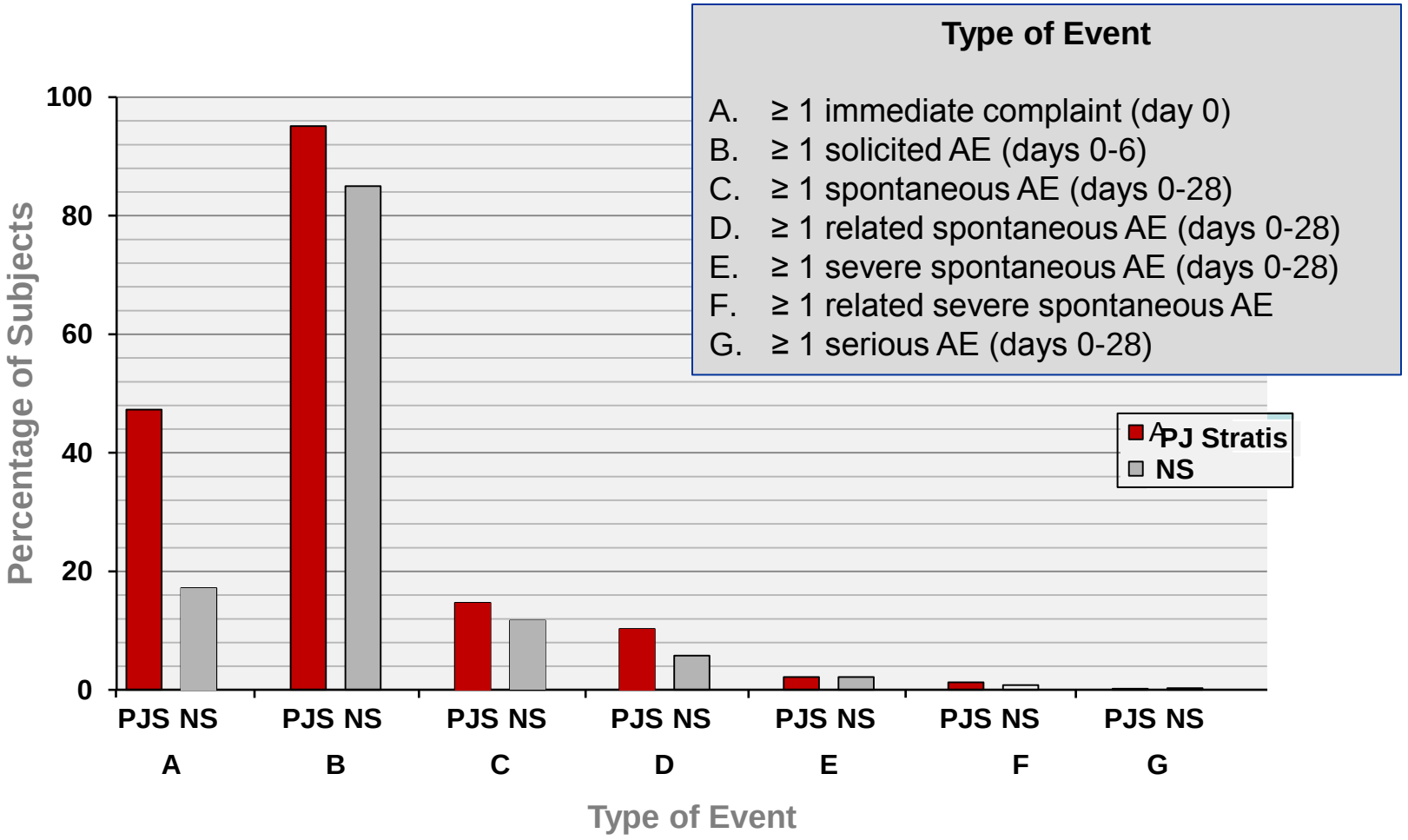
28 days post-vaccination

Seroprotection rate comparable in both groups



Safety

Immediate Complaints and Adverse Events

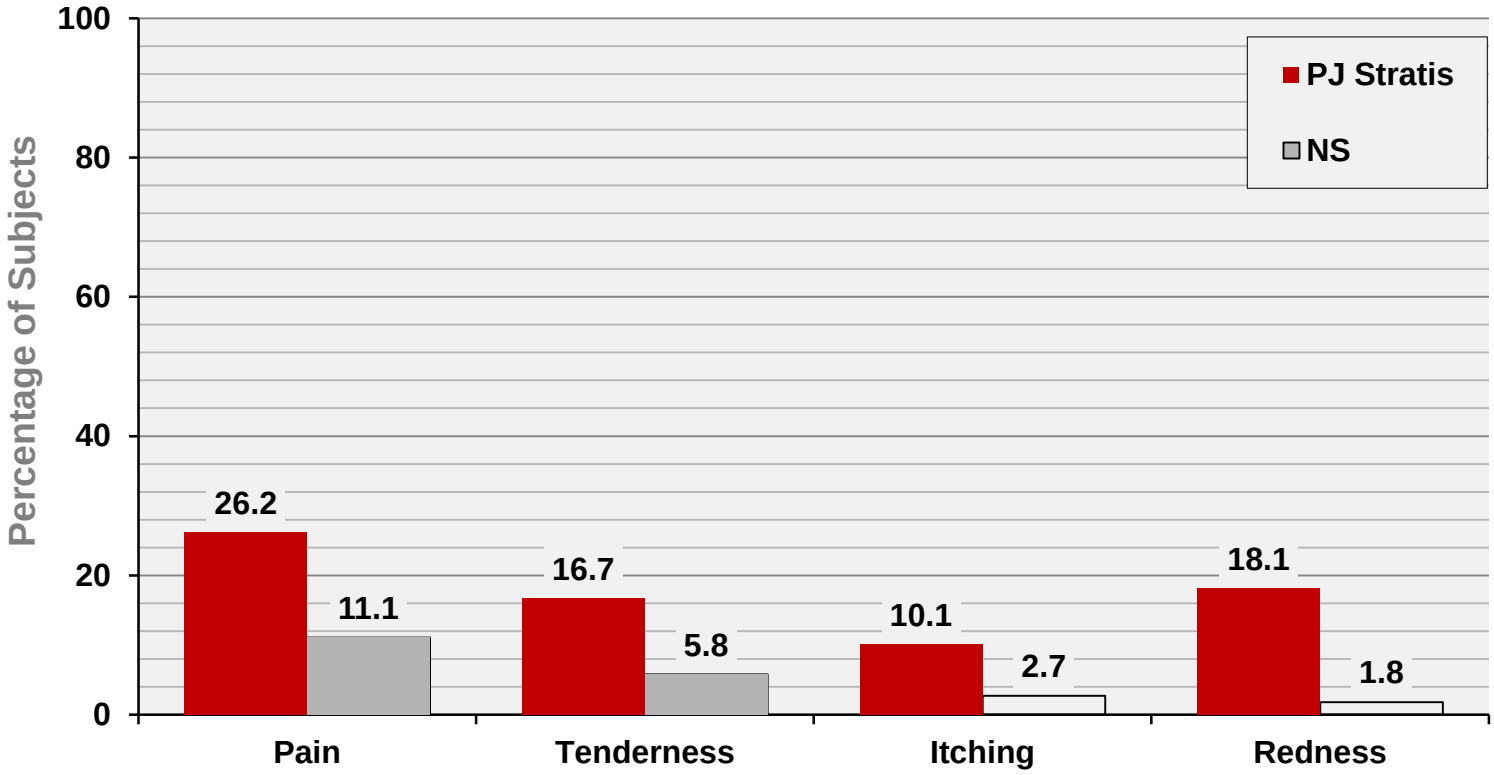


Safety

Immediate Local Reactions (≤ 30 min)

Higher frequency with PJ Stratis, but all were grade 1 or 2 (mild/moderate)

- **No bruising noted in either group**
- **No difference in swelling between groups (both < 1.0%)**

