

# Influenza Updates

*The newsletter of the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne*

Volume 6, Issue 3, November 2017

## Reflection on 2017: thank you and happy holidays

As the year draws to a close we would like to thank all of the laboratories who have sent us influenza samples during 2017. It has been an extremely busy year and we have received and processed more than 5,500 samples this year - this is the largest annual number of samples we have received since the pandemic in 2009.

In 2017 we marked our 25th anniversary as a WHO Collaborating Centre. We thank everyone who has supported and worked with us over the years.

In addition to a busy surveillance season we have been very active in other areas during 2017, with highlights including:

- a week-long Workshop on Virus Isolation and Characterisation for National Influenza Centre Staff in the Western Pacific Region, involving 17 scientists from the Asia-Pacific region;
- hosting the WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2018 at the Doherty Institute;
- the inclusion of a virus which was submitted by the National Public Health Laboratory (Singapore) and isolated as a candidate vaccine virus at the Centre in the WHO recommended vaccine strains for the Southern Hemisphere in 2018;
- the 12th Australian Influenza Symposium, which was attended by approximately 200 delegates; and
- the development and co-ordination of an External Quality Assurance Project (EQAP) to test proficiency of virus isolation techniques in National Influenza Centres (NICs) in the WHO Regions of the Eastern Mediterranean (EMRO), Africa (AFRO) and the Americas (AMRO).

We wish you all the best for the holiday season and look forward to working with you again in 2018.



*Pictured: Participants and instructors at the Workshop on Virus Isolation and Characterisation for NIC staff in the Western Pacific Region, May 2017*



## Social media: should we connect?

We would like to canvass your interest in being updated about the Centre's news and activities through social media channels. Please complete this online survey below - it should only take about 30 seconds of your time.

<https://whoflu.wufoo.eu/forms/social-media-survey/>

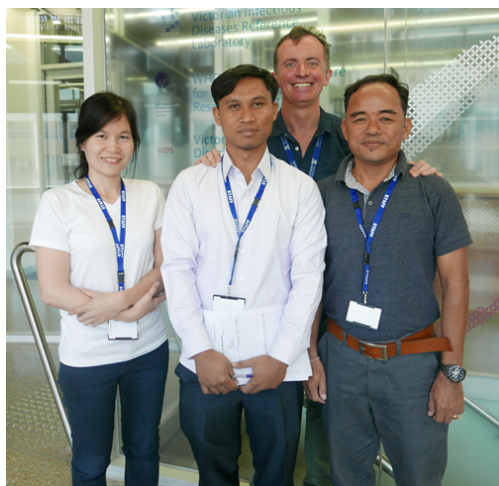


*Note: if you have already completed this survey via other forums such as the Australian Influenza Symposium, then please do not complete it again.*

## Training activities at the Centre

We welcome Ms Phalla Y and Mr Songha Tok from Institut Pasteur du Cambodge (Phnom Penh, Cambodia), as well as Mr Siyeatra Sok, from the National Public Health Laboratory (Phnom Penh, Cambodia), who are visiting the Centre from 20 November to 1 December.

Phalla, Songha and Siyeatra are undertaking training in surveillance techniques, including serological analysis, genetic analysis and antiviral resistance testing.



*Left to right: Phalla Y, Songha Tok and Siyeatra Sok, pictured with Centre Educator Patrick Reading (at rear)*

## Visiting scientists at the Centre

We were pleased to host Dr Barnaby Young, Ms Jung Pu Hsu and Ms Rachel Lim and Ms Yazid Nurhidayah, from Tan Tock Seng Hospital (Singapore), who recently spent a week at the Centre to perform large scale serological analyses on serum samples for a study they are currently conducting at their hospital.



*Left to right: Jung Pu Hsu, Yazid Nurhidayah, Rachel Lim and Barnaby Young*

## External Quality Assurance Project (EQAP) for Viral Isolation 2017

In 2016 the Centre developed and coordinated an external quality assurance project (EQAP) to test the proficiency of virus isolation techniques in National Influenza Centres (NICs) in the WHO Western Pacific Region (WPR) and South-East Asia Region (SEAR). Results of this EQAP have recently been published: <https://www.ncbi.nlm.nih.gov/pubmed/29127947>

Following the success of the EQAP in 2016, we are now conducting a similar EQAP for NICs in the WHO Regions of Africa (AFRO), the Americas (AMRO) and the Eastern Mediterranean (EMRO).

