Influenza Updates

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

Volume 7, Issue 2, October 2018

We've joined Twitter!

The Centre has recently a opened Twitter account through which we hope to further connect to others in the global influenza surveillance and research community. You can follow us at https://twitter.com/WHOCCFluMelb and tag us @WHOCCFluMelb.

WHO Recommendations for the Southern Hemisphere 2019 influenza vaccines

The WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2019 was held in Atlanta GA, USA, on 24-26 September 2018. Following the Consultation, WHO made the following recommendation:

> It is recommended that egg based quadrivalent vaccines for use in the 2019 southern hemisphere influenza season contain the following:
>
> - an A/Michigan/45/2015 (H1N1)pdm09-like virus;
> - an A/Switzerland/8060/2017 (H3N2)-like virus;
> - a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage); and
> - a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).
>
> It is recommended that egg based trivalent vaccines for use in the 2019 southern hemisphere influenza season contain the following:
>
> - an A/Michigan/45/2015 (H1N1)pdm09-like virus;
> - an A/Switzerland/8060/2017 (H3N2)-like virus; and
> - a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage).
>
> It is recommended that the A(H3N2) component of non-egg based vaccines for use in the 2019 southern hemisphere influenza season be an A/Singapore/INFIMH-16-0019/2016-like virus together with the other vaccine components as indicated above.

The recommendation includes a change in the A(H3N2) component of the egg-based vaccine. This is because a larger proportion of recently circulating viruses were well inhibited by ferret antisera raised against egg-propagated A/Switzerland/8060/2017 compared to the previous vaccine strain (A/Singapore/INFIMH-16-0019/2016). The new vaccine strain belongs to an antigenically distinguishable genetic subclade compared to the previous vaccine strain. The recommended B/Victoria component of the vaccine was also changed because globally, an increasing proportion of circulating viruses are antigenically similar to B/Colorado/6/2017 and different from the previous vaccine virus (B/Brisbane/60/2008).

(continued next page...)

Photo courtesy of Centers for Disease Control and Prevention

WHO Collaborating Centre
for Reference and
Research on Influenza
VIDRL

Doherty Institute
A joint venture between the University of Melbourne and the Royal Melbourne Hospital

Recommendations for the Southern Hemisphere 2019 influenza vaccines (continued)

While WHO makes recommendations for the influenza vaccine, it is up to national authorities to decide on the final composition for their individual countries. The Australian Influenza Vaccine Committee met in Canberra in October made the same recommendations as by WHO for the quadrivalent vaccine. However, the recommendation for the Australian trivalent vaccine includes a B/Yamagata lineage virus, rather than the B/Victoria lineage virus. This is because in Australia, the vast majority of recently circulating influenza B viruses have been of the B/Yamagata lineage and few B/Victoria lineage viruses have been detected.

The full WHO recommendations are here:
http://www.who.int/influenza/vaccines/virus/recommendations/2019_south/en/

Recommendations for the Australian influenza vaccine in 2019 are here:
https://www.tga.gov.au/aivc-recommendations-composition-influenza-vaccine-australia-2019

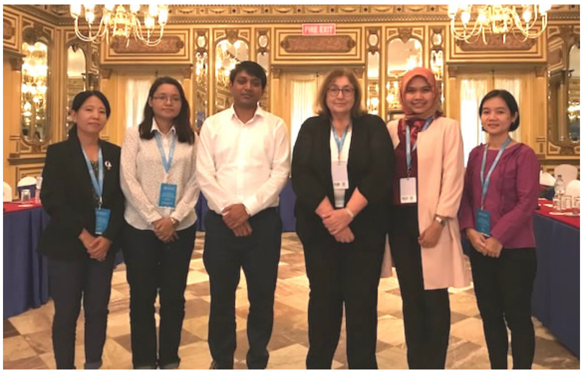
Thank you to everyone who sent us influenza samples in the months prior to the Consultation. Your viruses provided essential data on circulating strains and helped to inform the choice of recommended vaccine strains. Please continue to send us your samples in a timely fashion, as circulating influenza viruses continue to evolve and the need for constant surveillance remains.

Recent Training Activities

Over the past few months we have engaged in several training activities, both in regional settings and at the Centre.

Regional workshops and training

Naomi Komadina (*below, third from right*) led a workshop on GISAID Bioinformatics Training at the WHO South-East Asia and Western Pacific Region National Influenza Centre Meeting on 13 July in Nepal, Kathmandu.



