

Fluzone[®]

Virocyt Virus Counter Use for Determining Viral Seed Selection & Viral Yield Information in Upstream Process Steps

SANOFI PASTEUR IN BRIEF

- World leader in vaccines
 - 20 diseases
 - More than 1 billion doses/year
 - More than 500 million people vaccinated/year
 - various vaccines in development
- Nearly 13,000 employees ⁽¹⁾
- 13 production/R&D sites
 - France (Marcy l'Etoile and Val de Reuil)
 - US (Swiftwater, Cambridge, Canton, Orlando and Rockville)
 - Canada (Toronto)
 - Argentina (Pilar)
 - China (Shenzhen)
 - India (Hyderabad)
 - Mexico (Ocoyoacac),
 - Thailand (Chachoengsao)

And 2 new facilities under construction:
France (Neuville) and China (Shenzhen)
- A worldwide presence
- A joint venture with Merck & Co. Inc. in Europe, Sanofi Pasteur MSD



● Sites Sanofi Pasteur

1. FTEs as of December 2011 – Vaccines activities

OUR COMMITMENT TO FIGHTING INFLUENZA

- Sanofi Pasteur is the world leader in the production of seasonal influenza vaccine
 - More than 200 million doses supplied in 2011
 - Vaccines registered and sold in over 150 countries
 - More than 2.5 billion doses of Sanofi Pasteur seasonal influenza vaccines administered worldwide over the past 60 years.
- Sanofi Pasteur innovates and proposes new flu vaccines tailored to people's needs
 - 2010: launch of the first micro-needle vaccine against influenza: Intanza® / IDflu®, in more than 30 countries
 - 2010: launch of Fluzone® High-Dose vaccine in the US, designed specifically for people 65 years of age and older
 - 2011: licensing of Fluzone® ID 9 µg, indicated for adults 18 to 64, by the U.S. Food and Drug Administration (FDA).
- Sanofi Pasteur has been steadily increasing its manufacturing capacity to fight against flu. Since 2003, capacity has increased by more than 40%.

Epidemics and outbreaks of influenza **infect about 5-15%** of the population each season

Between **3 and 5 million cases** of **severe illness**

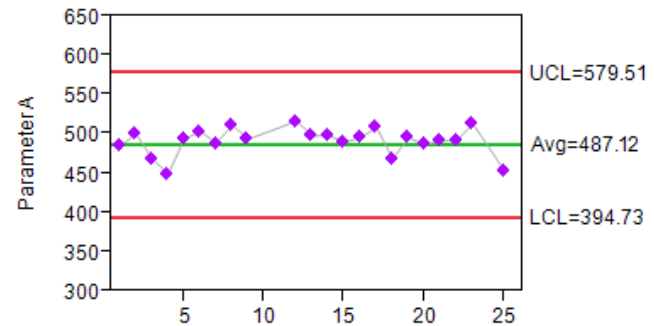
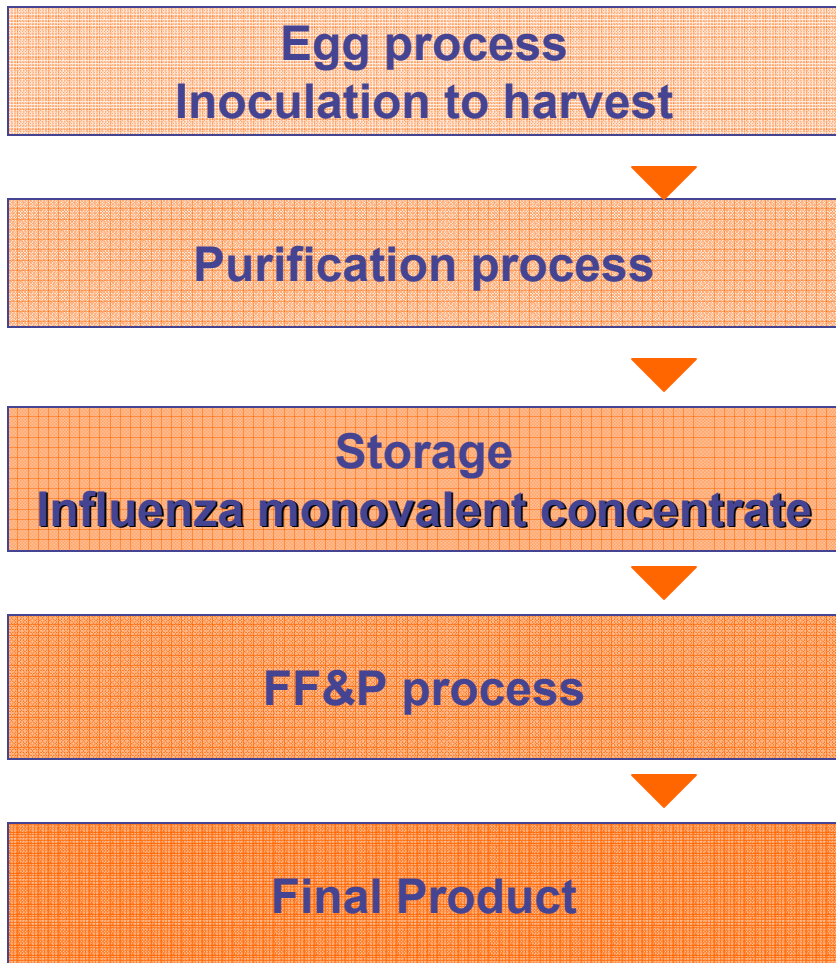
250,000 to 500,000 estimated deaths every year around the world