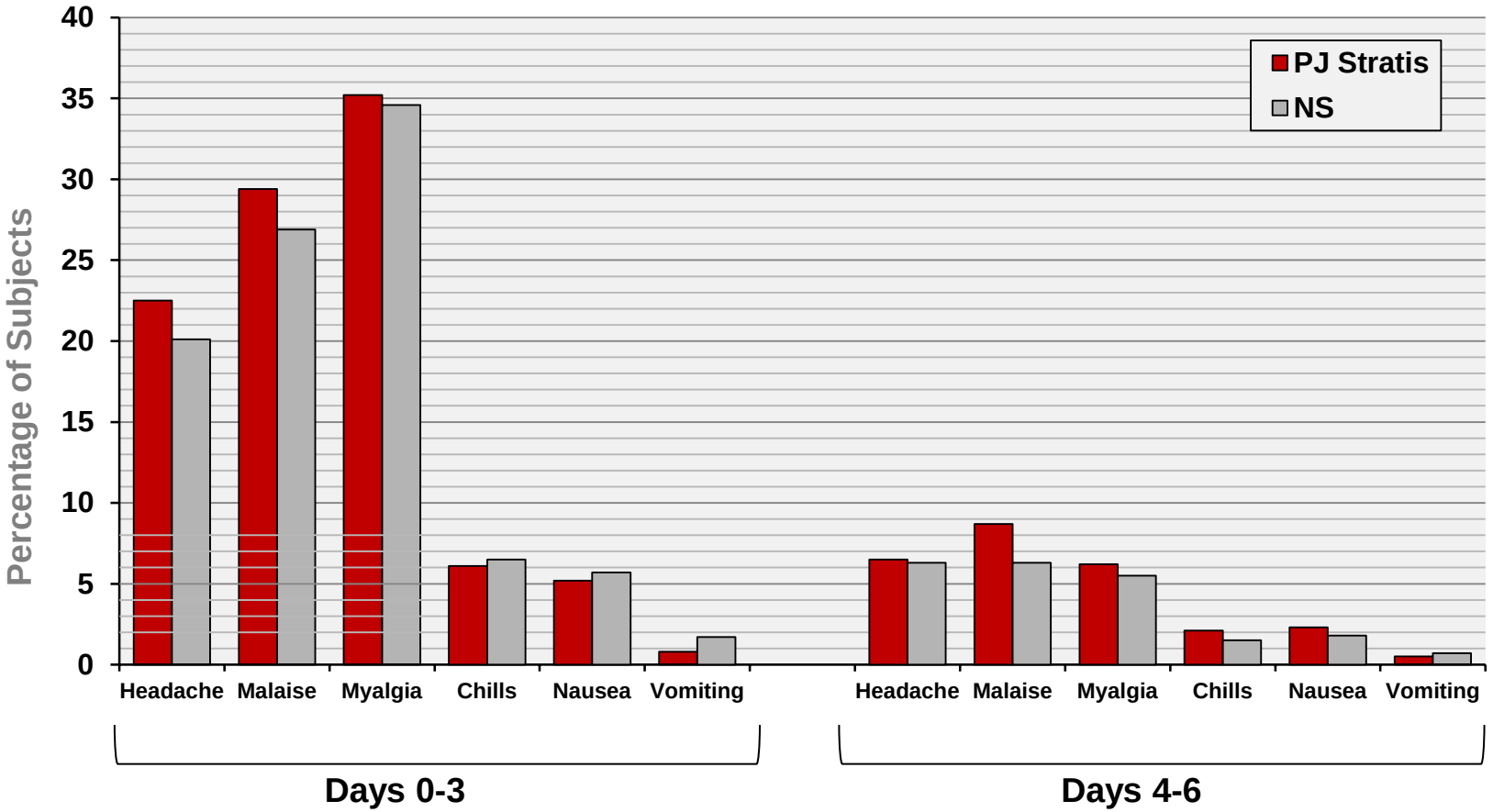


Safety

Solicited Systemic Adverse Events

days 0-3 and days 4-6

Systemic adverse events were comparable between groups



Mild fever (<100.4º F ,<38.0º C) in 2 subjects in each group, none had moderate or severe fever

Safety

Serious Adverse Events

- 3 subjects experienced 6 serious adverse events
- All were unrelated to the study drug/injection procedure

Event	Relationship	Outcome
Perforated duodenal ulcer and peritonitis	Unrelated	Resolved
Viral meningitis	Unrelated	Resolved
CAD, MI, arterial injury	Unrelated	Resolved

CAD = coronary artery disease; MI = myocardial infarction.

