Influenza Updates

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

@WHOCCFluMelb

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WHO Recommendations for the Southern Hemisphere 2023 Influenza Vaccines

The WHO Consultation on the Composition of Influenza Vaccines for the Southern Hemisphere 2023 was held in Dublin, Ireland between 19-22 September 2022.

Following the Consultation, the WHO made the following recommendations:

It is recommended that ***quadrivalent*** vaccines for use in the 2023 Southern Hemisphere influenza season contain the following:

Egg-based vaccines

- an A/Sydney/5/2021 (H1N1)pdm09-like virus;
- an A/Darwin/9/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Cell- or recombinant-based vaccines

- an A/Sydney/5/2021 (H1N1)pdm09-like virus;
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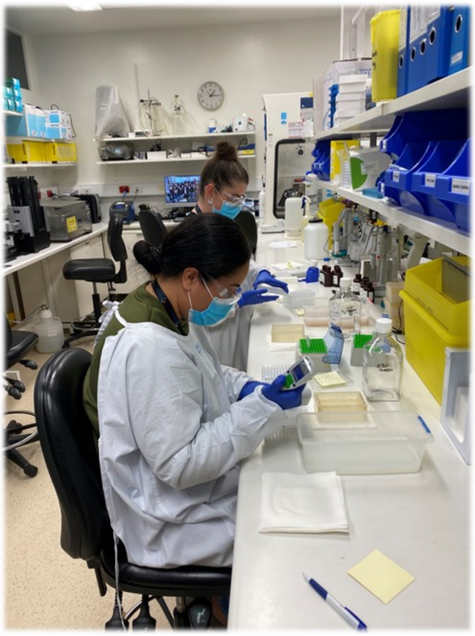
More details about the recommendations can be found here.

AIVC recommendation for the composition of influenza vaccine for Australia in 2022

The Australian Influenza Vaccine Committee (AIVC) met on 5 October 2022 to recommend the composition of the influenza virus vaccines for 2023. The full statement can be accessed here.

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.



We are especially pleased that the most recently added A(H1N1)pdm09 virus in the vaccine recommendation, A/Sydney/5/2021 (egg, cell, or recombinant), was originally submitted to our Centre by the WHO National Influenza Centre in Sydney, NSW, Australia, which is located at the **Centre for Infectious Diseases and Microbiology Laboratory Services** at ICPMR, Westmead Hospital.

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. The need for constant surveillance remains as the influenza virus continues to circulate and evolve.

Notable upcoming conferences

AVS11 Meeting

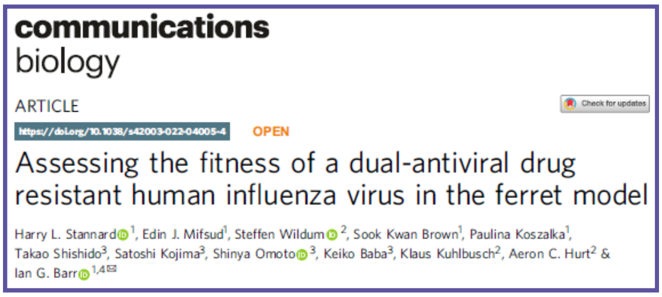
5-8 December 2022
Gold Coast, Queensland

This year's meeting will also celebrate the 21st anniversary of the Australian Virology Society's founding. Key topics will include epidemic/pandemic threats, virus-host interactions, agricultural veterinary and plant virology, vaccines, therapeutics, and diagnostic developments. Invited speakers include Centre Director Kanta Subbarao and Michelle Wille. Abstract submissions have closed, but further details on registration and the program are available here.