A total of 27 NICs — 12 in AFRO, 5 in AMRO and 10 in EMRO — are participating in the current EQAP. Laboratories will receive the panel during November and December 2017 and should return their results in the months following. We will inform all participating NICs of the provisional results as soon as all results have been received. Detailed analysis of results and completed questionnaires will be conducted in 2018.

We thank all of the laboratories who are participating in the EQAP. The information provided through your results and feedback will help us to assess the capacity of NICs around the world and further enable the organisation of appropriate training opportunities to support the global influenza surveillance network.







## Australian Influenza Symposium

The Centre hosted the 12th Australian Influenza Symposium at the Peter Doherty Institute for Infection and Immunity in Melbourne on 1 – 2 November 2017. The Symposium was attended by approximately 200 participants from Australia and other countries including the United States, China, Taiwan and the United Kingdom. Delegates enjoyed a range of presentations across a broad spectrum of topics, including:

- Evolution and spread of zoonotic influenza viruses
- Influenza vaccinations for maternal, paediatric and elderly populations
- Attitudes towards influenza vaccination
- Epidemiological studies of influenza
- New and emerging technologies in influenza vaccines, diagnostics and treatments
- Recent research developments in understanding influenza biology and the immune response
- A roundtable discussion on ways to reduce the impact of seasonal influenza epidemics in Australia.

The Symposium was also followed by a special joint session with the Australian Respiratory Virology Meeting on Respiratory Syncytial Virus (RSV).

More information and photos can be found at:

[http://www.influenzacentre.org/news\\_symposium.htm](http://www.influenzacentre.org/news_symposium.htm)

The next Australian Influenza Symposium will be held in 2019. For enquiries about future Symposiums, please email us at [symposium@influenzacentre.org](mailto:symposium@influenzacentre.org).





## Recommendations for Southern Hemisphere 2018 vaccine

As we previously reported, the WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2018 was held on 25-27 September 2017. Following the Consultation, WHO made the following recommendation:

*It is recommended that trivalent vaccines for use in the 2018 influenza season (southern hemisphere winter) contain the following:*

- an A/Michigan/45/2015 (H1N1)pdm09-like virus;
- an A/Singapore/INFIMH-16-0019 (H3N2)-like virus;
- a B/Phuket/3073/2013-like virus.

*It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.*

This differs from the previous vaccine recommendations (for the northern hemisphere 2017-2018), reflecting changes in circulating A(H3N2) viruses and a growing proportion B/Yamagata lineage viruses. We are particularly pleased that **A/Singapore/INFIMH-16-0019**, the most recently added virus in the vaccine recommendation, was originally submitted to our Centre by the National Public Health Laboratory (Singapore) and first isolated in eggs at our Centre.

The change in virus recommendations is also consistent with our recently published findings of low interim influenza vaccine effectiveness in Australia during the most recent influenza season (May-September 2017) and in particular for A(H3N2) viruses:

<http://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.43.17-00707>

More details about the most recent WHO recommendations can be found at:

[http://www.who.int/influenza/vaccines/virus/recommendations/2018\\_south/en/](http://www.who.int/influenza/vaccines/virus/recommendations/2018_south/en/)

## RECENT ACTIVITY AT THE CENTRE: 1 August — 31 October 2017

Below is a summary of surveillance activities at the Centre from 1 August to 31 October 2017. August was our busiest month of the year as the Southern Hemisphere influenza season reached its peak, followed by a gradual reduction in the number of samples received during the following two months.

**Samples received:** The Centre received 2894 influenza samples from the laboratories and institutions listed below during the period 1 August —31 October, 2017.