Patient Vaccination Experience

Subjects interviewed immediately post-immunization

- Question: Would you chose to receive this type of injection again?
- Response: Of those that received PJ Stratis, 89% indicated that they would receive the PJ Stratis injection again for their next immunization

Results of Recent Post-marketing Surveys on PharmaJet Stratis Use

Conclusions

- Needle fears and needle stick injuries are barriers to flu immunization
- Afluria TIV influenza vaccine delivered by PJ Stratis needle-free jet injector met noninferiority criteria for immunogenicity versus NS
  - Local injection-site reactions were reported more frequently in PJ Stratis injector group- all were mild/moderate
  - Systemic AEs were comparable between Afluria given with NS and with jet injector
- Post-marketing surveys support patient and health care provider satisfaction with needle-free flu immunization
- Overall goal is to support increased flu immunization coverage

TIV = trivalent inactivated vaccine.

AFL-10-0040 10/2014

IMPORTANT SAFETY INFORMATION

AFLURIA®, influenza vaccine, is an inactivated influenza vaccine indicated for active immunization against influenza disease caused by influenza virus subtypes A and type B present in the vaccine. Administration of AFLURIA with a needle and syringe is approved for use in persons 5 years of age and older. Administration of AFLURIA with the PharmaJet® Stratis® Needle-Free Injection System is approved for use in persons 18 through 64 years of age only.

AFLURIA is contraindicated in individuals with known severe allergic reactions (eg, anaphylaxis) to any component of the vaccine including egg protein, or to a previous dose of any influenza vaccine.

Administration of CSL's 2010 Southern Hemisphere influenza vaccine was associated with postmarketing reports of increased rates of fever and febrile seizures in children predominantly below the age of 5 years as compared to previous years; these increased rates were confirmed by postmarketing studies. Febrile events were also observed in children 5 to less than 9 years of age.

If Guillain-Barré Syndrome (GBS) has occurred within 6 weeks of previous influenza vaccination, the decision to give AFLURIA should be based on careful consideration of the potential benefits and risks.

IMPORTANT SAFETY INFORMATION

If AFLURIA is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.

AFLURIA should be given to a pregnant woman only if clearly needed.

AFLURIA has not been evaluated in nursing mothers. It is not known whether AFLURIA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AFLURIA is administered to a nursing woman.

Antibody responses in persons 65 years of age and older were lower after administration of AFLURIA as compared to younger adult subjects.

In children 5 through 17 years of age, most common injection-site adverse reactions observed in clinical studies of AFLURIA when administered by needle and syringe were pain, redness, and swelling. The most common systemic adverse events were headache, myalgia, irritability, malaise, and fever.

In adults 18 through 64 years of age, the most common injection-site adverse reactions observed in clinical studies of AFLURIA when administered by needle and syringe were tenderness, pain, swelling, and redness, itching. The most common systemic adverse reactions observed were muscle aches, headache and malaise.

IMPORTANT SAFETY INFORMATION

In adults 18 through 64 years of age, the most common injection-site adverse reactions observed in clinical studies with AFLURIA when administered by the PharmaJet Stratis Needle-Free Injection System up to 7 days post-vaccination were tenderness, swelling, pain, redness, itching and bruising. The most common systemic adverse events within this period were myalgia, malaise, and headache.

In adults 65 years of age and older, the most common injection-site adverse reactions observed in clinical studies of AFLURIA when administered by needle and syringe were tenderness and pain.

Vaccination with AFLURIA may not protect all individuals.

Please see full prescribing information for AFLURIA which is provided in the meeting handout.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch or call 1-800-FDA-1088.