Dr Patrick Reading (*below, at lectern)*, was an influenza specialist at the Workshop to Strengthen Influenza-like Illness (ILI) & Severe Acute Respiratory Infections (SARI) Surveillance, held in Suva, Fiji, on 6–10 August. The meeting was attended by laboratory representatives from the Cook Islands, Fiji, French Polynesia, Kiribati, New Caledonia, Niue, Samoa, Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, Wallis and Futuna and Guam.

Photo courtesy of The Secretariat of the Pacific Community

Photo courtesy of Jude Jayamaha, Medical Research Centre

Dr Patrick Reading visited the Sri Lankan National Influenza Centre at the Medical Research Centre in Colombo, Sri Lanka, on 25 August – 9 September. He trained staff in cell culture and virus isolation techniques.

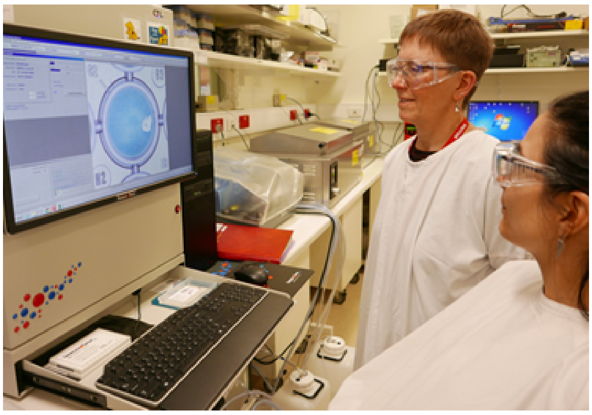
Dr Patrick Reading was an influenza specialist at the Workshop to Strengthen Influenza-like Illness & Severe Acute Respiratory Infections (SARI) Surveillance in the Solomon Islands on 2–4 October. The workshop was attended by over 30 doctors, nurses and surveillance representatives from different provinces of the Solomon Islands.

Recent Training Activities (continued)

Training at the Centre

Dr Anja Werno (*right*), from Canterbury Health Services, Christchurch, New Zealand, visited the Centre on 6–10 August. During her visit she learned techniques in genetic analysis, HI assays, focus reduction assays and data analysis.

Jacqui Ralston (*left*), from the Institute of Environmental Science and Research, Wellington, New Zealand, visited the Centre on September 3 – 15 to undertake training in focus reduction assays.



Songha Tok (*left*) and Sonita Kol (*centre*), from Institute Pasteur, Phnom Penh, Cambodia, and Sovandara Om (*right*), from the National Institute of Public Health, Phnom Penh, Cambodia, are visiting the Centre on October 22 – 2 November. Sonita and Sovandara are undertaking training in surveillance techniques for influenza detection and characterisation, while Songha is training in specialised serology techniques for the characterisation of viral isolates.

National Influenza Centres meeting in Kathmandu

Photo courtesy of SEARO

Four staff members from the Centre attended the 12th Bi-regional Meeting of the National Influenza Centres (NICs) and Influenza Surveillance of the South-East and Western Pacific Region, held in Kathmandu, Nepal in July.

Topics discussed included: global and regional updates on influenza activity; historical perspectives and strategies to prioritise influenza; supporting the introduction of vaccines; laboratory developments in influenza surveillance; shipping and sharing samples; pandemic preparedness planning; progress of the five-year influenza strategy in the Asia-Pacific; quality control systems; implementation of the PIP Framework; strengthening reporting, virus tracking and data usage.

We were pleased to catch up with many of you there and thank SEARO for organising the meeting.

Recent activity at the Centre (1 April — 30 September 2018)

Below is a summary of surveillance activities at the Centre from 1 April to 30 September. After a relatively quiet start to the Southern Hemisphere influenza season in 2018, we have been increasingly busy during the past couple months.

Samples received

The Centre received 1932 influenza samples from the laboratories and institutions listed below:

AUSTRALIA: Canberra Hospital, Westmead Hospital, John Hunter Hospital, Prince of Wales Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services, SA Pathology, Australian Clinical Labs, Royal Children's Hospital, Alfred Hospital, Dorevitch Pathology, Royal Melbourne Hospital, VIDRL, Pathwest QE II Medical Centre

CAMBODIA: Institut Pasteur du Cambodge

FIJI: Center For Communicable Disease Control

INDONESIA: National Institute of Health Research and Development

MALAYSIA: Institute for Medical Research

NEW CALEDONIA: Centre Hospitalier de Nouvelle Calédonie

NEW ZEALAND: Canterbury Health Laboratories, Institute of Environmental Science and Research