Featured Research Article

'Assessing the fitness of a dual-antiviral drug resistant human influenza virus in the ferret model'

Featuring Harry Stannard and many others from the Centre



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ARTICLE

https://doi.org/10.1038/s42003-022-04005-4 OPEN

Check for updates

Assessing the fitness of a dual-antiviral drug resistant human influenza virus in the ferret model

Harry L. Stannard[1], Edin J. Mifsud[1], Steffen Wildum[2], Sook Kwan Brown[1], Paulina Koszalka[1], Takao Shishido[3], Satoshi Kojima[3], Shinya Omoto[3], Keiko Baba[3], Klaus Kuhlbusch[2], Aeron C. Hurt[2] & Ian G. Barr[1,4]✉

Published in *Communications Biology* this September, the study assessed the replicative fitness and transmissibility of a patient-isolated A(H1N1)pdm09 influenza virus. This virus contained mutations that indicated it was resistant to both neuraminidase inhibitors and baloxavir marboxil, which are antivirals that are currently used to treat influenza infection. The study indicated that, while the overall replicative fitness of this mutant was reduced (suggesting reduced risk of widespread community transmission), person-to-person transmission could potentially still occur. The study highlights the need for continued surveillance of drug-resistant influenza viruses that may emerge in the community. It also highlights the importance of implementing measures (e.g. combination therapy) that reduce the likelihood of these drug-resistant influenza viruses from arising, particularly in immunocompromised individuals.

Stannard HL, Mifsud EJ, Wildum S, Brown SK, Koszalka P, Shishido T, Kojima S, Omoto S, Baba K, Kuhlbusch K, Hurt AC, Barr IG. Assessing the fitness of a dual-antiviral drug resistant human influenza virus in the ferret model. Commun Biol. 2022 Sep 28;5(1):1026. doi: 10.1038/s42003-022-04005-4. PubMed link.

Farewell and good luck

It is with sadness but good wishes that we announce the departure of Naomi Komadina, Mariana Baz, and Jean Moselen. We thank Naomi, Mariana, and Jean for their significant contributions to the Centre, and wish them all the very best for their futures.

Dr Naomi Komadina was the Bioinformatics Head and had worked at the Centre for almost 28 years. She retired from the Centre at the start of July.

Dr Mariana Baz was the Senior Scientist for the Antiviral group for around 16 months. She has now returned to Canada to pursue a new professional opportunity.

Ms Jean Moselen was a Medical Scientist with the Molecular group for three years. She has now taken on a role as a Medical Scientist with the Translational Diagnostics lab at VIDRL.

Recent activities at the Centre (1 January — 30 September 2022)

Below is a summary of surveillance activities at the Centre during this current reporting period. The Southern Hemisphere influenza season in 2022 has been especially busy for us, particularly with high levels of influenza in Australia. We have received and processed an unprecedented number of samples this year, with further isolation and characterisation of samples still underway.

Samples received:

The Centre received 11095 influenza samples from the laboratories and institutions listed below during the period 1 January — 30 September 2022.

AUSTRALIA: Canberra Hospital, John Hunter Hospital, 4Cyte Pathology, The Children's Hospital at Westmead, Prince of Wales Hospital, Westmead Hospital, Royal Darwin Hospital, Pathology Queensland (Cairns), Queensland Children's Hospital, Queensland Health Forensic and Scientific Services (QHFSS), SA Pathology, Hobart Pathology, Royal Hobart Hospital, Alfred Hospital, Australian Clinical Labs, Australian Clinical Labs (Geelong), Austin Pathology, Box Hill Hospital, Dorevitch Pathology (Heidelberg), Eastern Health Pathology, Melbourne Pathology, Monash Medical Centre, Royal Children's Hospital Molecular Microbiology Department (Bio21), Royal Children's Hospital, Royal Melbourne Hospital, St Vincent's Hospital, VIDRL, PathWest QEII Medical Centre

CAMBODIA: Institut Pasteur du Cambodge

FIJI: Center for Communicable Disease Control

INDIA: National Institute of Virology

MALAYSIA: Institute for Medical Research

NEW CALEDONIA: Centre Hospitalier de Nouvelle Calédonie

NEW ZEALAND: Institute of Environmental Science and Research

PHILIPPINES: Research Institute for Tropical Medicine

SINGAPORE: National Public Health Laboratory

SOUTH AFRICA: National Institute for Communicable Diseases

SRI LANKA: Medical Research Institute

THAILAND: Thai National Influenza Center

TIMOR-LESTE: Laboratório Nacional de Saúde

VANUATU: Vila Central Hospital Laboratory Department

Isolation of viruses in eggs:

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January — 30 September 2022, 12 A(H1N1)pdm09 and 8 A(H3N2) viruses were successfully isolated in eggs at the Centre.

