



SEQIRUS: MANUFACTURER'S UPDATE

2016 National Adult and Influenza Immunization Summit
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Seqirus 2016 NAIIS GMCC-903_2016-05-10

Agenda

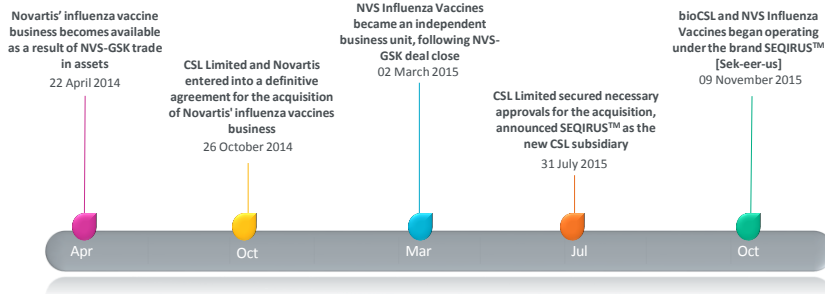
- Introduction to Seqirus
- Review of 2015/16 Influenza Season Performance
- Product Offerings 2016/17 Influenza Season
- Upcoming Directions in Vaccine Research and Development
- Areas for Consideration for the Summit

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About SEQIRUS™

Timeline



On 31 July 2015, bioCSL and NVS Influenza Vaccines joined forces to create Seqirus, now the second largest influenza vaccine company in the world.

Sources: CSL Limited and Novartis press releases. <https://www.novartis.com/news/media-releases/novartis-announces-divestiture-influenza-vaccines-business-csl-usd-275-million>, <http://www.csl.com.au/Investors/UPDATE-Novartis-Influenza-Vaccines-acquisition.htm>, <http://www.seqirus-us.com/news-room/CSL-brands-worlds-no-2-influenza-vaccine-as-seqirus>. Accessed Nov 19, 2015

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SEQIRUS: A Leader in the Prevention and Control of Influenza Globally and Pandemic Preparedness

- Reliable supplier of seasonal influenza vaccine and anti-viral treatment with the potential to rapidly respond to pandemic threats
- Significant manufacturing capacity with networks on three continents and the flexibility of two production technologies
- Differentiated seasonal and pre/pandemic influenza portfolio
- Only vaccine company completely focused on influenza
- CSL celebrates its 100th Anniversary in 2016 - A century of experience in helping to combat influenza



Holly Springs, NC, US

- Cell-based platform
- Primary and secondary production



Kankakee, IL, US

- Secondary production



Liverpool, UK

- Egg-based platform
- Primary production



Marburg, Germany

- Secondary production
- Adjuvant production



Parkville, AUSTRALIA

- Egg-based platform
- Primary production

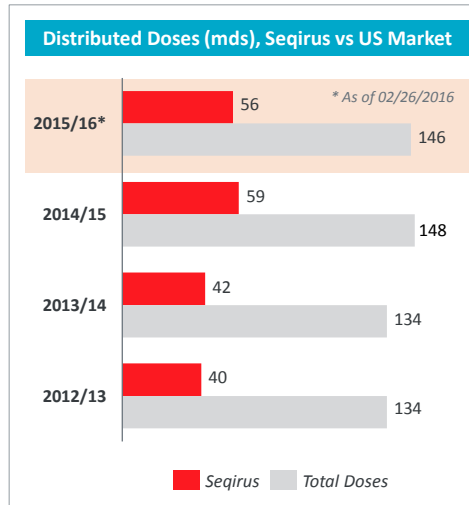
Source: SEQIRUS. Data on file.

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SEQIRUS: A Consistent and Reliable Manufacturer

- First to ship flu doses in the US
 - 2015-16: July 13, 2015
 - 2014-15: July 02, 2014
 - 2011-12: July 15, 2011
 - 2010-11: July 29, 2010
- Legacy Novartis shipped 41 mds during the 2015-2016 season
- Legacy bioCSL shipped 15 mds during the 2015-2016 season







Source: CDC. Seasonal Influenza Vaccine Doses Distributed in the US, By Season. <http://www.cdc.gov/flu/professionals/vaccination/vaccinesupply.htm>. Accessed April 26, 2016.

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SEQIRUS Provides a Differentiated Portfolio of Vaccines and Treatment for Influenza for the US

Brand	Current Presentation	Age Indication	Under FDA Review
 afluria INFLUENZA VACCINE	TIV MDV, PFS	5+ years*	QIV 18+ years
 FLUAD influenza vaccine, adjuvanted	TIV PFS	65+ years	
 FLUCELVAX Influenza Vaccine	TIV PFS	18+ years	QIV 4+ years
Influenza Virus Vaccine Fluvirin®	TIV MDV, PFS	4+ years	
 Rapivab peramivir injection	Three single-use vials	18+ years	