(1) WHO – Influenza Factsheet n° 211 – Revised April 2009

FLUZONE® PRODUCTION PROCESS

EGG RECEIPT TO FINAL PRODUCT

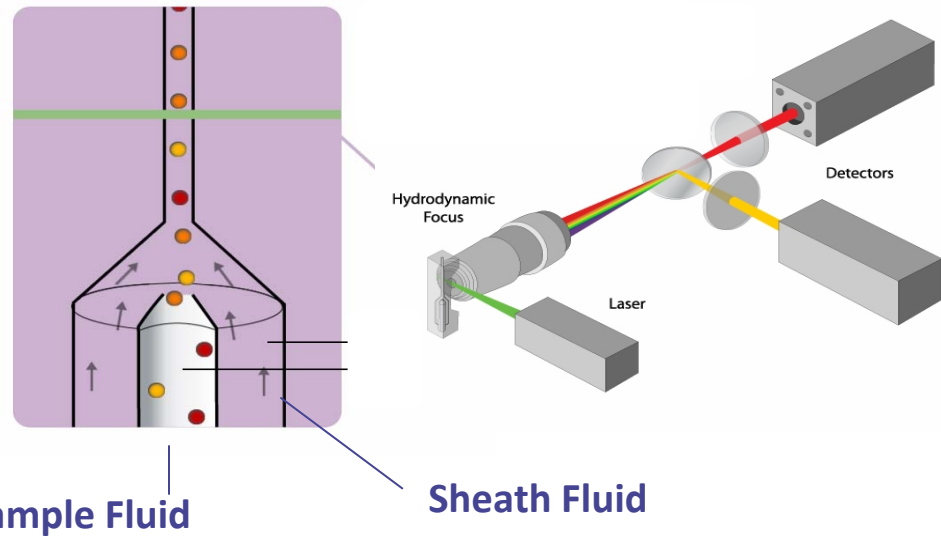
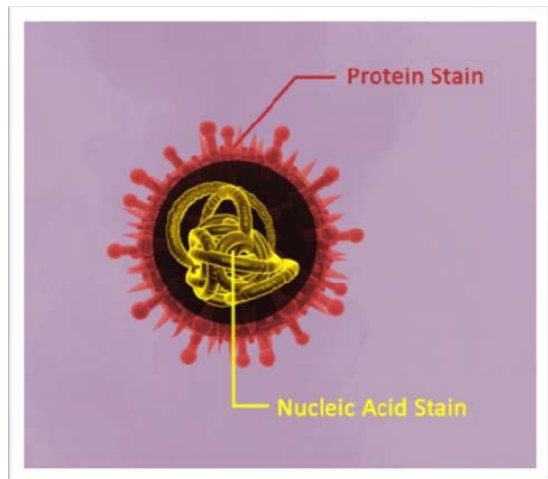