Recent activities at the Centre (1 January — 30 September 2022) continued

Antigenic analysis
3038 viruses analysed by haemagglutination inhibition (HI) assay

Antiviral drug susceptibility
2676 viruses analysed by neuraminidase inhibition (NAI) assay

Sequencing
1428 viruses analysed
1414 HA genes
1418 NA genes
1354 MP genes
712 NS genes

Country of submitting laboratory	No. of viruses analysed by HI assay*				No. of viruses tested by NAI assay*				No. of viruses sequenced by NGS or Sanger sequencing*		
	A(H1N1)pdm09	A(H3N2)	B lineage undetermined	B/Victoria	A(H1N1)pdm09	A(H3N2)	B lineage undetermined	B/Victoria	A(H1N1)pdm09	A(H3N2)	B/Victoria
Australia	551	1972		7	521	1595		6	350	713	5
Fiji		21				21				30	
India	17	14		17	17	14		17	16	8	10
Malaysia		47				89				15	
New Caledonia		44				43				39	
New Zealand	4	91			4	144			3	79	
Philippines	2	15		3		5		2		10	3
Singapore		46	1	28		44	1	28		1	
South Africa	37	14		4	37	14		4	33	14	4
Thailand		9				9				9	
Timor-Leste		64		26		61				60	19
Vanuatu		4									
Total	**611**	**2341**	**1**	**85**	**579**	**2039**	**1**	**57**	**402**	**984**	**42**

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

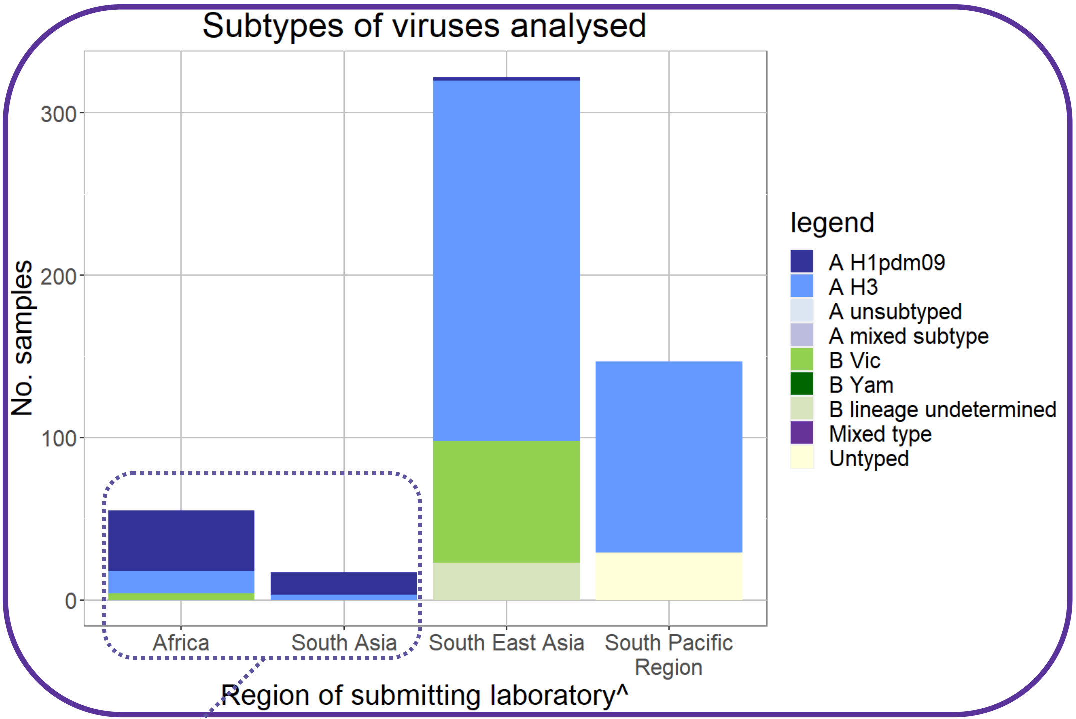
Surveillance update: Virus activity 1 January—30 September 2022

