

Monitoring Changes in the Influenza Virus at the National Level

Wendy Sessions, MPH

Virus Surveillance and Diagnosis Branch
Influenza Division, CDC

2013 DSHS Influenza Surveillance Workshop
July 16, 2013

OBJECTIVES

- **Discuss the World Health Organization's Global Influenza Surveillance and Response System and the vaccine strain selection process**
- **Describe the virologic surveillance of influenza**
- **Describe the methods for monitoring the evolution of influenza viruses by genetic and antigenic characterization**

Influenza Surveillance

- **Global:**
 - **Global Influenza Surveillance and Response System (GISRS)**



- **US**
 - **CDC, FluView**

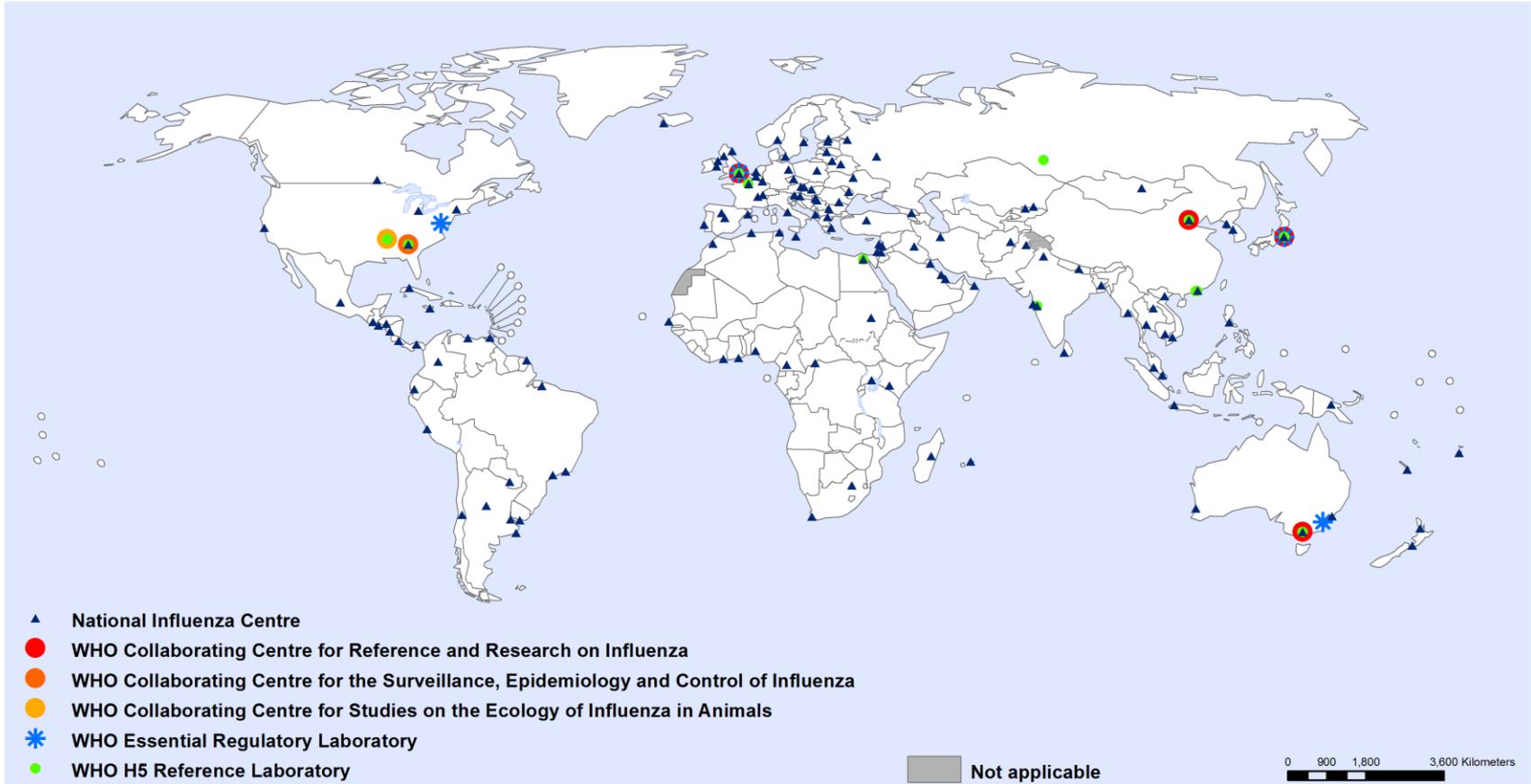


WHO Influenza Network

- **Six WHO Collaborating Centers (WHO CCs) on Influenza**
- **Four WHO Essential Regulatory Laboratories**
- **141 Institutions that are National Influenza Centers (NICs)**
 - Designated by national Ministries of Health and recognized by WHO
 - Collect virus specimens in their country and perform preliminary analysis
 - Ship representative clinical specimens and isolated viruses to WHO CCs for advanced antigenic and genetic analysis
- **Ad hoc groups designed to address emerging issues**

WHO Global Influenza Surveillance and Response System

25 April 2013



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), WHO
Map Production: WHO GISRS Team
World Health Organization



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Global Influenza Surveillance and Response System (GISRS)

- **Monitors the evolution of influenza viruses and provides recommendations in areas including laboratory diagnostics, vaccines, antiviral susceptibility and risk assessment**
- **Serves as a global alert mechanism for the emergence of influenza viruses with pandemic potential**

