The Case for Public Health

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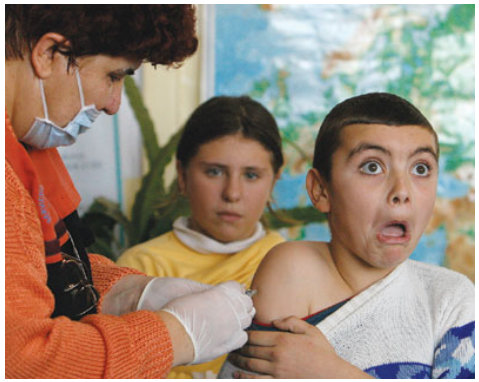

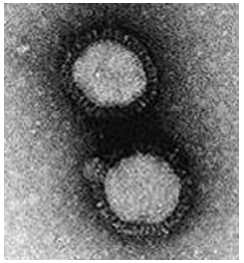

Finding cures. Saving children.

Background

- Member (professor) of infectious diseases
- “Virologist” specializing in pathogenesis
- Influenza and enteric viruses
- Co-PI of SJCEIRS

Figure 1. Location of proposed SJCEIRS surveillance activities

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Background

- Member (professor) of infectious diseases
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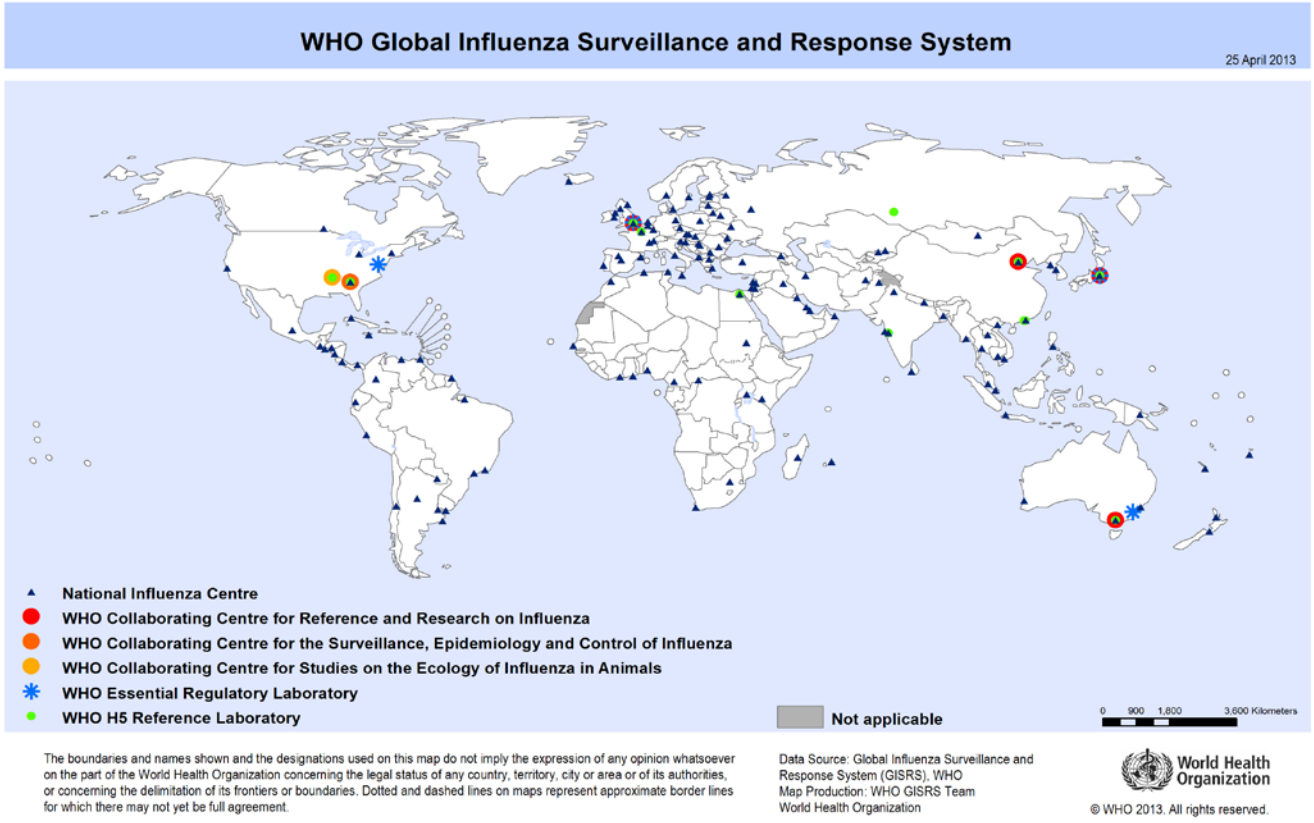
Deputy Director SJ WHO Collaborating Center for studies on the ecology of influenza in animals and birds