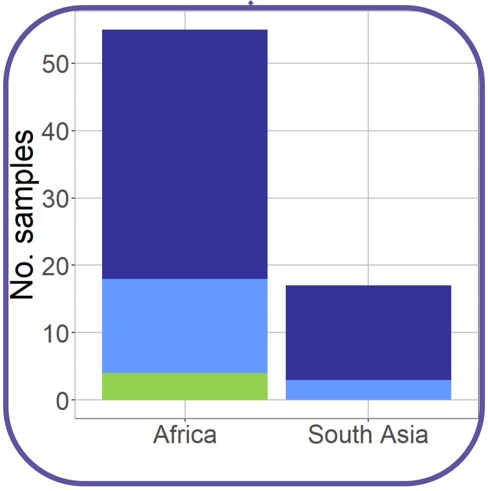
The data below are results for viruses collected between 1 January and 30 September 2022 that have been analysed at the Centre as of 4 October 2022.

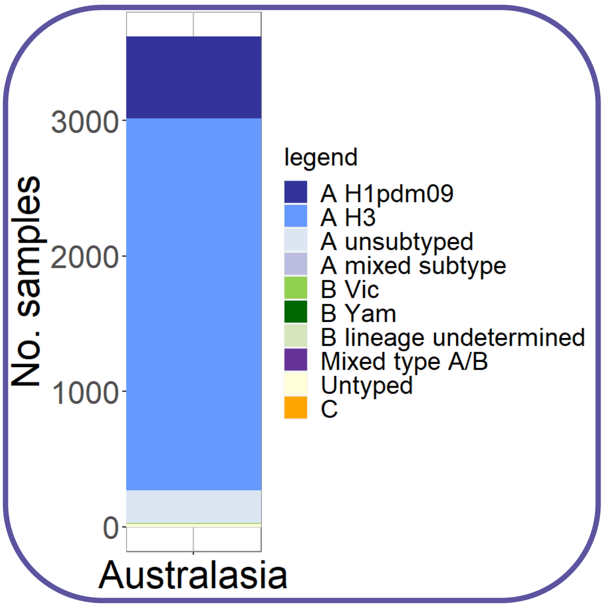
Virus types/subtypes*

The type and subtype/lineage of 4161 viruses have been determined.

15.8% A(H1N1)pdm09
74.5% A(H3N2)
2.0% B/Victoria







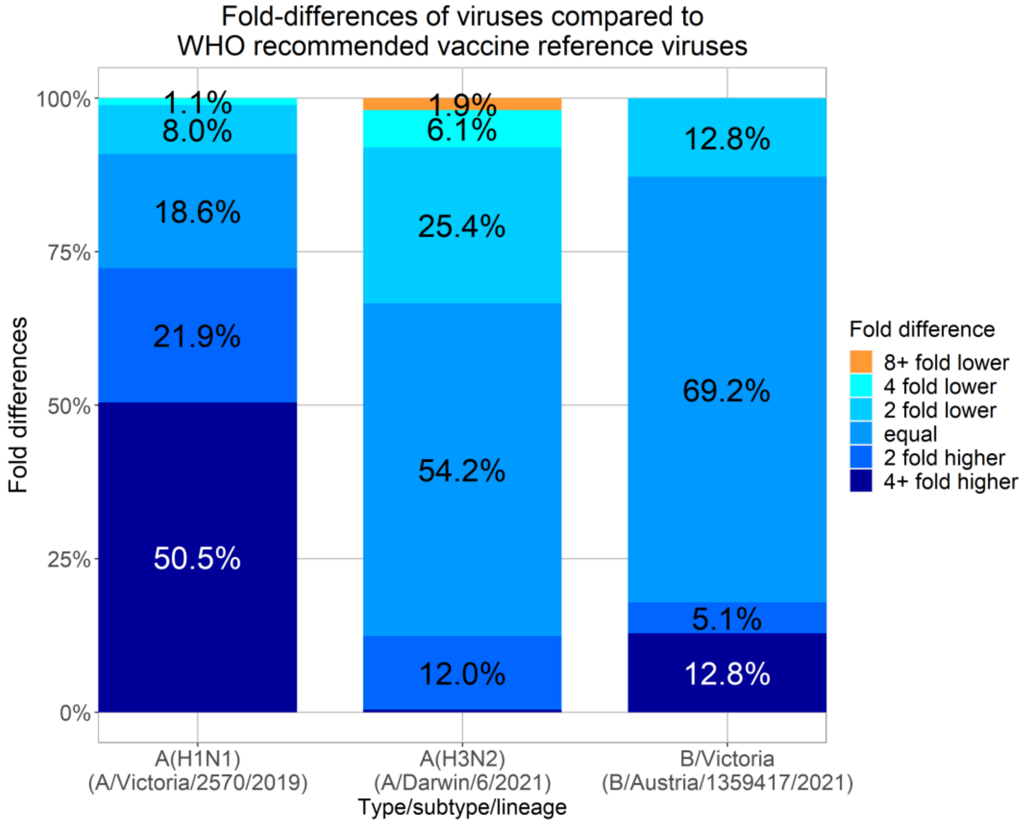
Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.