Process monitoring
Process performance

DATA COLLECTION
TESTING



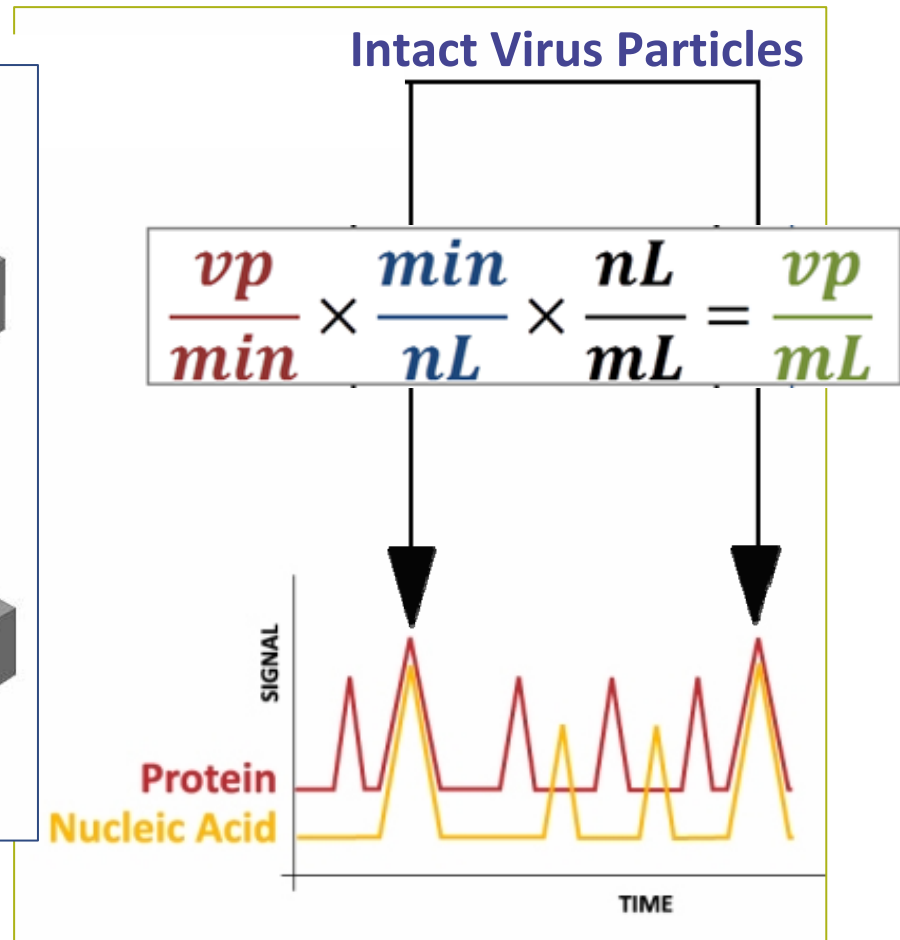
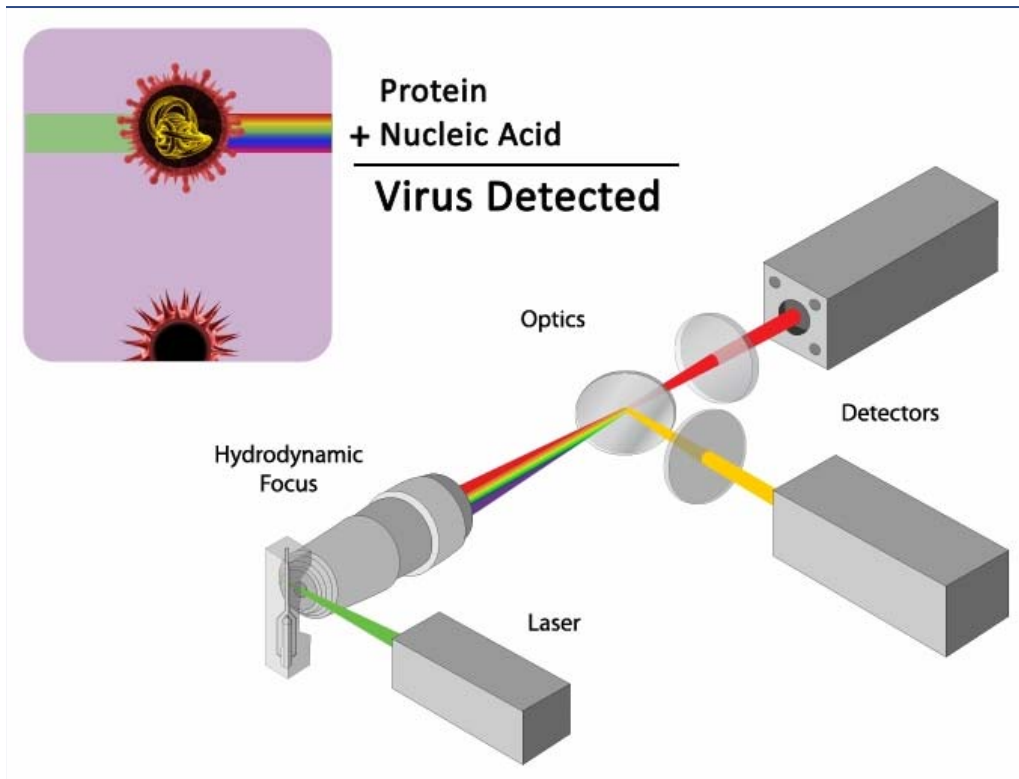
Virocyt Instrument Principle