World Health Organization



2014, 89, 457–464 No. 42

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

17 OCTOBER 2014, 89th YEAR / 17 OCTOBRE 2014, 89e ANNÉE
No. 42, 2014, 89, 457–464
http://www.who.int/wer

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Antigenic and genetic characteristics of zoonotic influenza viruses and development of candidate vaccine viruses for pandemic preparedness

September 2014

The development of representative candidate influenza vaccine viruses (CVV), coordinated by WHO, remains an essential component of the overall global strategy for pandemic preparedness.

Zoonotic influenza viruses continue to be identified and often evolve both genetically and antigenically, leading to the need for update of CVVs for pandemic preparedness purposes. Evaluation of the genetic and antigenic characteristics of these viruses, their relationship to existing CVVs, and their potential risks to public health, justify the need to select and develop new CVVs.

Selection and development of a CVV represents a first step only towards timely vaccine production and does not imply a recommendation for initiating manufacture. National authorities may consider the use of one or more of these CVVs for pilot lot vaccine production, clinical trials and other pandemic preparedness purposes based on their assessment of public health risk and need.

This document summarizes the genetic and antigenic characteristics of recent zoonotic influenza viruses and related viruses circulating in animals and updates the availability of CVVs. Institutions that wish to receive these CVVs should contact WHO at gisrs-wholsp@who.int or the institutions listed in announcements published on the WHO website.[1]

[1] See http://www.who.int/influenza/vaccines/viruses

Caractéristiques génétiques et antigéniques des virus grippaux zoonotiques et mise au point de virus vaccinaux candidats pour se préparer à une pandémie

Septembre 2014

La mise au point de virus grippaux vaccinaux candidats représentatifs, coordonnée par l'OMS, reste une composante essentielle de la stratégie mondiale globale de préparation à une pandémie.

Des virus grippaux zoonotiques continuent d'être identifiés et ces virus évoluent souvent à la fois sur le plan génétique et antigénique, ce qui impose une actualisation des virus vaccinaux candidats destinés à la préparation à une pandémie. L'évaluation des caractéristiques génétiques et antigéniques de ces virus, de leur parenté avec les virus vaccinaux candidats existants et de leurs risques potentiels pour la santé publique justifie que l'on sélectionne et que l'on mette au point de nouveaux virus vaccinaux candidats.

La sélection et la préparation d'un virus vaccinal candidat représentent une première étape vers la production en temps utile de vaccins et ne supposent pas qu'il ait été recommandé de mettre en route la fabrication. Les autorités nationales peuvent envisager d'utiliser un ou plusieurs de ces virus vaccinaux candidats pour la production de lots pilotes de vaccins, la réalisation d'essais cliniques et d'autres opérations de préparation à une pandémie, en fonction de leur évaluation des risques et des besoins pour la santé publique.