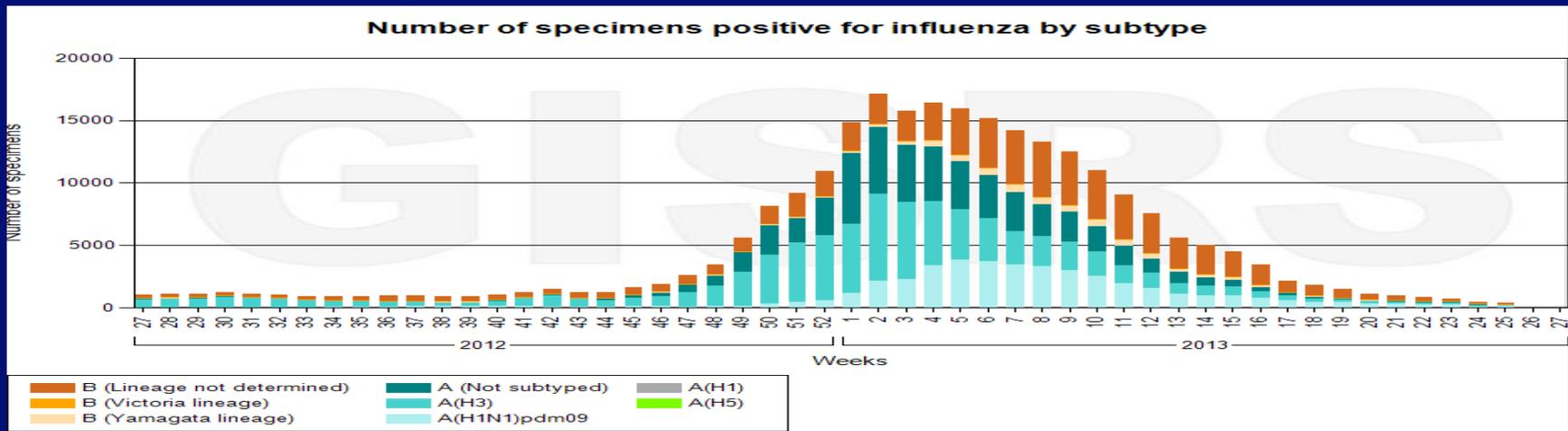


**World Health
Organization**

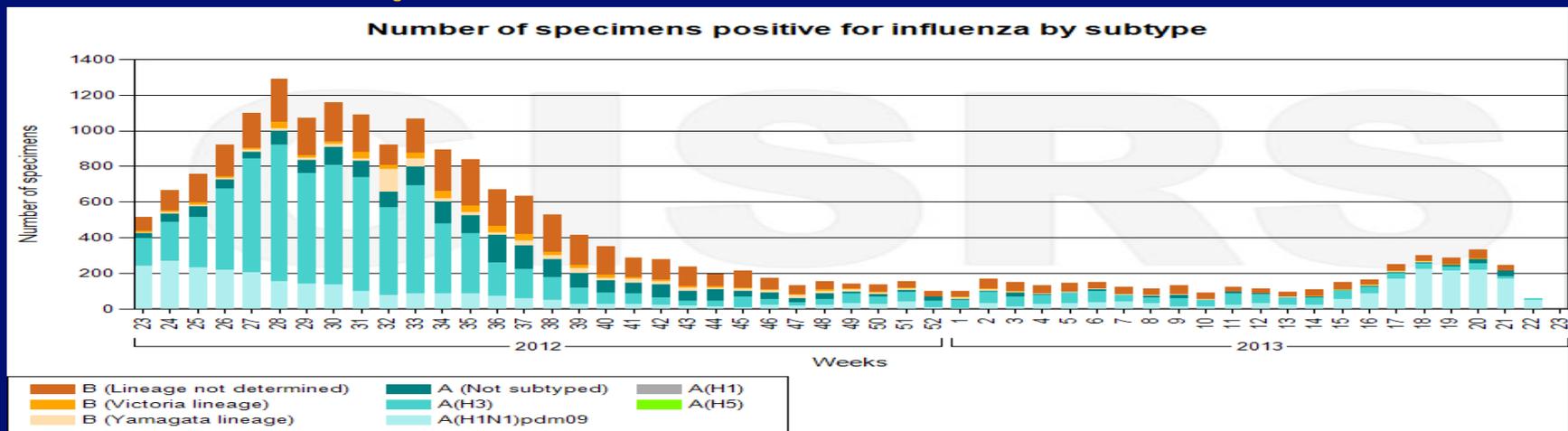
Influenza Laboratory Surveillance Information

(by GISRS)

Northern Hemisphere



Southern Hemisphere



U.S. Influenza Surveillance Systems

- **Outpatient Illness Surveillance**
- **Mortality Surveillance**
- **Hospitalization Surveillance**
- **Summary of the Geographic Spread of Influenza**
- **Virologic Surveillance**