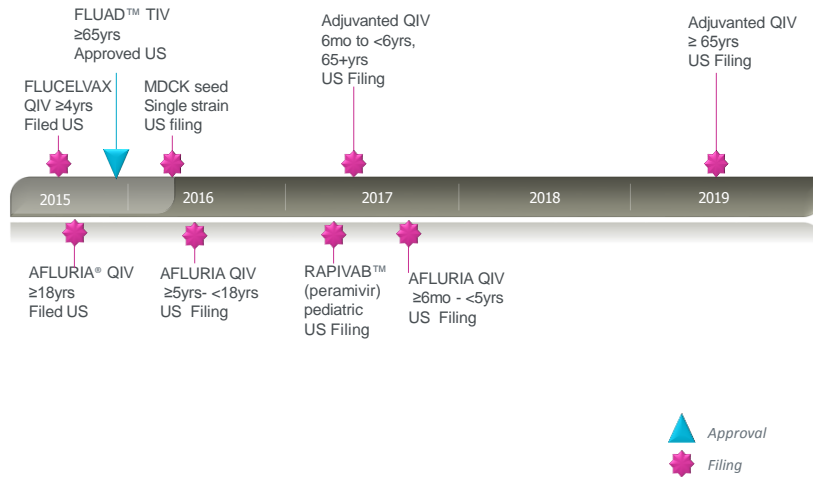
* ACIP Recommendation is for use in individuals 9+ years of age

Source: SEQIRUS. Data on file.

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Current and Anticipated Directions in Research and Development



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Areas for Consideration for the Summit

- Annual US Flu associated deaths range from 3,300-48,600¹
- Flu results in ~226,000 associated hospitalizations annually²
- Certain people are at greater risk for serious complications if they get the flu. This includes older people, young children, and people with certain health conditions
- Yet, despite universal recommendations since 2010, influenza vaccination rates remain sub-optimal, and flat for many vulnerable populations

What is the Next Level of Engagement to Improve Immunization Rates?

1. "Estimates of Deaths Associated with Seasonal Influenza — United States, 1976–2007", *MMWR*, 27 August 2010.
 2. Thompson W et al., "Influenza-Associated Hospitalizations in the United States", *JAMA*, 15 September 2004.

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Vaccination Rates for 65+ Population are Largely Unchanged for the Last Decade

2006	2007	2008	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016 *
64.1%	66.4%	67.0%	69.6%	66.6%	64.9%	66.2%	65.0%	66.7%	60.2%

*Interim November 2015 data

SOURCE

2006-2008: NHIS: http://www.cdc.gov/flu/pdf/professionals/nhis89_08fluvaxtrendtab.pdf

2009: BRFS: http://www.cdc.gov/flu/fluview/coverage_1011estimates.htm

2010: BRFS: http://www.cdc.gov/flu/fluview/coverage_1011estimates.htm

2011: BRFS: http://www.cdc.gov/flu/fluview/coverage_1112estimates.htm#data

2012: BRFS: <http://www.cdc.gov/flu/fluview/coverage-1213estimates.htm>

2013: BRFS: <http://www.cdc.gov/flu/fluview/coverage-1314estimates.htm#age-group-adults>

2014: BRFS: <http://www.cdc.gov/flu/fluview/coverage-1415estimates.htm#age-group-adults>

2015: <http://www.cdc.gov/flu/fluview/nifs-estimates-nov2015.htm>

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Pediatric Influenza Rates: Can We Do Better?

Children: 6 months to 4 years	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016 *
	63.6%	67.6%	69.8%	70.4%	70.4%	51.7%

*Interim November 2015 data

SOURCE:

2010: NIS: http://www.cdc.gov/flu/fluview/coverage_1011estimates.htm

2011: NIS-FLU: http://www.cdc.gov/flu/fluview/coverage_1112estimates.htm

2012: NIS-FLU: <http://www.cdc.gov/flu/fluview/coverage-1213estimates.htm>

2013: NIS-FLU: <http://www.cdc.gov/flu/fluview/coverage-1314estimates.htm#age-group-adults>

2014: NIS-FLU: <http://www.cdc.gov/flu/fluview/coverage-1415estimates.htm#age-group-children>

2015: <http://www.cdc.gov/flu/fluview/nifs-estimates-nov2015.htm#age-children>

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Conclusion

- SEQIRUS combines Novartis Influenza Vaccines and bioCSL into a dynamic company that is the second largest influenza vaccine manufacturer in the world
 - Significant manufacturing capacity on three continents
 - 100 years of experience in helping to combat influenza
- Four vaccines and an antiviral are planned for manufacturing for the 2016-2017 influenza season
 - This includes both cell and egg-based technologies
- Investing in products to help reduce the burden of influenza, especially in the most vulnerable populations
 - Expansion into quadrivalent vaccines and additional adjuvanted vaccines
- Look forward to partnering with the Summit to identify new levels of engagement and increase immunization rates across the US

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AFLURIA® 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 (e.g., 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 post marketing 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 post marketing 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.
- If Afluria is administered to immunocompromised persons, including those receiving immunosuppressive therapy, the immune response may be diminished.