AUSTRALIA: Royal Darwin Hospital, John Hunter Hospital, Prince of Wales Hospital, Westmead Hospital, Queensland Health Forensic and Scientific Services, SA Pathology, Hobart Pathology, Lismore Base Hospital, Alfred Hospital, Austin Health, Monash Medical Centre, Royal Children's Hospital (Molecular Microbiology Dept), Royal Children's Hospital, St Vincent's Hospital, VIDRL, Pathwest QEII Medical Centre, Canberra Hospital, Dorevitch Pathology, Royal Melbourne Hospital

Fiji: Fiji Centre for Communicable Disease Control

MALAYSIA: Institute for Medical Research

NEW CALEDONIA: Institut Pasteur

NEW ZEALAND: Auckland Hospital, Institute of Environmental Science and Research

PAPUA NEW GUINEA: Institute of Medical Research

SOLOMON ISLANDS: National Referral Hospital

SOUTH AFRICA: National Institute for Communicable Disease

SRI LANKA: Medical Research Institute



## RECENT ACTIVITY AT THE CENTRE: 1 August — 31 October 2017, continued

	<b>Antigenic analysis:</b> A total of 1078 influenza isolates were analysed by HI assay.				<b>Neuraminidase inhibitor susceptibility:</b> A total of 1342 influenza isolates were tested by neuraminidase inhibition (NAI) assay for susceptibility to oseltamivir, zanamivir, peramivir and laninamivir.				
Country of submitting laboratory	<b>No. of viruses analysed by HI assay*</b>				<b>No. of viruses tested by NAI assay*</b>				
	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	A (unsubtyped)	B/Victoria	B/Yamagata
Australia	182	317	12	354	162	622	1	17	309
Cambodia	22	3	18		22	3		18	
New Caledonia		2	2	8		3		2	8
New Zealand	13	41	2	39	12	59		2	39
Papua New Guinea		17		2		19			2
Singapore	11			3		1			
Solomon Islands				1					1
South Africa	3	12		3	3	18			3
Sri Lanka	5	3	1	1	5	9		1	1
Thailand				1					
<b>Total</b>	<b>236</b>	<b>395</b>	<b>35</b>	<b>412</b>	<b>204</b>	<b>734</b>	<b>1</b>	<b>40</b>	<b>363</b>

\* Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.

**Genetic analysis:** Viruses were sequenced using Sanger sequencing and Next Generation Sequencing (NGS) techniques. In total, 616 HA, 480 NA, 422 MP and 63 NS genes were sequenced. This includes full genome sequencing of 39 viruses by NGS.

Country of submitting laboratory	<b>No. of viruses with individual genes (HA/NA/MP/NS) analysed by Sanger sequencing or NGS.</b>			
	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata
Australia	48	455	11	40
Cambodia	6		2	
New Caledonia		1		1
New Zealand	4	28	1	1
Papua New Guinea		1		2
Singapore	1	1		
South Africa	2	7		2
Sri Lanka	2	2		
<b>Total</b>	<b>63</b>	<b>495</b>	<b>14</b>	<b>46</b>

### Isolation of viruses in eggs

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 August to 31 October 2017, 4 A(H1N1)pdm09, 5 A(H3N2) and 6 B/Yamagata viruses were successfully isolated in eggs at the Centre.

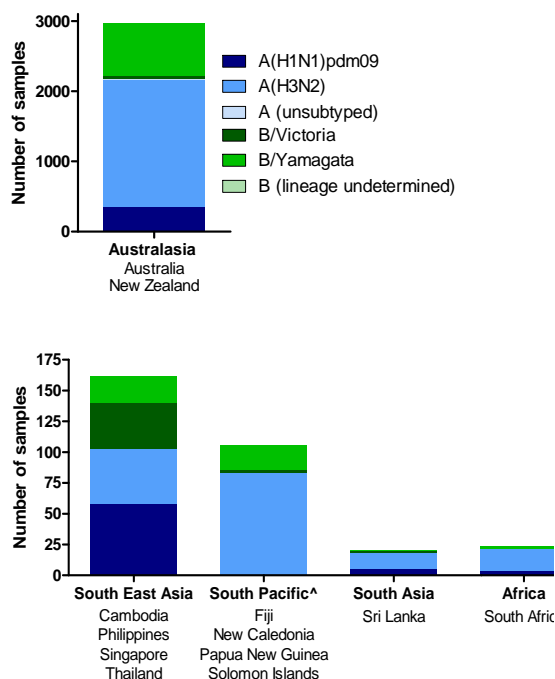


## SURVEILLANCE UPDATE: Virus activity 1 January—31 October 2017

The data below are results for viruses collected between 1 January and 31 October 2017 that have been analysed at the Centre as of 21 November 2017.