FLUVIEW

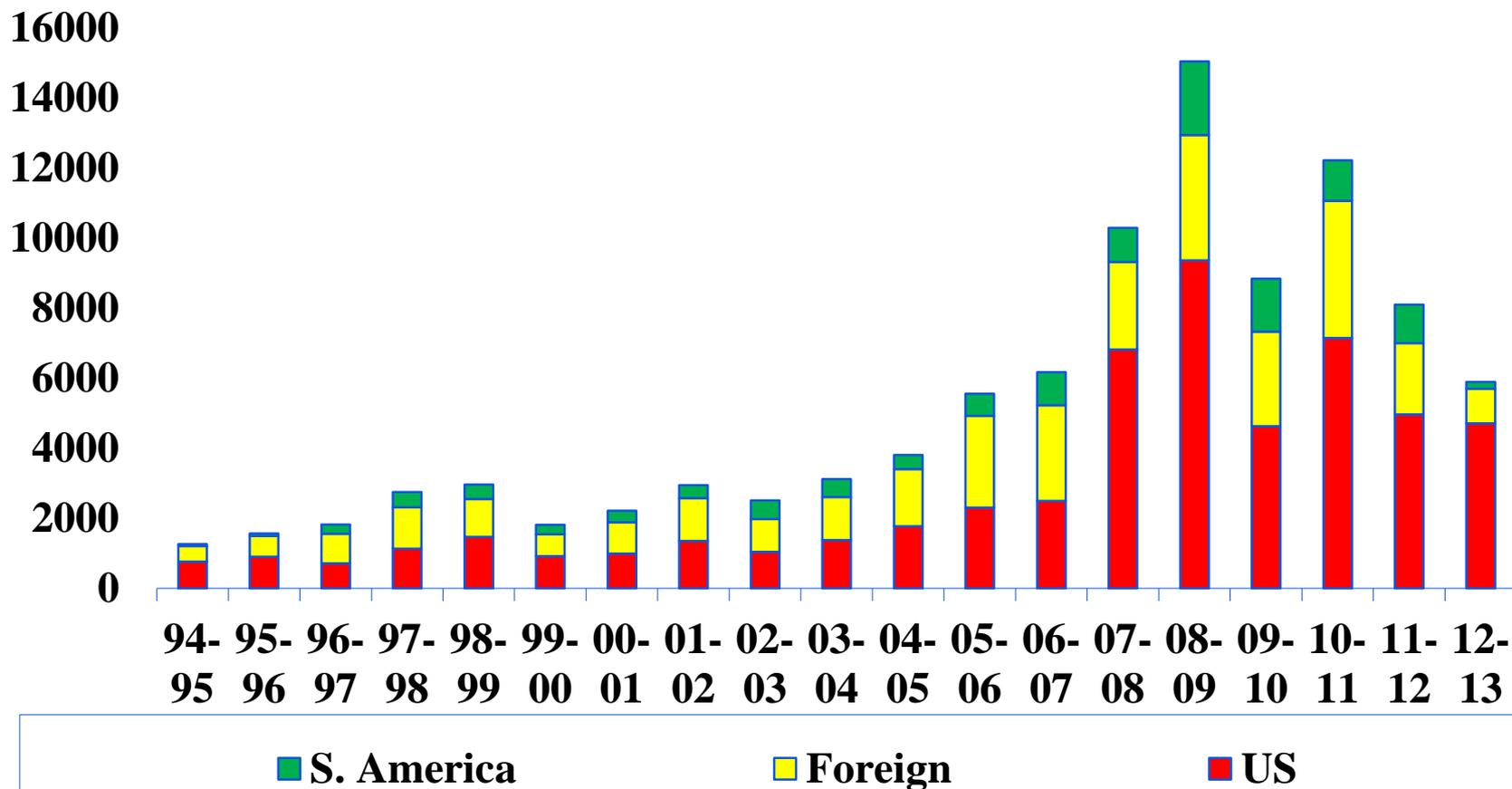
A Weekly Influenza Surveillance Report Prepared by the Influenza Division



U.S. Virologic Surveillance

- **Approximately 60 NREVSS and 85 WHO collaborating laboratories report:**
 - Weekly total of positive influenza tests by type/subtype
 - Percent positive for influenza
- **A subset of viruses collected are sent to CDC for further characterization**
- **Published weekly in FluView**