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

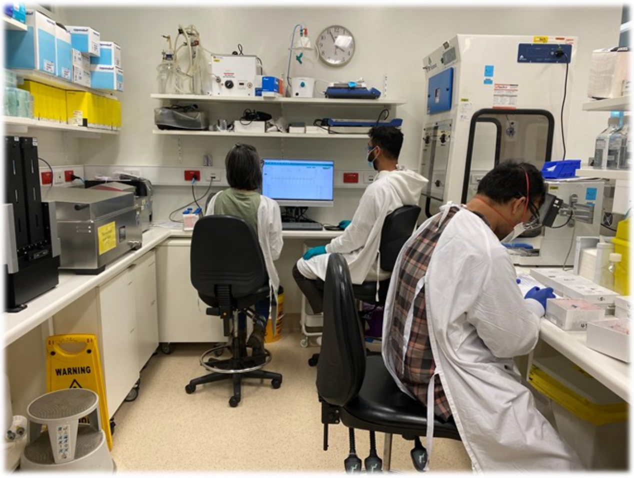
Antigenic analysis*

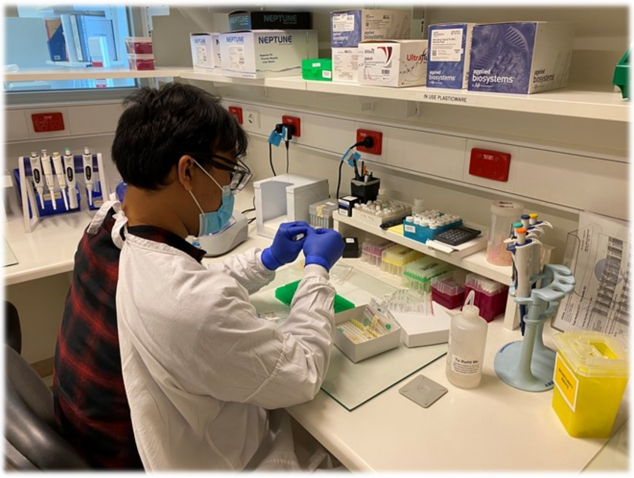
A total of 2830 viruses were tested using the haemagglutination inhibition (HI) assay.

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. The vast majority of A (H1N1)pdm09, A(H3N2), and B/Victoria lineage viruses were antigenically similar to their respective reference viruses.