PAPUA NEW GUINEA: Institute of Medical Research

PHILIPPINES: Research Institute for Tropical Medicine

SINGAPORE: National Public Health Laboratory

SOLOMON ISLANDS: National Referral Hospital

SOUTH AFRICA: National Institute for Communicable Diseases

SRI LANKA: Medical Research Institute

THAILAND: Thai National Influenza Center

TIMOR-LESTE: Laboratório Nacional da Saúde

	Antigenic analysis: A total of 1333 influenza isolates were analysed by HI assay.				**Genetic analysis:** Sequencing was performed on 646 HA, 643 NA, 482 MP and 52 NS genes from 646 viruses by Sanger sequencing or Next Generation Sequencing (NGS) techniques.				
	No. of viruses analysed by HI assay*[*]*				**No. of viruses sequenced by NGS or Sanger sequencing**				
Country of submitting laboratory	A(H1N1) pdm09	A(H3N2)	B/Victoria	B/Yamagata	A(H1N1) pdm09	A(H3N2)	A (mixed subtype)	B/Victoria	B/Yamagata
Australia	369	150	8	143	145	146	1	5	45
Cambodia	26	1	2	12	20	1		2	5
Fiji	25	8		12	10	12			8
Indonesia	6	1	3		6	2		3	
Macau SAR	23	15	1	3	9	5			3
Malaysia	77	59	2	21	12	5			1
New Caledonia	20	3	28	25	9	6		9	15
New Zealand	53	5	3	38	26	12		3	19
Papua New Guinea	4				4			2	
Philippines	5	11	1	2	4	8			
Singapore	20	24	10	8				5	
South Africa	38	2		2	27	2			2
Sri Lanka	14	6	2	3	10	4		2	2
Thailand	12	13		14	11	13			5
Total	**692**	**298**	**60**	**283**	293	216	1	31	105

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

Recent activity at the Centre (1 April — 30 September 2018, continued)

	Neuraminidase inhibitor susceptibility: A total of 652 influenza isolates were tested by neuraminidase inhibition (NAI) assay for susceptibility to oseltamivir, zanamivir, peramivir and laninamivr.			
Country of submitting laboratory	**No. of viruses tested by NAI assay***			
	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata
Australia	208	53	5	75
Cambodia	25		2	6
Fiji	20			
Macau SAR	23	13	2	3
Malaysia	33		2	17
New Caledonia	10		23	4
New Zealand	28			7
Papua New Guinea	5			
Singapore	14	8	11	8
South Africa	30	2		2
Sri Lanka	6			
Thailand	7			
Total	**409**	**76**	**45**	**122**

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

Isolation of viruses in eggs

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 April to 30 September 2018, 9 A(H1N1)pdm09, 20 A(H3N2), 5 B/Victoria and 2 B/Yamagata viruses were successfully isolated in eggs at the Centre. One of the A(H3N2) viruses (A/Brisbane/1/2018) was reassorted at the New York Medical Centre and is a candidate vaccine virus (antigenically like A/Switzerland/8060/2017) for the 2019 Southern Hemisphere vaccine.

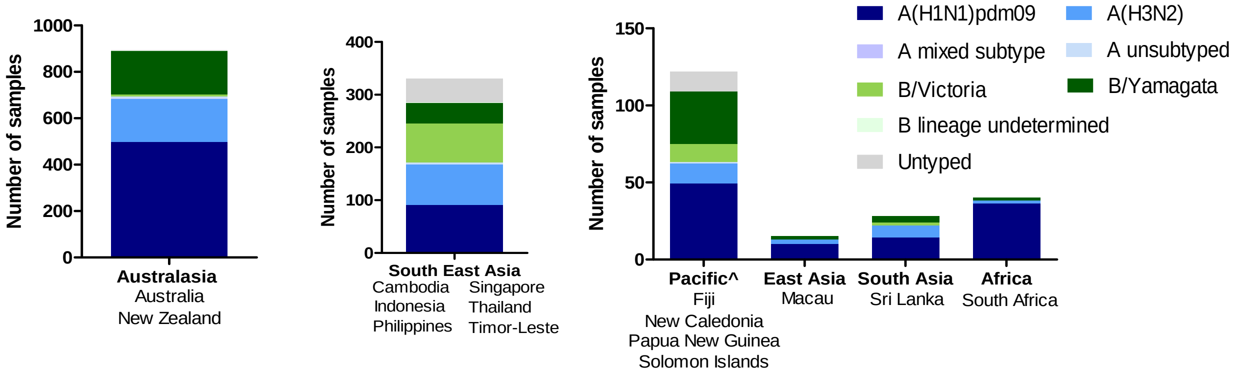
Surveillance update: Virus activity 1 January—30 September 2018

The data below are results for viruses collected between 1 January and 30 September 2018 that have been analysed at the Centre as of 10 October 2018.