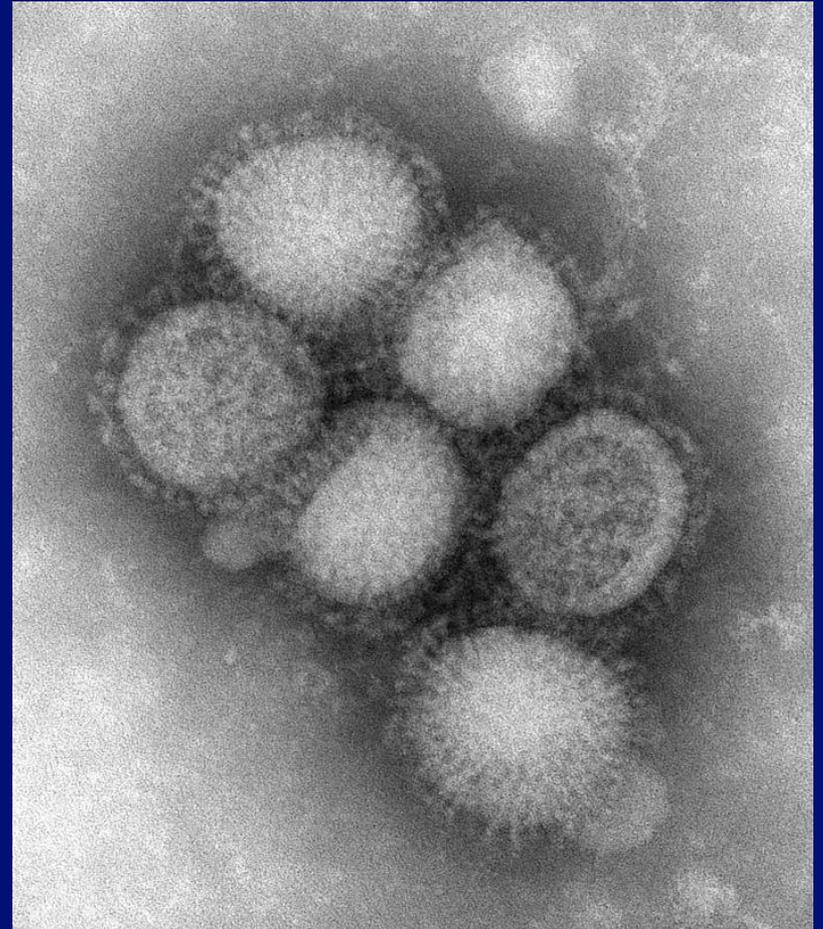
Number of specimens received by CDC



as of 06/25/2013

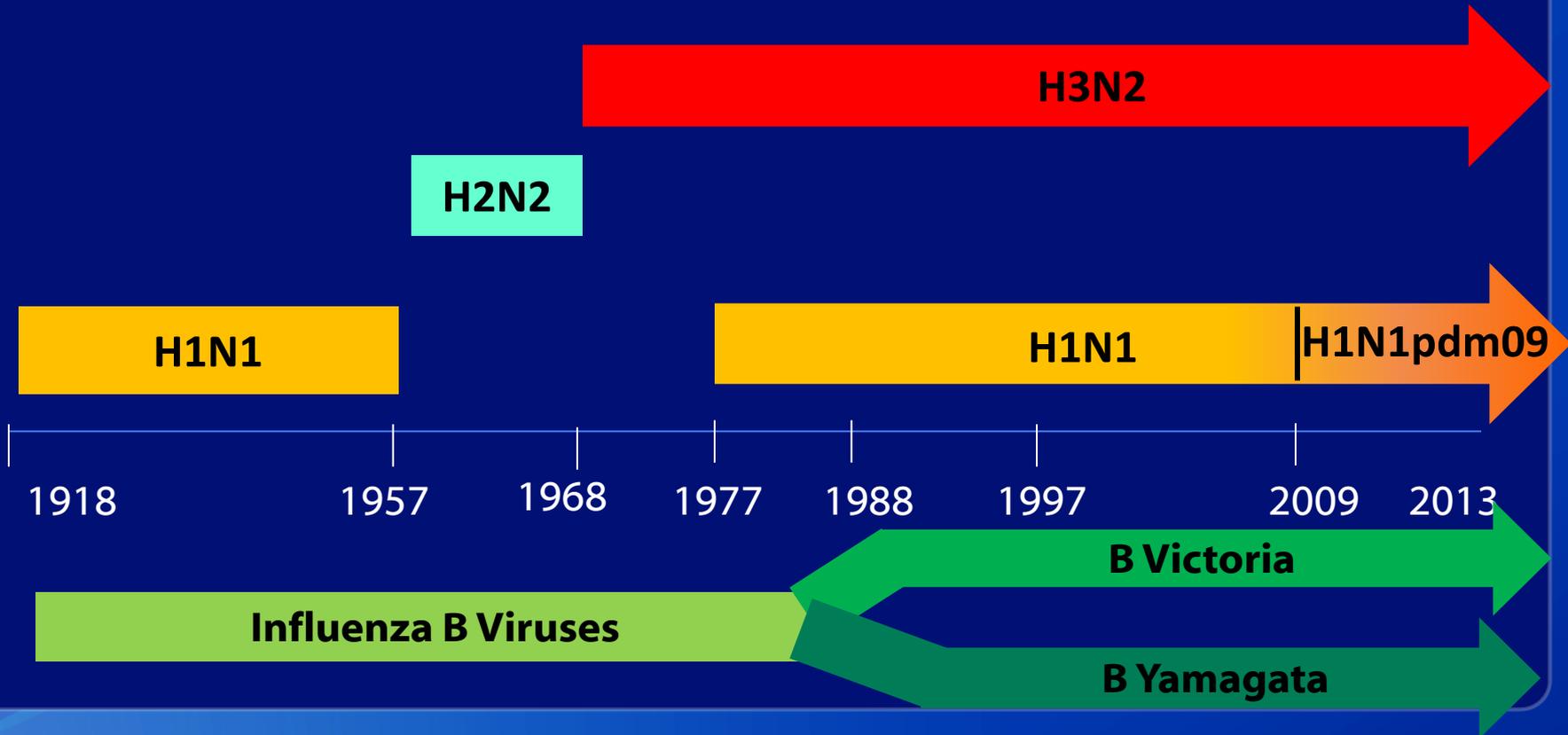
Influenza Virus

- Negative strand virus
- Three types (A, B, and C)
- Segmented genome
- Influenza A viruses have different subtypes of each:
 - Hemagglutinin (H 1-17)
 - Neuraminidase (N 1-10)
- All known subtypes of Influenza A can infect birds, with the exception of H17N10 which has only been found in bats



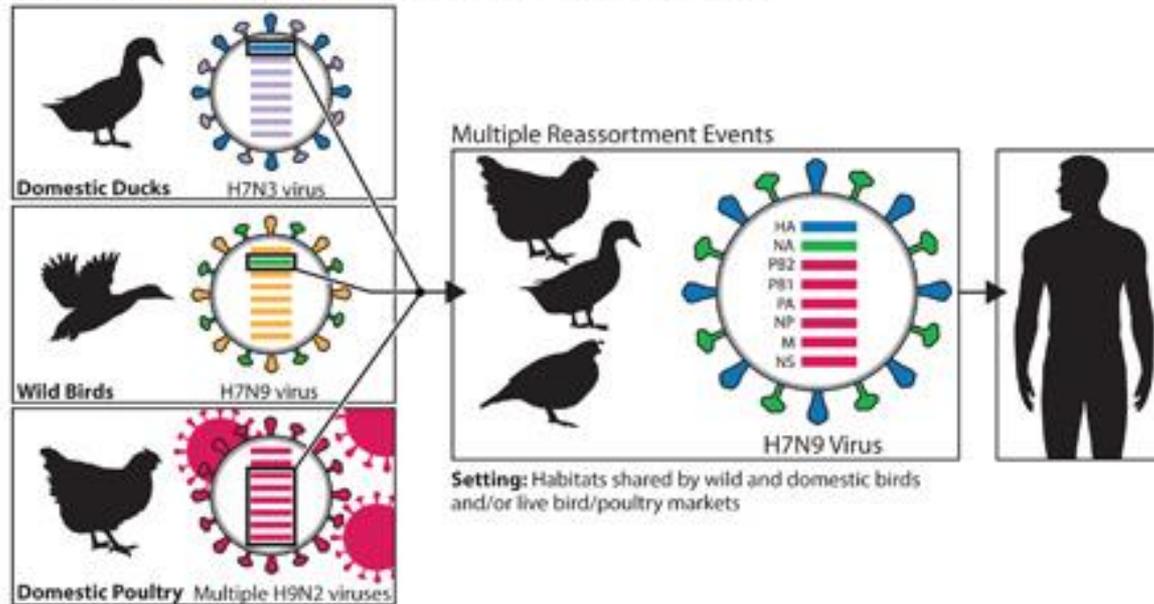
Circulation of Influenza Viruses in Humans