Sample Prep / Analysis

- Add two fluorescent dyes (Combo Dye)
- 30 min incubation (multiple samples at once)
- Analyze on Virus Counter (<15 min/sample)

Virocyt Instrument Principle



Virocyt Instrument Principle

Automated threshold determination using proprietary algorithm.

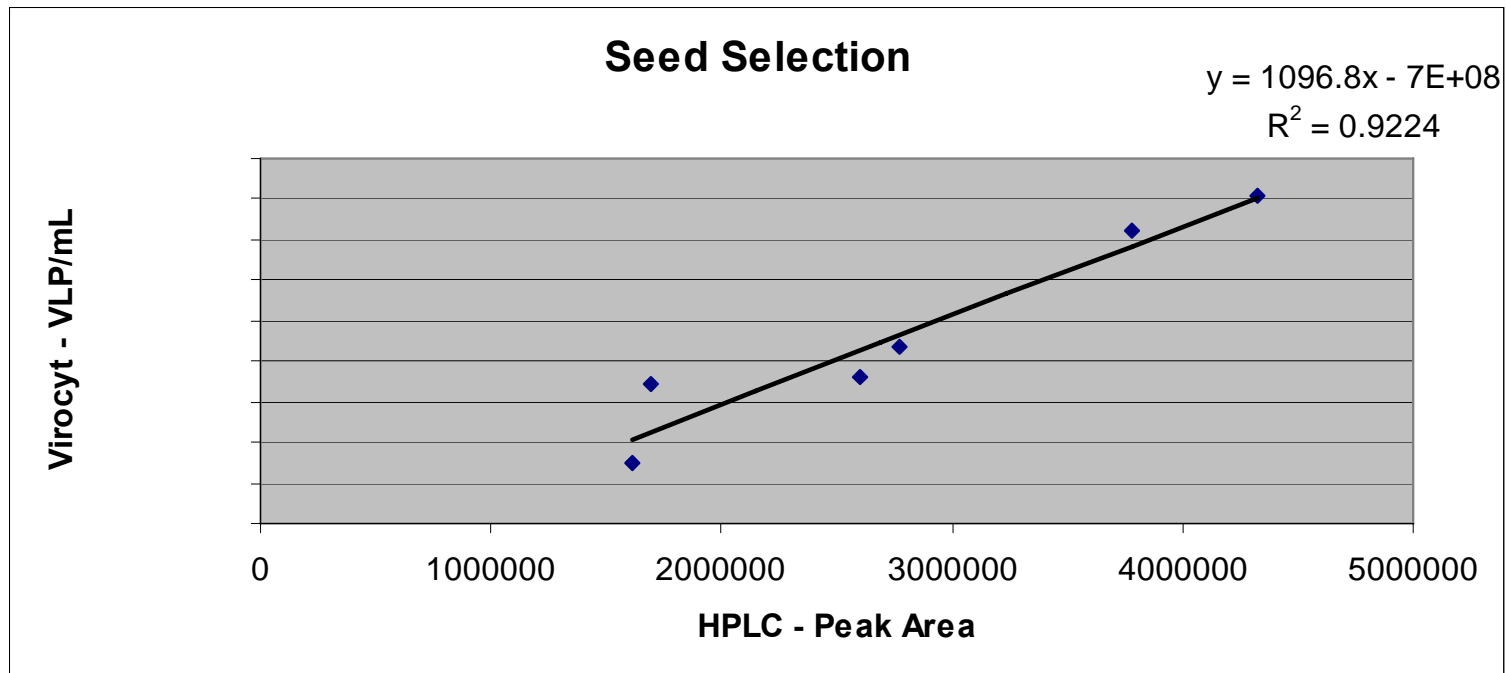


Business Need / Request

- To be able to perform seed analysis to determine high yield seed lots for implementation into production.
- To be able to perform yield information on early upstream production process steps either with or without a cleanup step.

Using Virocyt for Seed Development

- Current Status
 - HPLC peak areas are used for determining viral seed selections.
- Proposed Change
 - Use Virocyt instead of HPLC peak areas for viral seed selections.