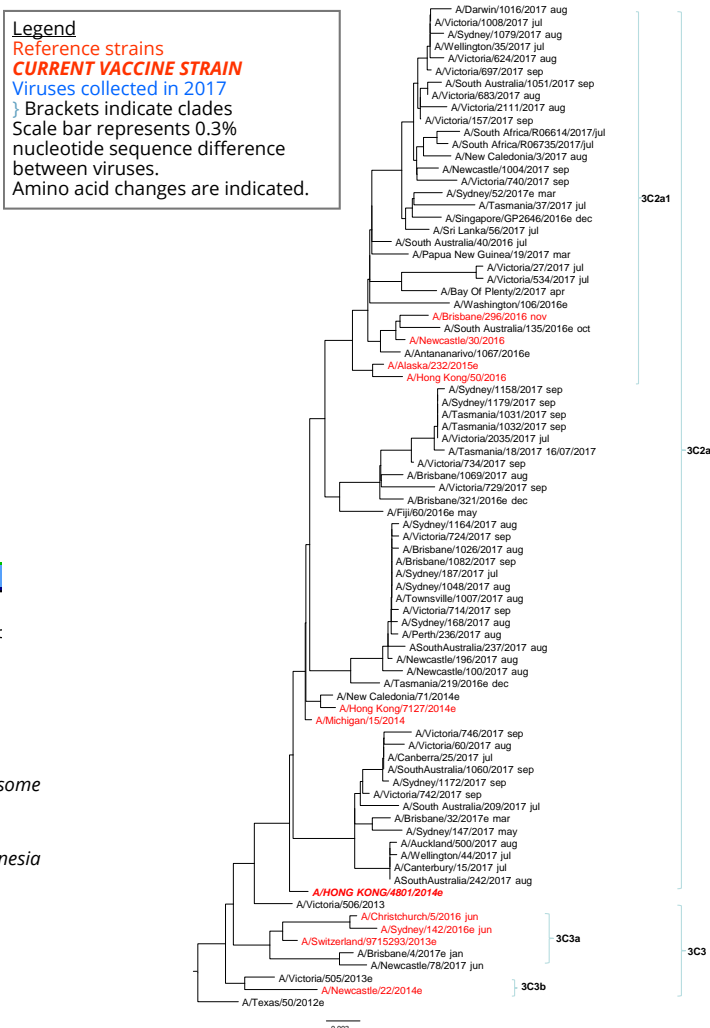
### Virus types/subtypes<sup>†</sup>

The type and subtype/lineage of 3296 viruses have been determined. The predominant type/subtype amongst viruses analysed to date is A(H3N2) (59.7%).



### Genetic analysis: focus on A(H3N2)

Sequencing and phylogenetic analysis of haemagglutinin (HA) genes from A(H3N2) collected during January–October 2017 show the continuing predominance of viruses in the 3C2a clade and 3C2a.1 subclade.