Virus types/subtypes*

The type and subtype/lineage of 1431 viruses have been determined. Of viruses analysed to date, the largest proportion have been A(H1N1)pdm09 (48.7%), followed by A(H3N2) (20.2%) and B/Yamagata viruses (18.9%).

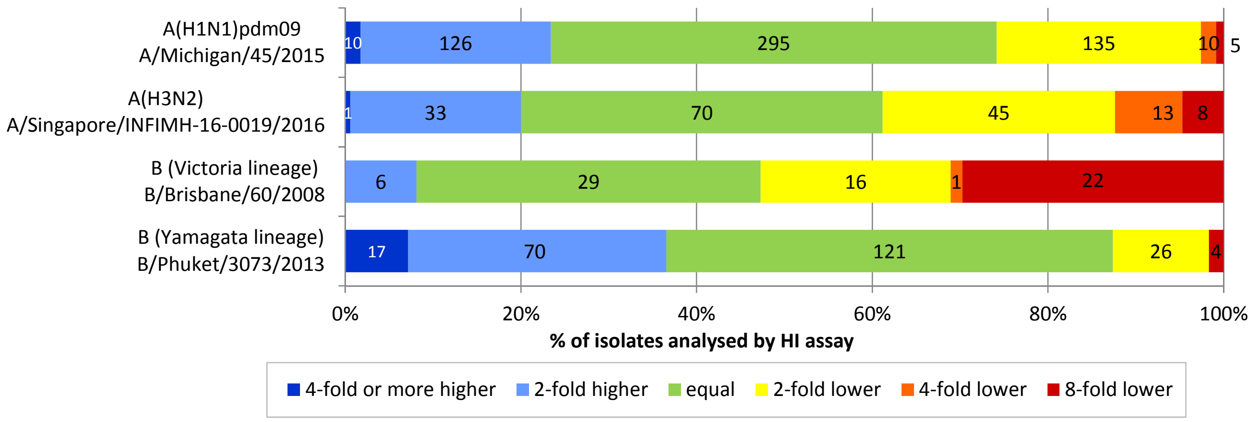
Samples collected 1 January—30 September 2018 and analysed at the Centre, by geographical region of submitting laboratory:



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

Antigenic analysis[*]

Haemagglutination inhibition (HI) assays indicate that the vast majority of A(H1N1)pdm09, A(H3N2) and B/Yamagata isolates tested were antigenically similar to the 2018 Southern Hemisphere vaccine strains. Approximately 30% of A/Victoria isolates had a titre 8-fold lower compared to the cell-propagated reference virus A/Brisbane/60/2008.



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

Neuraminidase inhibitor susceptibility

Viral isolates are routinely tested for their susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir and laninamivir using the neuraminidase inhibition (NAI) assay. Viruses with reduced inhibition by antiviral drugs in the NAI assay undergo genetic analysis of the neuraminidase gene to detect mutations associated with the functional change.