Le présent document récapitule les caractéristiques génétiques et antigéniques des virus grippaux zoonotiques circulant chez des animaux et fait le point sur les virus vaccinaux candidats disponibles. Les institutions souhaitant recevoir des virus vaccinaux candidats devront prendre contact avec l'OMS à l'adresse gisrs-wholsp@who.int ou avec les institutions dont les noms figurent dans les communiqués publiés sur le site Web de l'OMS.[1]

[1] Se référer à l'adresse http://www.who.int/influenza/vaccines/viruses/

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Responsible for CVV Decisions

Decide on the Strains

- WHO VCM Feb & Sept
- Prepare seed virus
- Vaccine manufacturers
- Regulatory agencies
- 6-9 months later have vaccine

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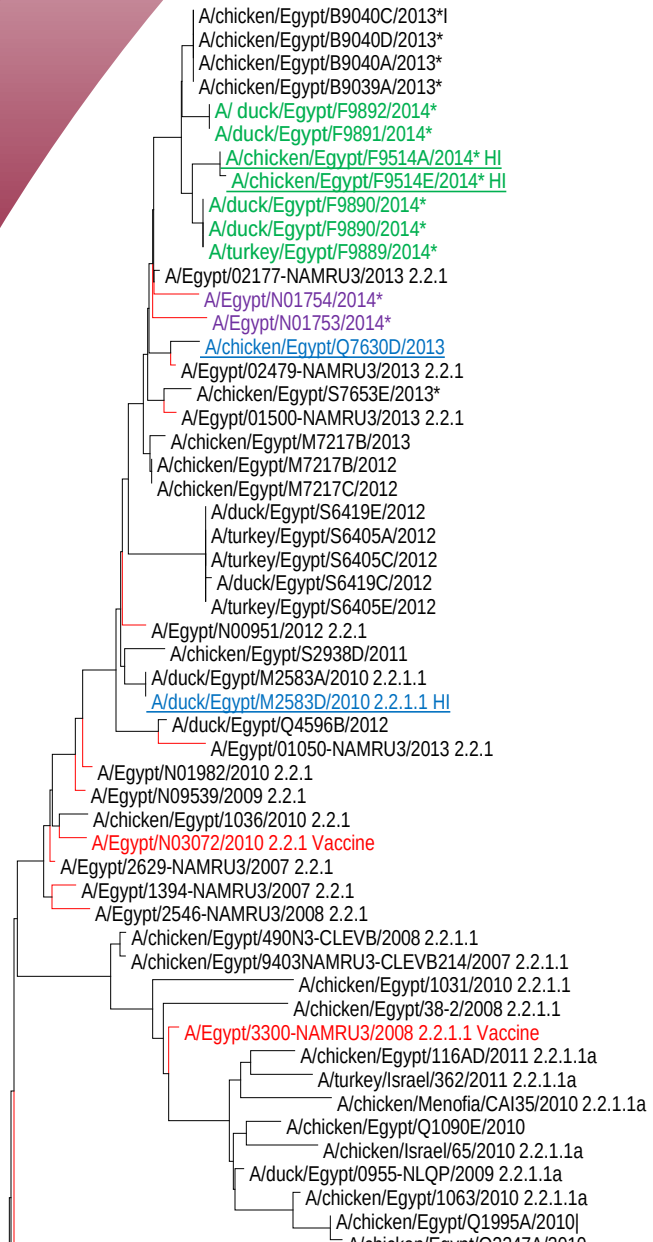
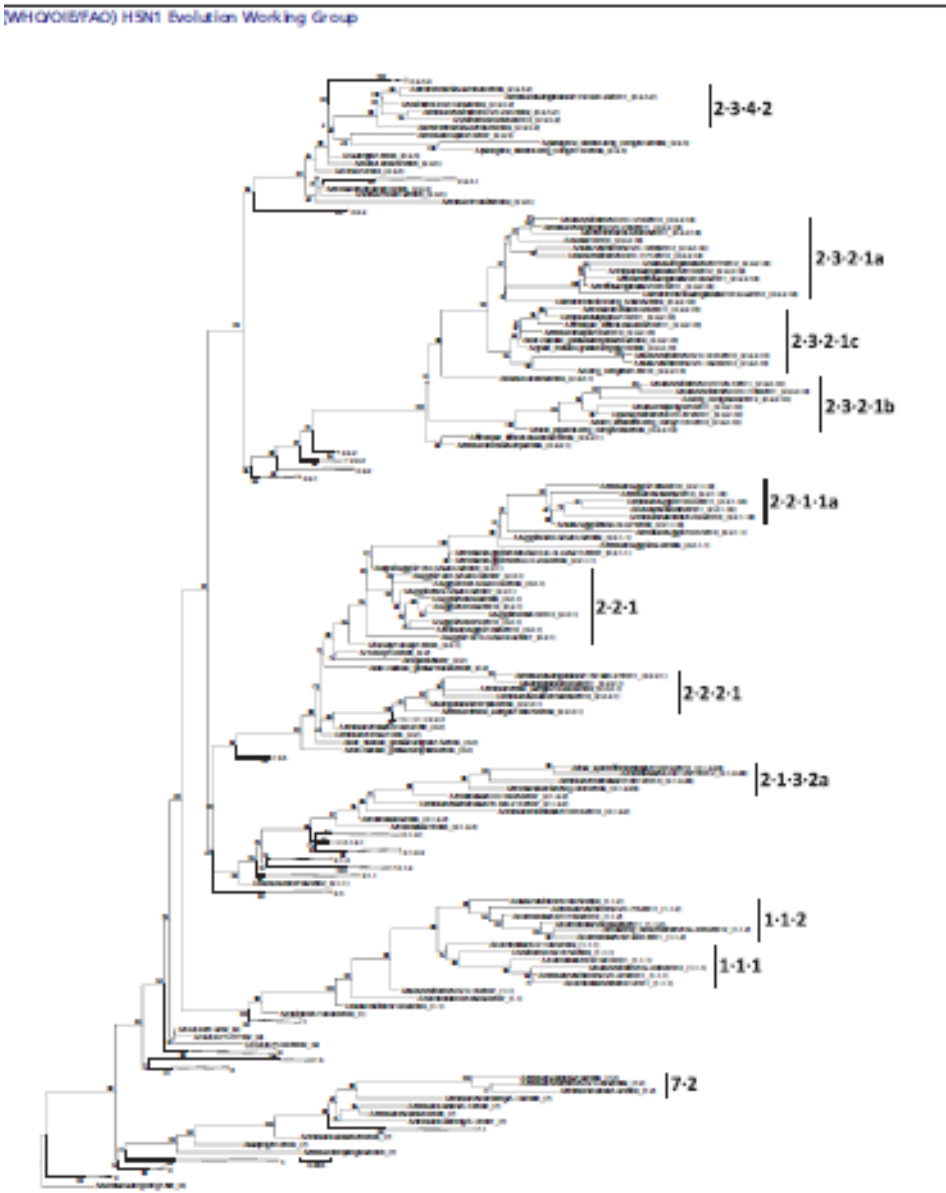
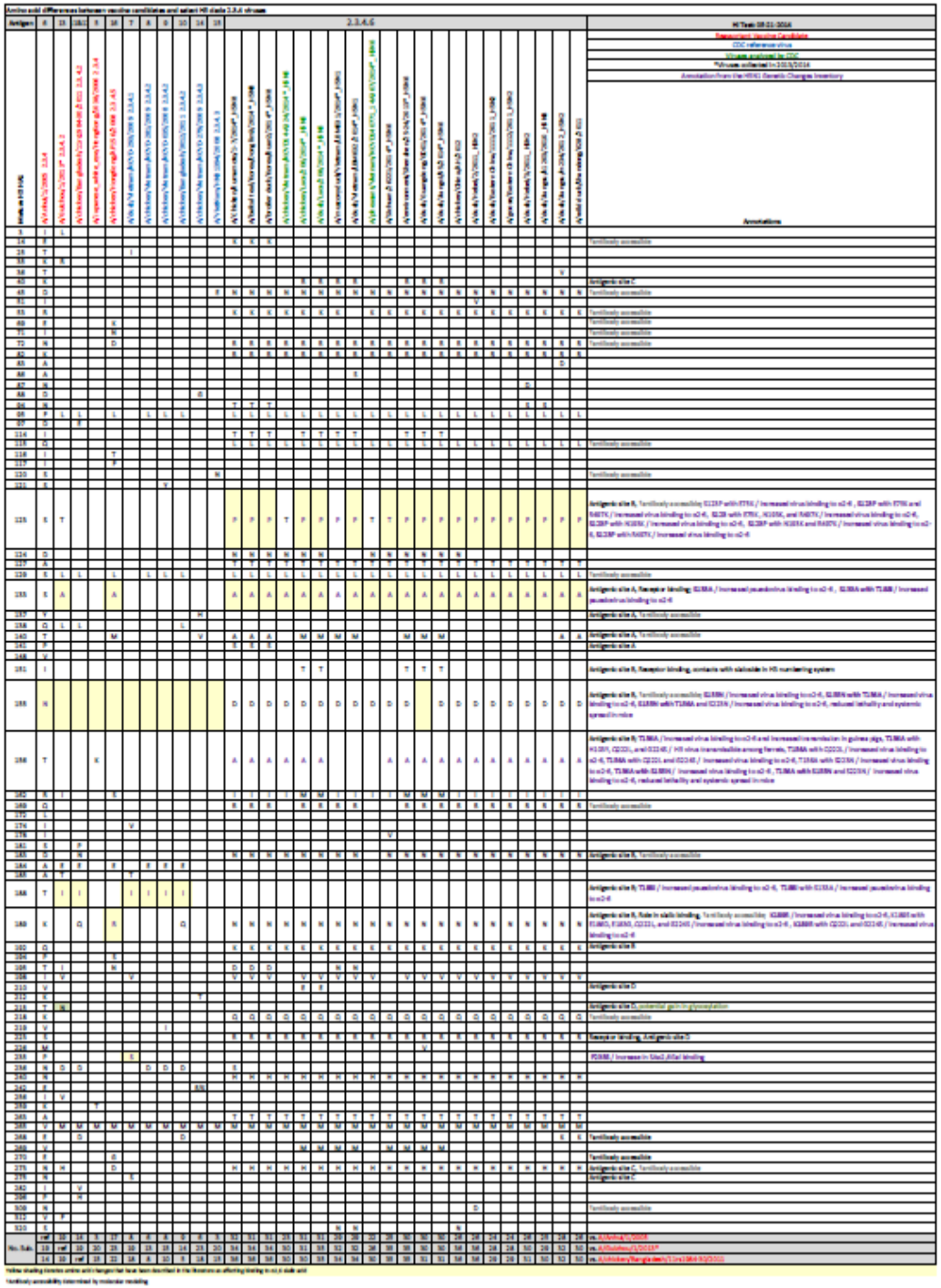
H5Nx, H7Nx, H9, H6, H10, vH3N2…