Influenza A
Viruses



Influenza viruses are capable of reassortment

Genetic Evolution of H7N9 Virus in China, 2013

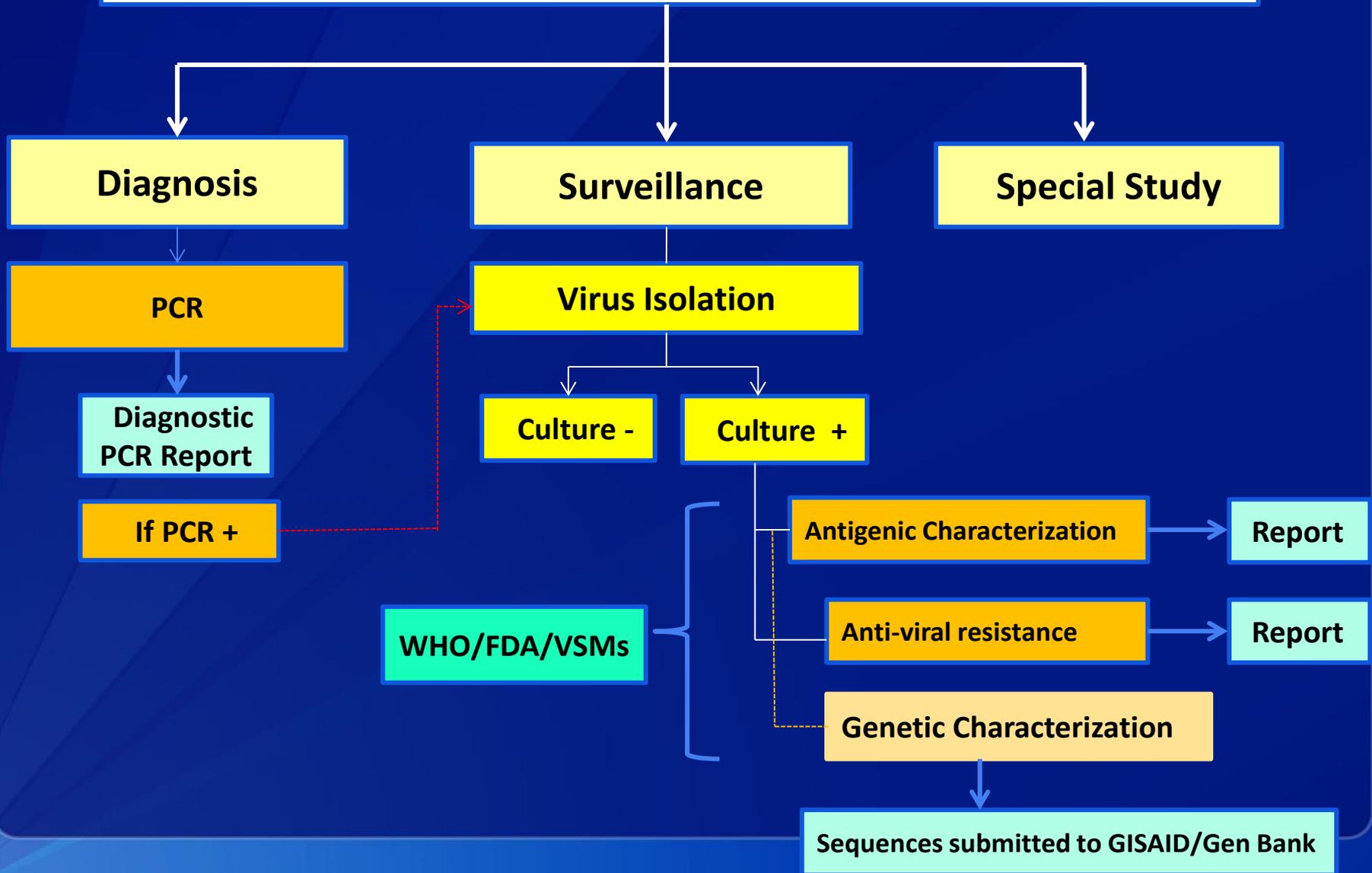


The eight genes of the H7N9 virus are closely related to avian influenza viruses found in domestic ducks, wild birds and domestic poultry in Asia. The virus likely emerged from "reassortment," a process in which two or more influenza viruses co-infect a single host and exchange genes. This can result in the creation of a new influenza virus. Experts think multiple reassortment events led to the creation of the H7N9 virus. These events may have occurred in habitats shared by wild and domestic birds and/or in live bird/poultry markets, where different species of birds are bought and sold for food. As the above diagram shows, the H7N9 virus likely obtained its HA (hemagglutinin) gene from domestic ducks, its NA (neuraminidase) gene from wild birds, and its six remaining genes from multiple related H9N2 influenza viruses in domestic poultry.