Using Virocyt for Yield Assessments in Upstream Process steps

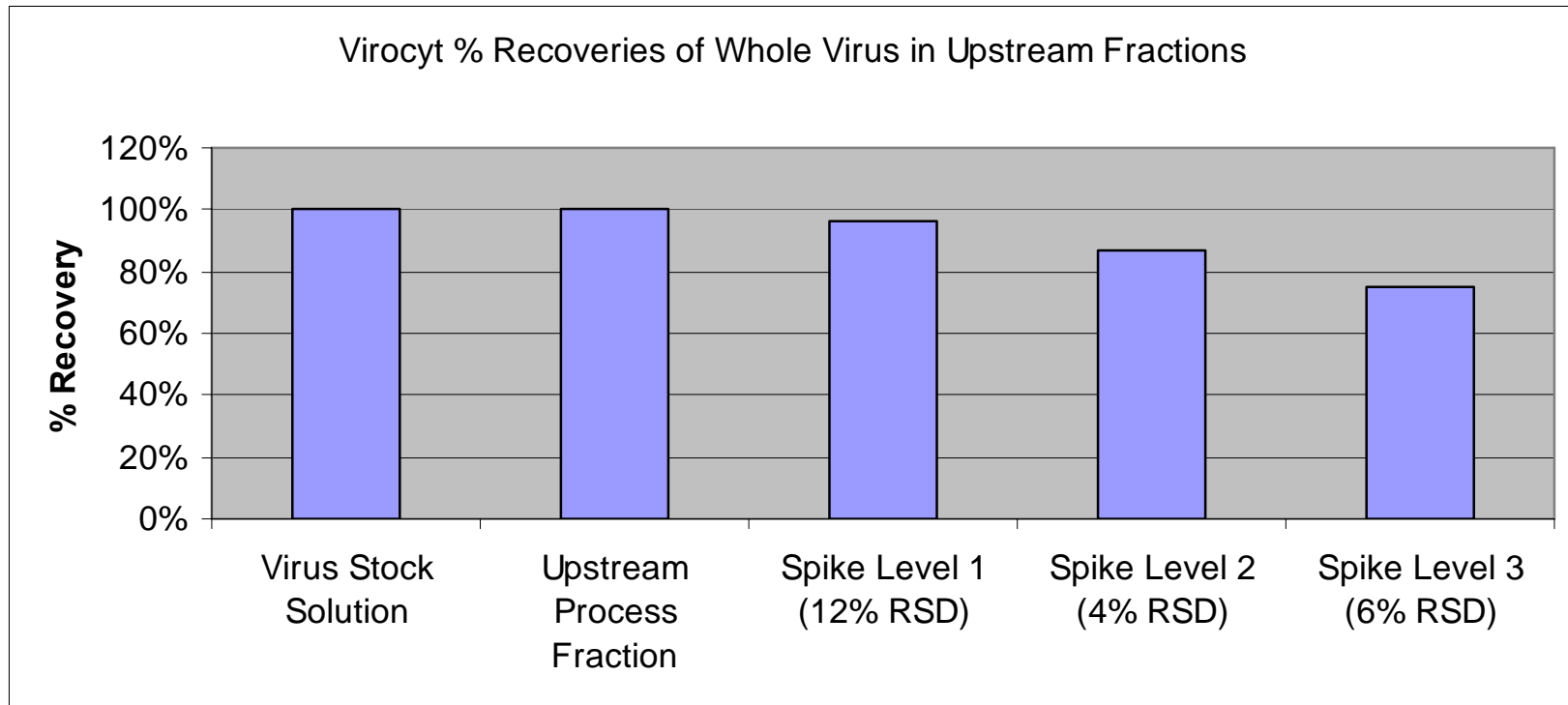
- **Current Status**

- **Quantitative HPLC results are used for determining viral yield assessments in upstream process steps.**
 - Concerns – High column protein loads make assessment difficult.

- **Proposed Change**

- **Use Virocyt instead of HPLC peak areas for determining viral yield assessments in upstream process steps.**
 - Possible solution – early assessment have determined it might be feasible to determine yield from upstream process steps by simple dilution of fluids without the need for a clean-up step.

Using Virocyt for Yield Assessments in Upstream Process steps - continued



Using Virocyt for Yield Assessments in Upstream Process steps - continued

virocyt™
Software 1.3

Ready

Exit Saved Data Mode

Sample

Start Analysis

Performance Verification

CVF PVS

Wash

ISW

Full Wash

Reverse Flush

Stop

Shutdown

InDev

Analysis | Charts | Results Summary

04/02/13 01:21 PM Result: 3.3E7 vp/mL Log: 7.52

Save Load

Notes:

Thresholds

Auto Thresholds Nucleic: 2.07 Protein: 0.65

Manual Thresholds Locked

Save Load Unlock Evaluate

Metrics	Nucleic	Protein	Simultaneous
Concentrations (#/mL)	4.4E7	7.0E7	3.3E7
Number of Events	17732	27869	13139
Peak Heights (V)	3.76 ± 3.20	2.22 ± 3.23	
Peak Widths (us)	38 ± 26	34 ± 21	

Scaling Print Freeze

Nucleic Acid Protein

Time (s)

Thank you