Antigenic site B, †antibody accessible; S123P with E75K / Increased virus binding to α2-6 , S123P with E75K and R497K / Increased virus binding to α2-6, S123 with E75K , N193K, and R497K / Increased virus binding to α2-6, S123P with N193K / Increased virus binding to α2-6, S123P with N193K and R497K / Increased virus binding to α2-6, S123P with R497K / Increased virus binding to α2-6

†antibody accessible

Antigenic site A, Receptor binding; S133A / Increased psuedovirus binding to α2-6 , S133A with T188I / Increased psuedovirus binding to α2-6

Antigenic site A, †antibody accessible

Antigenic site A, †antibody accessible

Antigenic site A

Antigenic site B, Receptor binding, contacts with sialoside in H3 numbering system

Antigenic site B, †antibody accessible; S155N / Increased virus binding to α2-6, S155N with T156A / Increased virus binding to α2-6, S155N with T156A and S223N / Increased virus binding to α2-6, reduced lethality and systemic spread in mice

Antigenic site B; T156A / Increased virus binding to α2-6 and increased transmission in guinea pigs, T156A with H103Y, Q222L, and G224S , H5 virus transmissible among ferrets, T156A with Q222L / Increased virus binding to α2-6, T156A with Q222L and G224S / Increased virus binding to α2-6, T156A with S223N / Increased virus binding to α2-6, T156A with S155N / Increased virus binding to α2-6 , T156A with S155N and S223N / Increased virus binding to α2-6, reduced lethality and systemic spread in mice

GOF studies crucial for selecting the CVV considered highest risk

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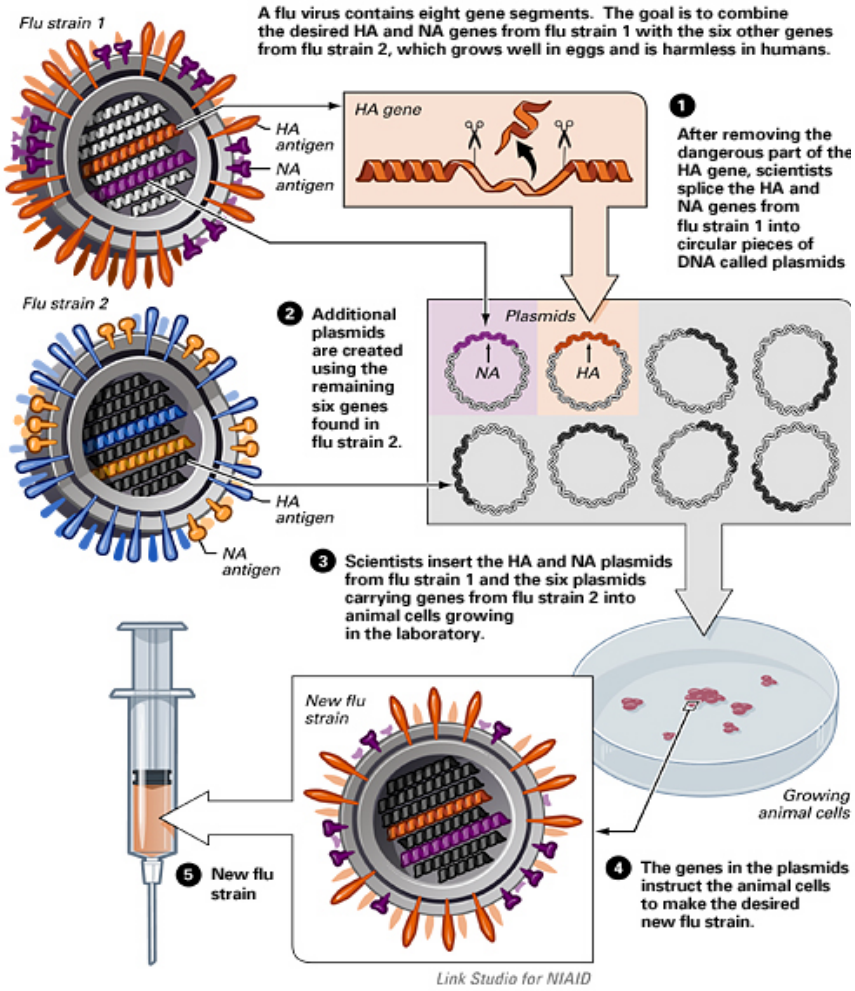
A(H5N1) candidate vaccine viruses