Centers for Disease
Control and Prevention
National Center for Immunization
and Respiratory Diseases

Specimen pathway: clinical respiratory specimens, and/or tissue culture/egg isolates

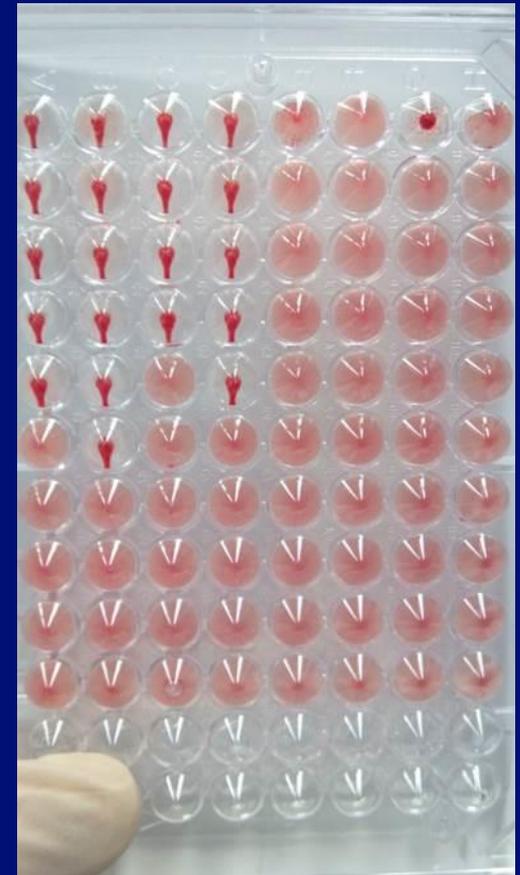


Virus propagation at CDC

- **Madin Darby Canine Kidney (MDCK) culture**
 - **High volume (T75 flask for ~20 ml available for harvest)**
 - **Permanent storage**
 - **Antigenic analysis**
 - **Antiviral analysis**
 - **Genetic analysis**
- **Embryonated egg culture**
 - **Currently licensed influenza vaccine requires egg isolate**
 - **Original clinical material used as inoculum**
 - **Egg isolates may be provided to vaccine manufacturers**
 - **Recovery rate of influenza viruses in egg culture ranges from ~10-50% depending on subtype**

Antigenic Analysis by Hemagglutination Inhibition (HI)

- **The HI assay is performed on influenza MDCK and egg virus isolates**
- **The hemagglutinin protein agglutinates red blood cells (RBCs) and is the basis for the HI assay**
- **The HI assay measures the inhibition of hemagglutination caused by influenza antisera at a standardized concentration of virus and RBCs**
- **The HI endpoint titer is the reciprocal of the dilution of antisera in the last well with complete inhibition of hemagglutination**



HI reactions of vaccine strain influenza A H3N2 viruses (1968-2009)

STRAIN DESIGNATION	Vaccine Strain (years)	FERRET ANTISERA AGAINST													
		HK/08	EN/42	TX/1	BA/01	PH/02	SH/11	BE/35 3	BE/32	JO/33	NA/933	SY/0 5	FU/41 1	BRI/10	PER/1 6
A/HONG KONG/08/1968	1968-1973	160	640	20	40	10	5	10	10	5	5	5	5	5	5
A/ENGLAND/42/1972	1973-1974	40	1280	40	40	10	5	20	10	5	5	5	5	5	5
A/TEXAS/01/1977	1978-1980	5	80	2560	320	640	10	20	40	5	5	5	5	5	5
A/BANGKOK/01/1979	1980-1983	5	10	640	640	640	10	40	40	5	5	5	5	5	5
A/PHILIPPINES/2/1982	1984-1986	5	10	20	40	320	10	10	10	5	5	5	5	5	5
A/SHANGHAI/11/1987	1989-1990	5	20	40	40	40	1280	160	80	10	5	5	5	5	5
A/BEIJING/353/1989	1991-1993	20	20	40	40	40	320	320	80	20	5	5	5	5	5
A/BEIJING/32/1992	1993-1994	5	10	40	40	20	10	40	640	80	10	5	5	5	5
A/JOHANNESBURG/33/1994	1995-1996	20	20	40	20	20	5	20	80	1280	40	5	5	5	5
A/NANCHANG/933/1995	1996-1998	5	10	20	20	20	5	10	80	80	1280	80	10	5	5
A/SYDNEY/05/1997	1998-2000	20	10	10	10	20	5	20	40	10	80	5120	320	5	5
A/FUJIAN/411/2002	2004-2005	5	5	5	5	5	5	5	5	5	5	80	1280	40	5
A/BRISBANE/10/2007	2008-2010	5	5	5	5	5	5	5	5	5	5	20	80	1280	5
A/PERTH/16/2009	2010-2011	5	5	5	5	5	5	5	5	5	5	5	5	10	320