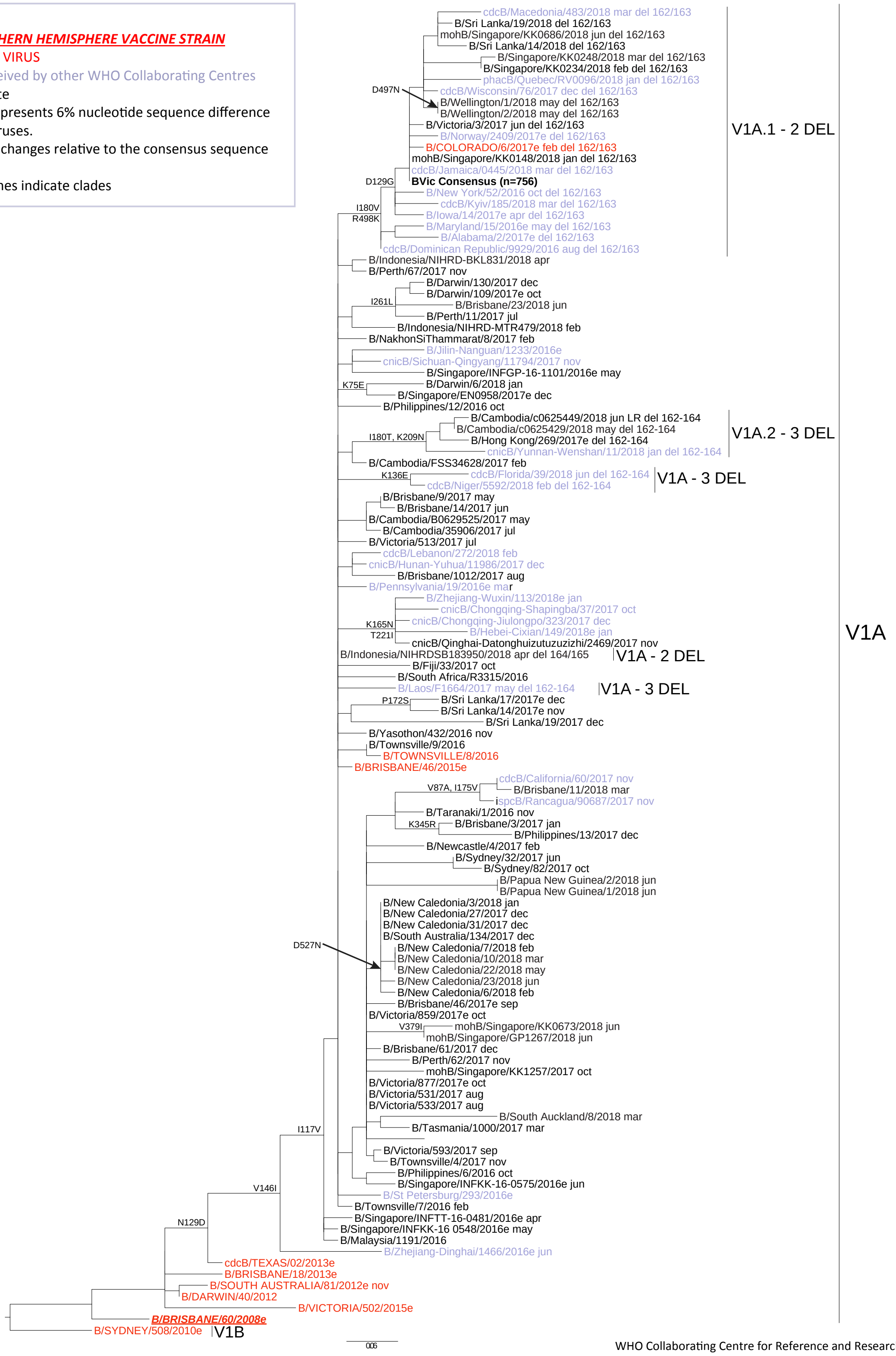
Of 1195 viruses tested, two A(H1N1)pdm09 viruses from Singapore showed highly reduced inhibition to oseltamivir and peramivr. Genetic analysis of both viruses showed that they contained the H275Y mutation which reduces inhibition of these viruses by oseltamivir and peramivir. The relationship between 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.

		Oseltamivir		Peramivir		Laninamivir		Zanamivir	
Type/Subtype[*]	No. tested	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition
A(H1N1)pdm09	624		2 (0.3%)		2 (0.3%)				
A(H3N2)	243	2 (0.8%)		1 (0.4%)		1 (0.4%)		2 (0.8%)	
A (unsubtyped)	1								
B/Victoria	75								
B/Yamagata	252	1 (0.4%)		1 (0.1%)					
TOTAL	**1195**	**3 (0.25%)**	**2 (0.2%)**	**2 (0.2%)**	**2 (0.2%)**	**1 (0.1%)**	**-**	**2 (0.2%)**	**-**

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

Genetic Analysis: Focus on B/Victoria lineage

Sequencing and phylogenetic analysis of haemagglutinin (HA) genes from B/Victoria viruses collected during January–October 2017 shows the expansion of the subclade V1A.1 at a global level. This subclade contains the new recommended vaccine strain B/Colorado/6/2017, which has two amino acid deletions in the HA gene and is genetically distinct from the previous vaccine strain (B/Brisbane/60/2008).



Legend
2018 SOUTHERN HEMISPHERE VACCINE STRAIN
REFERENCE VIRUS
Viruses received by other WHO Collaborating Centres
e: egg isolate
Scale bar represents 6% nucleotide sequence difference between viruses.
Amino acid changes relative to the consensus sequence are shown.
| Vertical lines indicate clades