$50,000

Candidate vaccine viruses	Clade	Institution*	Available
A/Viet Nam/1203/2004 (CDC-RG; SJRG-161052)	1	CDC and SJCRH	Yes
A/Viet Nam/1194/2004 (NIBRG-14)	1	NIBSC	Yes
A/Cambodia/R0405050/2007 (NIBRG-88)	1.1	NIBSC	Yes
A/duck/Hunan/795/2002 (SJRG-166614)	2.1	SJCRH	Yes
A/Indonesia/5/2005 (CDC-RG2)	2.1.3.2	CDC	Yes
A/bar-headed goose/Qinghai/1A/2005 (SJRG-163222)	2.2	SJCRH	Yes
A/chicken/India/NIV33487/2006 (IBCDC-RG7)	2.2	CDC/NIV	Yes
A/whooper swan/Mongolia/244/2005 (SJRG-163243)	2.2	SJCRH	Yes
A/Egypt/2321-NAMRU3/2007 (IDCDC-RG11)	2.2.1	CDC	Yes
A/turkey/Turkey/1/2005 (NIBRG-23)	2.2.1	NIBSC	Yes
A/Egypt/N03072/2010 (IDCDC-RG29)	2.2.1	CDC	Yes
A/Egypt/3300-NAMRU3/2008 (IDCDC-RG13)	2.2.1.1	CDC	Yes
A/common magpie/Hong Kong/5052/2007 (SJRG-166615)	2.3.2.1	SJCRH	Yes
A/Hubei/1/2010 (IDCDC-RG30)	2.3.2.1	CDC	Yes
A/barn swallow/Hong Kong/D10-1161/2010 (SJ-003)	2.3.2.1	SJCRH	Yes
A/chicken/Hong Kong/AP156/2008 (SJ-002)	2.3.4	SJCRH	Yes
A/Anhui/1/2005 (IBCDC-RG6)	2.3.4	CDC	Yes
A/duck/Laos/3295/2006 (CBER-RG1)	2.3.4	FDA	Yes
A/Japanese white eye/Hong Kong/1038/2006 (SJRG-164281)	2.3.4	SJCRH	Yes
A/goose/Guiyang/337/2006 (SJRG-165396)	4	SJCRH	Yes
A/chicken/Viet Nam/NCVD-016/2008 (IDCDC-RG12)	7.1	CDC	Yes
A/chicken/Viet Nam/NCDV-03/2008 (IDCDC-RG25A)	7.1	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Institution**	**Availability**
A/chicken/Bangladesh/11RS1984-30/2011-like	2.3.4.2	CDC	Pending
A/Indonesia/NIHRD11771/2011-like	2.1.3.2	NIID	Pending
A/Guizhou/1/2013-like	2.3.4.2	CDC/CCDC	Pending

Beyond CVV Selection… GOF studies crucial for producing HPAI vaccines



HA0 cleavage

HPAI	A/seal/Mass/1/1980	PENPKKEHPSAGKDPKKTGGPIYRRTRG
	A/turkey/Oregon/1971	PENPKTSLSPLYPGRTTDLQVPTA--RG
	A/chicken/Chile/2002	PENPKTCSPLSRCRET----------RG
	A/chicken/Jalisco/CPA1/2012	PENPKDRKSRHRRT----------RG
	A/Mexico/InDRE7218/2012	PENPKDRKSRHRRT----------RG
	A/chicken/BC/2004	PENPKQAYQKRMT----------RG
	A/Canada/rv504/2004	PENPKQAYQKRMT----------RG
	A/Canada/rv444/2004	PENPKQAYQKQMT----------RG
	A/chicken/SK/HR-00011/2007	PENPKTTKPRPR----------RG
	A/chicken/Germany/01/1979	PEIPKKKKKK----------RG
	A/chicken/Italy/5074/1999	PEIPKGSRVR----------RG
	A/chicken/Victoria/1976	PEIPKKREK----------RG
	A/starling/Victoria/1985	PEIPKKREK----------RG
	A/fowl/Dobson/1927	PELPKKRRK----------RG
	A/chicken/Germany/R28/2003	PEIPKRRR----------RG
	A/chicken/Belgium/06600/2003	PEIPKRRR----------RG
	A/Netherlands/127/2003	PEIPKRRR----------RG
	A/chicken/Netherlands/2586/2003	PEIPKRRR----------RG
	A/goose/Leipzig/137/8/1979	PEIPKRKK----------RG
	A/chicken/Victoria/1/1992	PEIPKKKK----------RG
	A/chicken/Queensland/667/1995	PEIPKRKK----------RG
	A/turkey/England/1963	PETPKRRR----------RG
	A/chicken/Murree/NARC-01/1995	PETPKRRK----------RG
LPAI	A/New York/107/2003	PEKPKP----------RG
	A/turkey/Virginia/4529/2002	PEKPKP----------RG
	A/env/New York/19495-1/2006	PEKPKP----------RG
	A/chicken/NY/3572/1998	PENPKP----------RG
	A/chicken/Chile/184240-2/2002	PEKPKT----------RG

