Influenza Updates

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

@WHOCCFluMelb

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Preparation for the upcoming influenza season

Winter and the influenza season is fast approaching over the next few months across many southern hemisphere countries. Under normal circumstances, we would expect that the number of samples submitted to the Centre will increase leading up to the next WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere in September 2020. However, given the current social distancing measures implemented across many countries to address the COVID-19 pandemic, the severity of the upcoming influenza season is likely to be significantly less than what has been observed for previous years.

Please note the following points:

- please send us your samples as soon as possible after collection, as they are most useful when they have been collected recently
- we accept both viral isolates and/or original clinical specimens
- we need to receive samples by the end of August at the very latest (and preferably earlier) in order to process them in time for the Consultation.
- the WHO Shipping Fund Project (SFP) is available to assist National Influenza Centres in covering the cost of shipping samples to WHO Collaborating Centres up to four times per year. It is recommended that one of the shipments be in July to mid-August. If you have any questions about shipping samples or would like information about accessing the WHO Shipping Fund, please contact us at whoflu@influenzacentre.org.



Timing for sending samples to a WHO Collaborating Centre

Number of specimens positive for influenza by subtype

Figure adapted from FluNet: https://www.who.int/influenza/gisrs_laboratory/flunet/charts/en/Influenza viruses detections, Western Pacific Region of WHO

WHO Collaborating Centre for Reference and **Research on Influenza** VIDRL



A joint venture between The University of Melbourne and The Royal Melbourne Hospital



Recommendations for Northern Hemisphere 2020-2021 vaccine announced

The WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2020-2021 was held in Geneva, Switzerland on 24-27 February 2020. Following the Consultation, WHO made the following recommendation:

It is recommended that egg based quadrivalent vaccines for use in the 2020-2021 northern hemisphere influenza season contain the following:

- an A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus;
- an A/Hong Kong/2671/2019 (H3N2)-like virus;
- a B/Washington/02/2019 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

The recommendations for the northern hemisphere 2020-2021 vaccine includes a change in the A(H1N1)pdm09 and A(H3N2) components of the egg-based vaccine compared to the previous vaccine recommendations for the southern hemisphere 2020. In addition, the B/Victoria component was changed compared to the previous vaccine recommendations for the northern hemisphere 2019-2020. The changes in the recommended A(H1N1)pdm09, A(H3N2) and B/Victoria components reflect increasing proportions of circulating virus that were similar to these updated strains, compared to previous vaccine viruses. More details about the most recent recommendations can be found at:

https://www.who.int/influenza/vaccines/virus/recommendations/2020-21_north/en/

Contribution of National Influenza Centres to the vaccine recommendations

We thank everyone who has sent us influenza samples prior to the Consultation. Your viruses provide essential data on recently circulating strains and help to inform the choice of recommended vaccine strains.

In this context, we would like to acknowledge the contribution and critical role played by WHO National Influenza Centres and other submitting laboratories in providing influenza samples to WHO Collaborating Centres, not only for the purposes of analysis and surveillance, but also for the provision of potential vaccine candidates. Please continue to send us your samples, as of course the influenza virus continues to circulate and evolve, and need for constant surveillance remains.

Upcoming meetings and conferences

Many upcoming meetings and conferences have been postponed due to COVID-19. Given the changing nature of travel restrictions, it is currently not possible to determine whether many of these conferences will still go ahead in a virtual setting, or whether they will be postponed.

Farewell and good luck

It is with sadness but good wishes that we announce the departure of three long-standing staff members from the Centre. We thank Michelle, Leo, and Michelle for their significant contributions to the Centre, and wish them all the very best for their future.



Dr Michelle Chow has been a part of the Centre as Communications Officer for the past nine years. She has contributed significantly to ensuring the Centre's work is showcased in reports, newsletters, website, and on social media.



Dr Michelle Wille has been involved in avian influenza research with the Centre for the past three and a half years. Last year she was awarded a Discovery Early Career Researcher Award (DECRA) from the Australian Research Council (ARC), and will now move to work at the University of Melbourne. She will also continue to assist with avian influenza surveillance for the Centre and other existing partners.



Mr Leo Lee has been a research assistant with the Centre for the last three years. His first author paper on the effects of Baloxavir against A(H1N1)pdm09 in ferrets was recently published in the journal PLoS Pathogens. This May he has joined Centre Director Kanta Subbarao's research laboratory within the Department of Microbiology and Immunology at the University of Melbourne, in order to work on COVID-19.