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AFLURIA® Important Safety Information

- 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, redness, and itching. The most common systemic adverse reactions observed were muscle aches, headache, and malaise.

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AFLURIA® Important Safety Information

- In adults 18 through 64 years of age, the most common injection-site adverse reactions observed in clinical studies of 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.
- 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.

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FLUAD™ Important Safety Information

Indication:

- FLUAD (influenza vaccine, adjuvanted) 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.

Contraindications

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

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

Adverse Reactions

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

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FLUVIRIN® Important Safety Information

- FLUVIRIN (influenza virus vaccine) should not be administered to anyone with known systemic hypersensitivity reactions to egg proteins (egg or egg products), or to any component of FLUVIRIN, or who has had a life-threatening reaction to previous influenza vaccinations
- If Guillain-Barré syndrome has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give FLUVIRIN should be based on careful consideration of the potential benefits and risks
- If FLUVIRIN is administered to immunocompromised persons, including individuals receiving immunosuppressive therapy, the expected immune response may not be obtained. Prior to administration of any dose of FLUVIRIN, the healthcare provider should review the patient's prior immunization history for possible adverse events, to determine the existence of any contraindication to immunization with FLUVIRIN and to allow an assessment of benefits and risks. Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine
- The tip caps of the FLUVIRIN prefilled syringes may contain natural rubber latex which may cause allergic reactions in latex sensitive individuals
- Vaccination with FLUVIRIN may not protect all individuals. In clinical trials, the most common adverse events in adults were headache, fatigue, injection site reaction (pain, mass, redness, and induration), and malaise

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FLUCELVAX® Important Safety Information

Contraindication

- Do not administer FLUCELVAX (influenza vaccine) to anyone with a history of severe allergic reaction (e.g. anaphylaxis) to any component of the vaccine.

Warnings & Precautions

- Guillain-Barré Syndrome (GBS): If GBS has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUCELVAX should be based on careful consideration of the potential benefits and risks.
- Latex: The tip caps of the pre-filled syringes may contain natural rubber latex which may cause allergic reactions in latex-sensitive individuals.
- Preventing and Managing Allergic Reactions: Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration of the vaccine.
- Syncope: Syncope (fainting) can occur in association with administration of injectable vaccines, including Flucelvax. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope by maintaining a supine or Trendelenburg position.

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FLUCELVAX® Important Safety Information

Warnings & Precautions

- Altered Immunocompetence: After vaccination with FLUCELVAX, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response.
- Limitations of Vaccine Effectiveness: Vaccination with FLUCELVAX may not protect all vaccine recipients against influenza disease.

Most Common Adverse Reactions

- The most common ($\geq 10\%$) solicited adverse reactions occurring in adults 18-64 years of age within 7 days of vaccination with FLUCELVAX were pain at the injection site, erythema at the injection site, headache, fatigue, myalgia and malaise. The most common ($\geq 10\%$) solicited adverse reactions occurring in adults ≥ 65 years of age within 7 days of vaccination were erythema at the injection site, fatigue, headache and malaise.

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RAPIVAB™ Important Safety Information

Rapivab™ (peramivir injection) is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days.

- Efficacy of Rapivab was based on clinical trials in which the predominant influenza virus type was influenza A; a limited number of subjects infected with influenza B virus were enrolled.
- Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Rapivab.
- Efficacy could not be established in patients with serious influenza requiring hospitalization.

Contraindications

None

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RAPIVAB™ Important Safety Information

Warnings and Precautions

- Rare cases of serious skin reactions, including Stevens-Johnson syndrome and erythema multiforme have occurred with Rapivab. Appropriate treatment should be instituted if a serious skin reaction occurs or is suspected.
- Patients with influenza may be at an increased risk of hallucinations, delirium and abnormal behavior early in their illness. There have been post-marketing reports (from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who were receiving neuraminidase inhibitors, including Rapivab. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made, but they appear to be uncommon. These events were reported primarily among pediatric patients. The contribution of RAPIVAB to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior.
- Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. Rapivab has not been shown to prevent such complications.

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RAPIVAB™ Important Safety Information

Adverse Reactions

The most common adverse reaction was diarrhea (8% Rapivab vs 7% placebo).

Lab abnormalities (incidence \geq 2%) occurring more commonly with Rapivab than placebo were elevated ALT 2.5 times the upper limit of normal (3% vs 2%), elevated serum glucose greater than 160 mg/dL (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (4% vs 2%) and neutrophils less than $1.0 \times 10^9/L$ (8% vs 6%).

Concurrent use with Live Attenuated Influenza Vaccine

Antiviral drugs may inhibit viral replication of a live attenuated influenza vaccine (LAIV). The concurrent use of Rapivab with LAIV intranasal has not been evaluated. Because of the potential for interference between these two products, avoid use of LAIV within 2 weeks before or 48 hours after administration of Rapivab unless medically indicated.

Please see full prescribing information for Rapivab.
You are encouraged to report negative side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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