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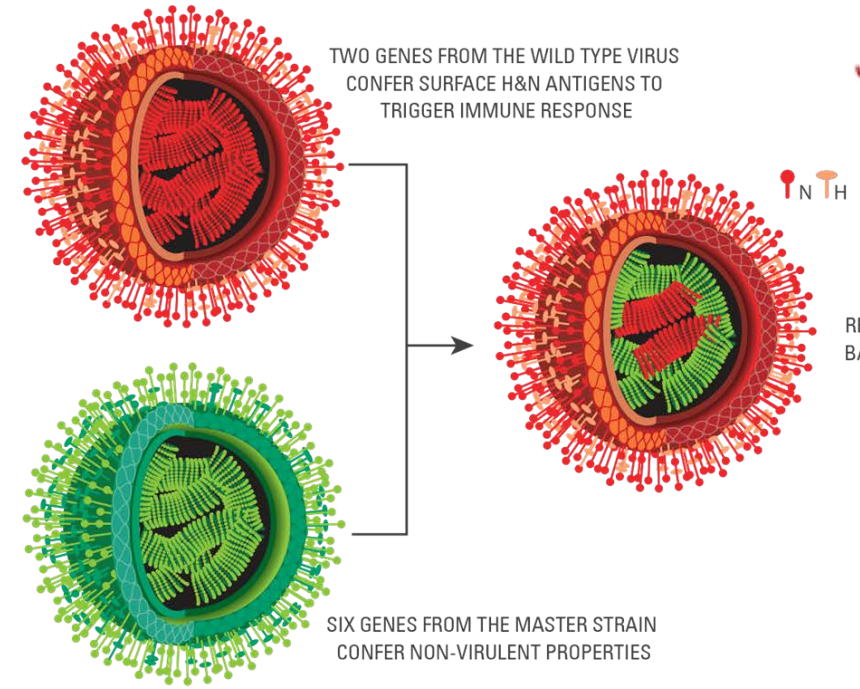
Beyond CVV Selection… GOF studies crucial for producing high yield vaccine seed viruses

Journal of Virology

Enhanced Growth of Influenza Vaccine Seed Viruses in Vero Cells Mediated by Broadening the Optimal pH Range for Virus Membrane Fusion

Shin Murakami, Taisuke Horimoto, Mutsumi Ito, Ryo Takano, Hiroaki Katsura, Masayuki Shimojima and Yoshihiro Kawaoka
J. Virol. 2012, 88(3):1405. DOI: 10.1128/JVI.06008-11.
Published A



Journal of Virology

Generation of Live Attenuated Novel Influenza Virus A/California/7/09 (H1N1) Vaccines with High Yield in Embryonated Chicken Eggs

Zhongying Chen, Weijia Wang, Helen Zhou, Amorsolo L. Suguitan Jr., Cindy Shambaugh, Lomi Kim, Jaokie Zhao, George Kemble and Hong Jin
J. Virol. 2010, 84(1):44. DOI: 10.1128/JVI.02108-09.
Published Ahead of Print 28 October 2009.

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