Recent activities at the Centre (1 January — 30 April 2020)

Below is a summary of surveillance activities at the Centre from 1 January to 30 April. Centre activities have been relatively quiet in recent months due to decreased influenza cases resulting from social distancing and travel restriction measures implemented in response to COVID-19 across many countries. We anticipate that this decrease in the number of samples will continue while these measures are in place.

Samples received: The Centre received 1063 influenza samples from the laboratories and institutions listed below during the period 1 January—30 April 2020.

AUSTRALIA: Canberra Hospital, Westmead Hospital, The MALAYSIA: Institute for Medical Research Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services, SA Pathology, Hobart Pathology, Alfred Hospital, Royal Children's SOLOMON ISLANDS: National Referral Hospital Hospital, Royal Melbourne Hospital, VIDRL, Pathwest QEII **Medical Centre**

SINGAPORE: National Public Health Laboratory SRI LANKA: Medical Research Institute THAILAND: Thai National Influenza Center

CAMBODIA: Institut Pasteur du Cambodge

	Antigenic analysis: A total of 655 influenza isolates were analysed by HI assay.						Neuraminidase inhibitor susceptibility: A total of 616 influenza isolates were tested by neuraminidase inhibition (NAI) assay for susceptibility to oseltamivir, zanamivir, peramivir and laninamivr.				Genetic analysis: Sequencing was performed on 249 HA, 230 NA, 188 MP and 52 NS genes from 251 viruses by Sanger sequencing or Next Generation Sequencing (NGS) techniques.			
	No. of viruses analysed by HI assay *							No. of viruses tested by NAI assay [*]				No. of viruses sequenced by NGS or Sanger sequencing		
Country of submitting laboratory	A(H1N1)pdm09	A(H3N2)	A mixed subtype	A unsubtyped	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	A mixed subtype	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	B/Victoria
Australia	247	80	1		27		216	79	1	20		87	45	20
Cambodia	18	20			32		18	20		32		9	11	10
Malaysia	87	12			3		87	12		3		16	3	2
Singapore	31	17			13	3	31	17		13	3			
Sri Lanka	2	8		1	11		2	8		11		3	2	8
Thailand	16	12			14		16	13		14		12	13	10
Total	401	149	1	1	100	3	370	149	1	93	3	127	74	50

* 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 January to 30 April 2020, 7 A(H1N1)pdm09, 8 A(H3N2) and 2 B/Victoria viruses were successfully isolated in eggs at the Centre.



The data below are results for viruses collected between 1 January and 30 April 2020 that have been analysed at the Centre as of 4 June 2020.



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

^ The Pacific region comprises countries in Polynesia, Melanesia and Micronesia.

Antigenic analysis[†]

A total of 220 viruses were tested using the haemagglutination inhibition (HI) assay. Viruses were identified as low-reactors if their titre with reference antiserum was at least 8-fold lower than the titre of the reference virus. A large proportion of A(H1N1) pdm09, and almost half of A(H3N2) viruses were low reactors to their respective reference strains.



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



Genetic analysis: focus on A(H1N1)

Sequencing and phylogenetic analysis of haemagglutinin (HA) genes of viruses circulating during January–April 2020, show an increasing proportion of viruses in the 6B.1A/183P-5A subclade.





Antiviral drug susceptibility testing:

234 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that 2 A(H1N1)pdm09 had highly reduced inhibition by one or more neuraminidase inhibitors (NAI).

Type/subtype/ lineage	Oseltamivir			Peramivir			Laninamivir			Zanamivir		
	Normal inhibition	Reduced inhibition	Highly reduced Inhibition									
A(H1N1)pdm09	176		2	175	1	2	178			177	1	
A(H3N2)	31			31			31			31		
A unsubtyped												
B/Victoria	25			25			25			25		
B/Yamagata												
B lineage undeter- mined												
Untyped												
Total	232		2	231	1	2	234			233	1	

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. 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/sub	tyne/lineage	Country of sub-	NAI(s) with highly reduced inhibition (marked with *)							
rype/sur	cype/ meage	mitting laboratory	Oseltamivir	Peramivir	Laninamivir	Zanamivir				
A(H1N1)pdm09	A/Perth/22/2020	Australia	*	*						
	A/Perth/24/2020	Australia	*	*						

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