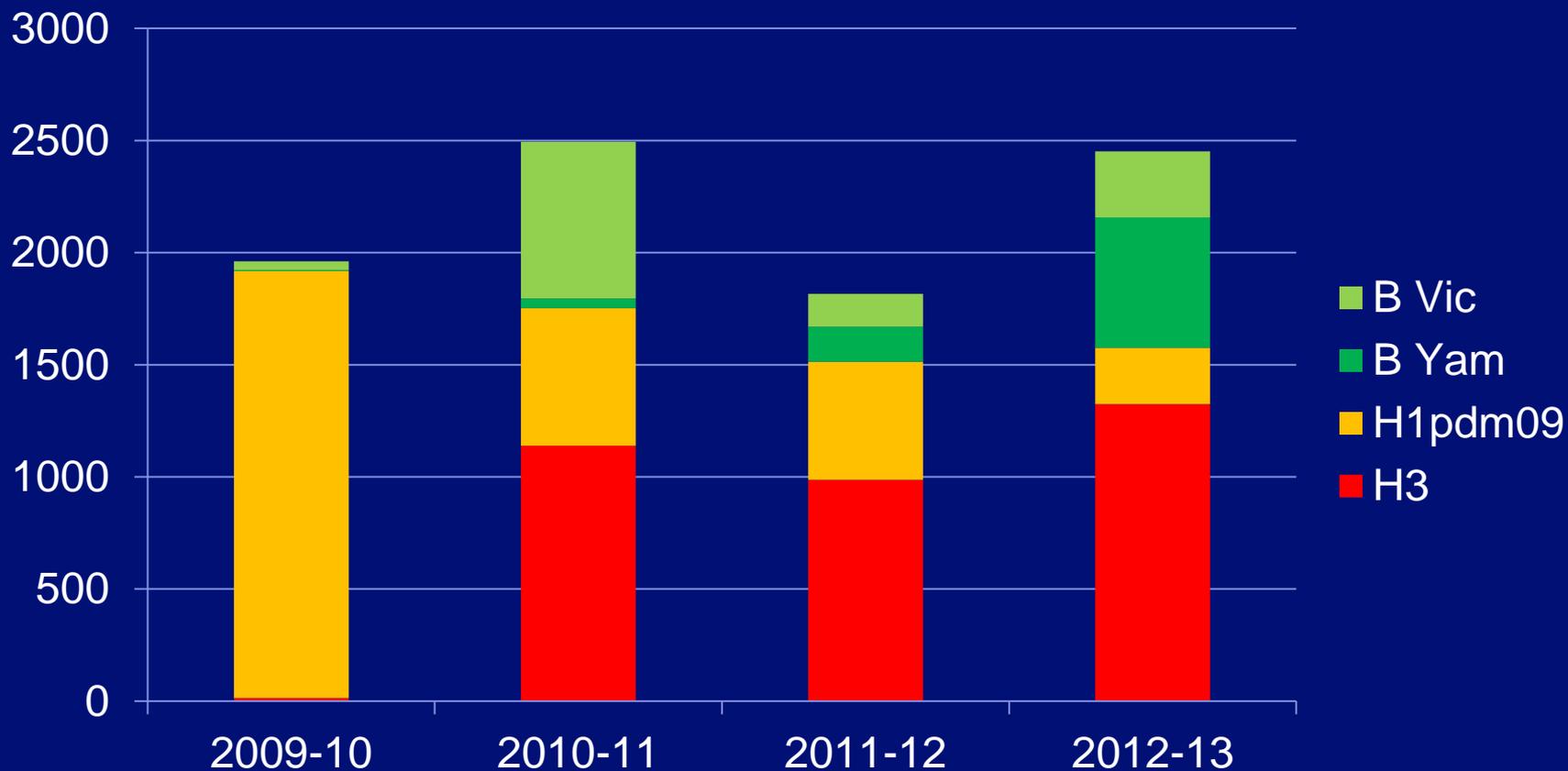
A virus is considered as low to the reference virus if there is an 8-fold or greater reduction in the HI titer when compared to the homologous HI titer (in red) of the reference strain.

Data Source: Serologic assays for influenza surveillance, diagnosis, and vaccine evaluation. Expert Rev. Anti Infect. Ther. 2011 June; 9(6): 669-683

U.S. Influenza Isolates Antigenically Characterized (Sept 2012-May 2013)

Type/Subtype	Total #
H3N2	
A/Victoria/361/2011	1281
A/Victoria/361/2011 (4 fold)	124
A/Victoria/361/2001 (8 fold) low	5
H1N1pdm09	
A/California/07/2009	260
A/California/07/2009 (4 fold)	17
A/California/07/2009 (8 fold) low	3
B/Yamagata lineage	
B/Wisconsin/01/2010	667
B/Wisconsin/01/2010 (4 fold)	1
B/Wisconsin/01/2010 (8 fold) low	0
B/Victoria lineage	
B/Brisbane/60/2008	141
B/Brisbane/60/2008 (4 fold)	197
B/Brisbane/60/2008 (8 fold) low	33

U.S. Viruses Antigenically Characterized by CDC



Genetic Analysis

- Subset (~10%) of cell culture isolates grown at CDC are sequenced. Isolates are chosen for sequencing primarily based on HI results, geographic location, and date of collection.
- Genes sequenced:

Influenza A

- HA
- NA
- M

Influenza B

- HA
- NA
- NS

Anti-Viral Analysis

Neuraminidase Inhibitor Resistance Testing Results on Samples Collected Since Oct. 1, 2012

	Oseltamivir		Zanamivir	
	Virus Samples tested (n)	Resistant Viruses, Number (%)	Virus Samples tested (n)	Resistant Viruses, Number (%)
Influenza A (H3N2)	2,123*	2 (0.1)	2,123*	1 (0.05)
Influenza B	961	0 (0.0)	961	0 (0.0)
2009 H1N1	542*	2 (0.4)	258	0 (0.0)

*Includes specimens tested in national surveillance and additional specimens tested at public health laboratories in 11 states (AZ, DE, HI, ME, MD, MI, MN, NY, PA, WA, and WI) who share testing results with CDC.