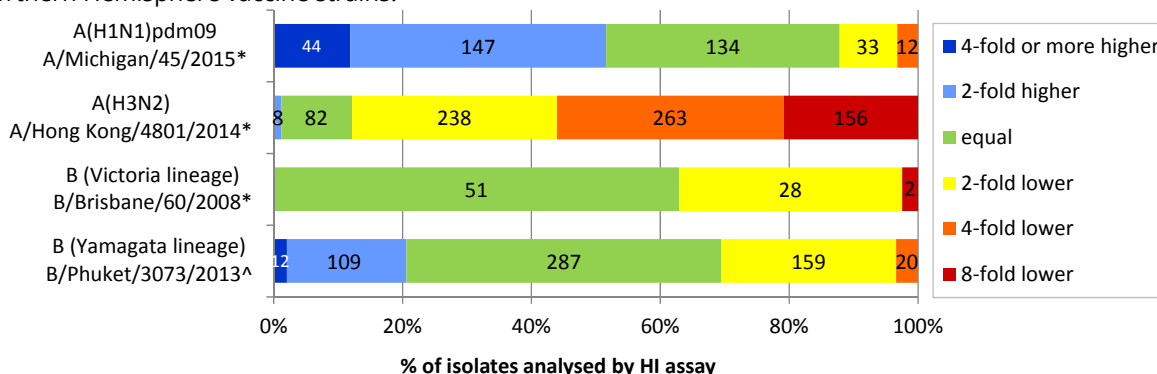


<sup>†</sup> Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.

<sup>^</sup> The South Pacific region comprises countries in Polynesia, Melanesia and Micronesia.

### Antigenic analysis

Haemagglutination inhibition (HI) assays indicate that with the exception of a number of A(H3N2) viruses and two B/Victoria viruses, all isolates were antigenically similar to the 2017 Southern Hemisphere and 2017–2018 Northern Hemisphere vaccine strains.



\* indicates strains included in the 2017 Southern Hemisphere and 2017–2018 Northern Hemisphere WHO vaccine recommendations.

<sup>^</sup> Indicates strains included in the WHO quadrivalent vaccine recommendations





## SURVEILLANCE UPDATE: 1 January –31 October 2017 (continued)

### Neuraminidase inhibitor susceptibility

The neuraminidase inhibition (NAI) assay was used to test 2473 viruses for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir and laninamivir. One A(H1N1)pdm09 virus from Singapore showed highly reduced inhibition by oseltamivir and peramivir, and one A(H1N1)pdm09 virus from Brisbane showed highly reduced inhibition by zanamivir. One B/Yamagata virus from Brisbane showed highly reduced inhibition by peramivir.

Viruses with reduced inhibition by antiviral drugs undergo genetic analysis of the NA gene to detect mutations associated with the functional change. The relationship between reduced inhibition and the clinical effectiveness of a neuraminidase inhibitor is not well understood. Further studies would be required to determine whether a virus with reduced inhibition in the NAI assay is clinically resistant.

Type/Subtype	No. tested	Oseltamivir		Peramivir		Laninamivir		Zanamivir	
		Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition
A(H1N1)pdm09	399		1 (0.3%)	1 (0.3%)	1 (0.3%)	1 (0.3%)			1 (0.3%)
A(H3N2)	1414								
A(unsubtyped)	1								
B/Victoria	76	1 (1.3%)		1 (1.3%)				1 (1.3%)	
B/Yamagata	581			1 (0.2%)	1 (0.2%)				
Mixed (sub)type	2								
<b>TOTAL</b>	<b>2473</b>	<b>1 (0.04%)</b>	<b>1 (0.04%)</b>	<b>3 (0.12%)</b>	<b>2 (0.08%)</b>	<b>1 (0.04%)</b>	<b>0</b>	<b>1 (0.04%)</b>	<b>1 (0.04%)</b>

### Adamantane resistance screening

The adamantane class of antiviral drugs (amantadine and rimantadine) were previously used to treat cases of influenza A, but are no longer recommended due to the almost universal adamantane resistance amongst circulating influenza A strains for the past decade. All five WHO Collaborating Centres for Influenza continue to screen submitted viruses for the most common resistance-conferring mutation, serine to alanine at position 31 (S31N), in the influenza A M2 protein.

From 2010 – 2017 both A(H1N1)pdm09 and A(H3N2) viruses have found to almost universally resistant to adamantanes. However, between July and September 2017, 15 A(H3N2) viruses from Australia and New Zealand were found to contain a serine residue at position 31 in the M2 protein, rendering them sensitive to adamantanes.

More information can be found in our recently published paper:

<http://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2017.22.47.17-00731>