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



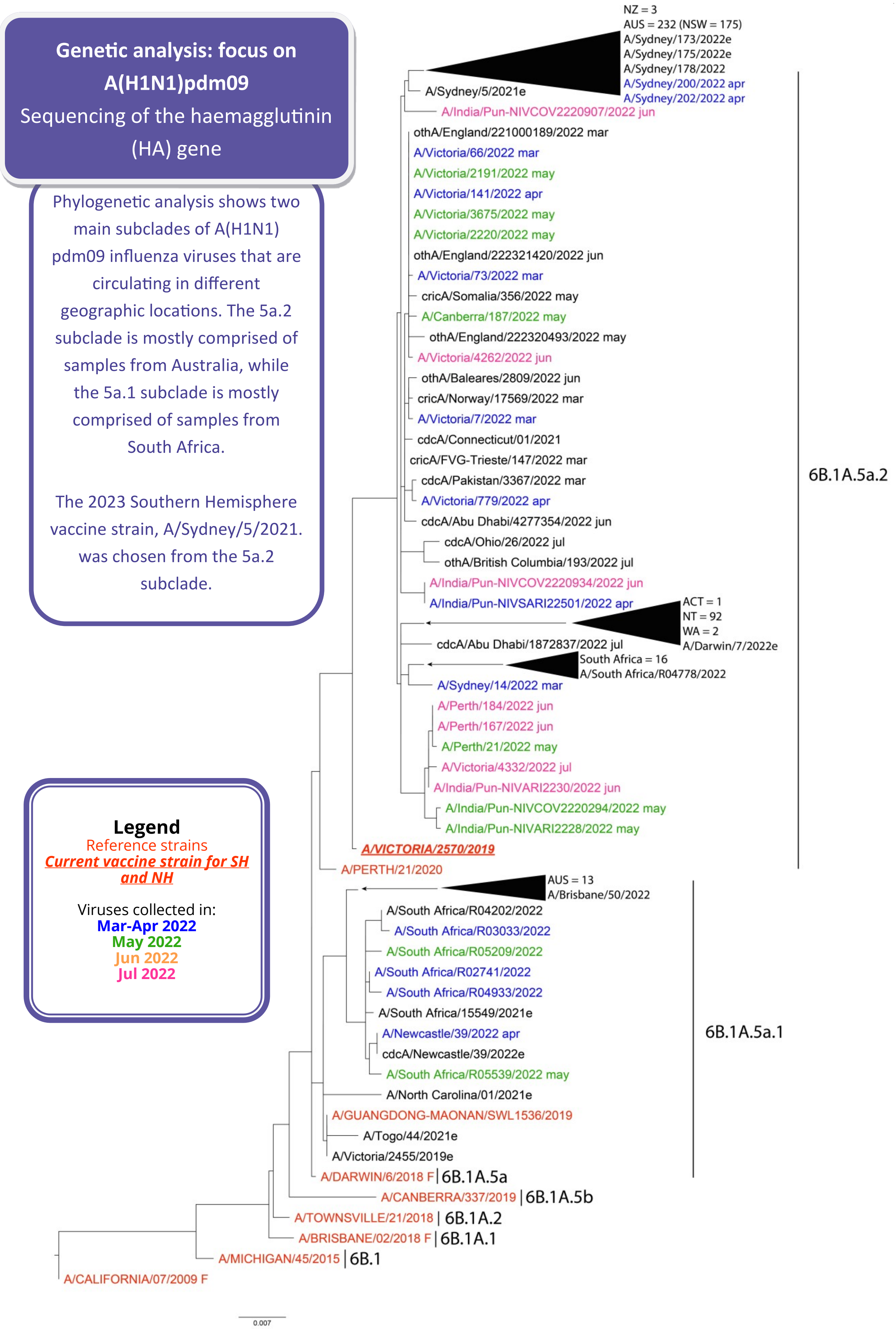


Genetic analysis: focus on A(H1N1)pdm09

Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows two main subclades of A(H1N1) pdm09 influenza viruses that are circulating in different geographic locations. The 5a.2 subclade is mostly comprised of samples from Australia, while the 5a.1 subclade is mostly comprised of samples from South Africa.

The 2023 Southern Hemisphere vaccine strain, A/Sydney/5/2021. was chosen from the 5a.2 subclade.



Surveillance update: Virus activity 1 January—30 September 2022 continued

Antiviral drug susceptibility testing:

2553 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that no viruses 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	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition	Normal inhibition	Reduced inhibition	Highly reduced Inhibition
A(H1N1) pdm09	567		2	567		2	569			569		
A(H3N2)	1972			1972			1972			1972		
B/Victoria	12			12			12			12		
Total	**2551**		**2**	**2551**		**2**	**2553**			**2553**		

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.

Viruses with highly reduced inhibition to one or more NAI

Type/subtype/lineage		Country of submitting laboratory	NAI(s) with highly reduced inhibition (marked with *)			
			Oseltamivir	Peramivir	Laninamivir	Zanamivir
A(H1N1) pdm09	A/Sydney/200/2022	Australia	*	*	Normal	Normal
	A/Sydney/202/2022	Australia	*	*	Normal	Normal