Seasonal Influenza Vaccine

- Continual evolution of influenza viruses may lead to antigenic drift of viruses. When this occurs an update in influenza vaccine viruses is necessary to maintain effectiveness

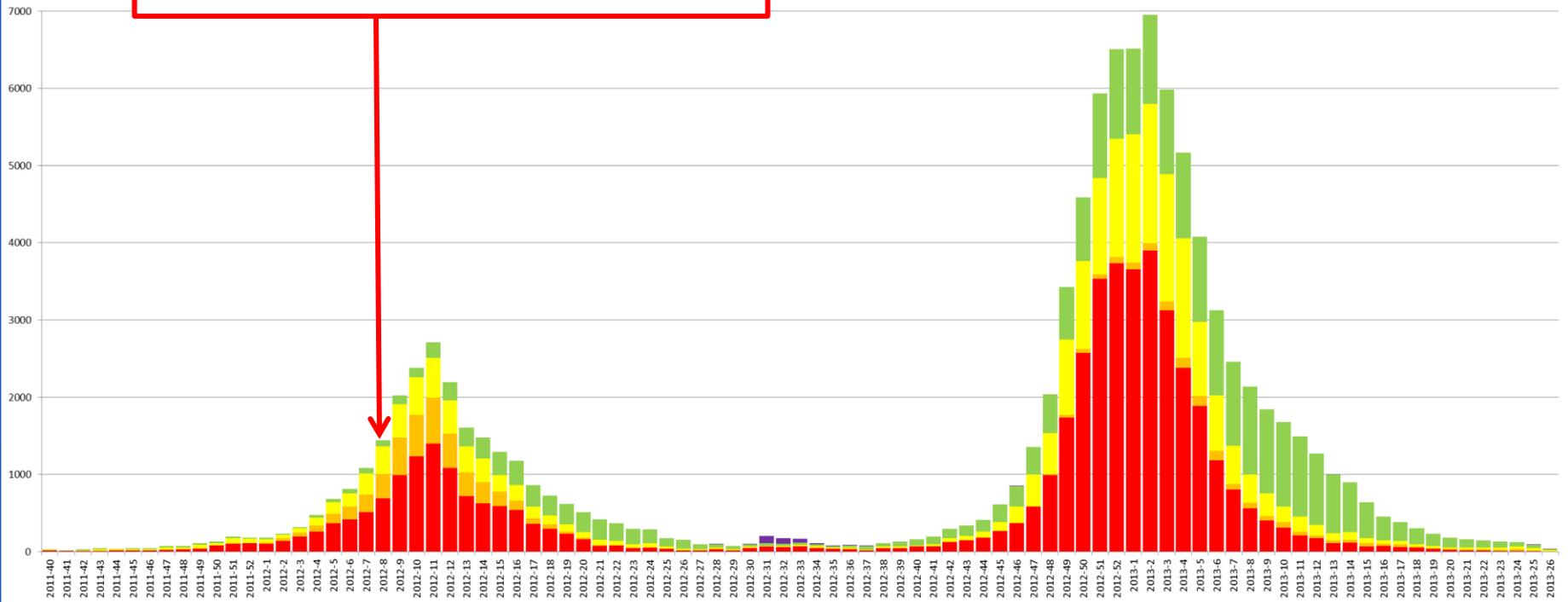
Season	H3N2	H1N1	B	B lineage
2012-13	A/Victoria/361/2011	A/California/07/2009 H1N1pdm09	B/Wisconsin/01/2010	Yamagata
2011-12	A/Perth/06/2009	A/California/07/2009 H1N1pdm09	B/Brisbane/60/2008	Victoria
2010-11	A/Perth/06/2009	A/California/07/2009 H1N1pdm09	B/Brisbane/60/2008	Victoria
2009-10	A/Brisbane/10/2007	A/Brisbane/59/2007 H1N1	B/Brisbane/60/2008	Victoria

WHO Consultation and Information Meeting on the Composition of Influenza Virus Vaccines

- **Biannual meeting held in:**
 - **February for northern hemisphere season**
 - **September for southern hemisphere season**
- **Participants include representatives from:**
 - **WHO CC's for influenza and WHO H5 Reference Laboratories**
 - **WHO Essential Regulatory Laboratories**
 - **National Influenza Centers**
 - **Experts on antigenic cartography; and representatives from the OIE/FAO Network of expertise on animal influenza (OFFLU)**
- **Recommendations are based on global influenza virus surveillance data related to epidemiology and antigenic characteristics, serology responses to seasonal vaccines, and availability of candidate strains and reagents.**

Vaccine strain selection meeting for Northern Hemisphere is held in February

February 23, 2012: vaccine recommendations announced for 2012-13 season



2011-2012 U.S. Influenza Season

2012-2013 U.S. Influenza Season

2013-2014 Northern Hemisphere Vaccine Recommendations

- **Trivalent**
 - **A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011***
 - **A/Texas/50/2012 H3N2**
 - **A/California/07/2009 H1N1pdm09**
 - **B/Massachusetts/02/2012* (Yamagata lineage)**
- **Quadrivalent will be comprised of the three components above and:**
 - **B/Brisbane/60/2008 (Victoria lineage)**

** Updated component from 2012-2013 vaccine*

A/Texas/50/2012 H3N2

- NP wash collected from patient in Fort Worth, April 2012
- Sent to TX DSHS lab in Austin, cell culture isolate grown from NP wash
- Both isolate and NP wash were sent to CA contract lab
- CA contract lab grew high volume MDCK isolate. Both isolate and remaining original specimens were sent from to CDC and antigenically and genetically characterized

- Original clinical specimen (NP wash) inoculated into eggs
- Resulting egg isolate sent to vaccine manufacturers for analysis as a potential vaccine seed

- *Recommended as new vaccine component at the February 2013 WHO Vaccine Strain Selection Meeting*

Thank You!

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

National Center for Immunization & Respiratory Diseases
Influenza Division

