Influenza Updates

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

@WHOCCFluMelb

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Reflection on 2024: Thank you for your hard work and support.

As the year draws to a close, we would like to thank all the laboratories that sent us influenza and RSV samples in 2024. It has been an exceptionally busy year for influenza around the world, as we have received more samples than any other year in the Centre's history. Some of the year highlights include:

- The Centre hosted the 2025 WHO Southern Hemisphere Vaccine Composition Meeting at the Doherty Institute in Melbourne
- The Options for the Control of Influenza XII Conference held in Brisbane was attended by a number of Centre staff, as well as colleagues working on influenza and other respiratory viruses from around the world
- Scientists from the Centre supported workshops and/or provided training to scientists in several countries, including in Kiribati, Philippines and India
- The Centre hosted staff from National Influenza Centres and other public health laboratories including scientists from China, Pakistan, Philippines and Vietnam for training in techniques relevant to laboratory-based surveillance of influenza and RSV
- The Centre, along with scientists from the University of Melbourne and AusBio, secured AUD$3.1 million in funding from the Novo Nordisk Foundation to develop a novel antiviral drug to counter pandemic influenza

Image made with Biorender.com

WHO Shipping Fund Project reminder

In anticipation of the WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2025-2026, which will be held in February 2025, this is a reminder that the WHO Shipping Fund Project (SFP) is available to assist National Influenza Centres in shipping samples to WHO Collaborating Centres up to four times per year.

The recommended timing of these shipments is:

- One between the end of December to mid-January and one between the end of June and mid-August, to support the WHO vaccine composition recommendation-making for each hemisphere;
- The third and fourth shipments can be used at your own judgement, which may depend on the seasonality, intensity of the season, the finding of unusual or untypable/ unsubtypable viruses, or notable outbreaks.

If you have any questions about shipping samples or would like information about accessing the WHO Shipping Fund, please contact us at enquiries@influenzacentre.org

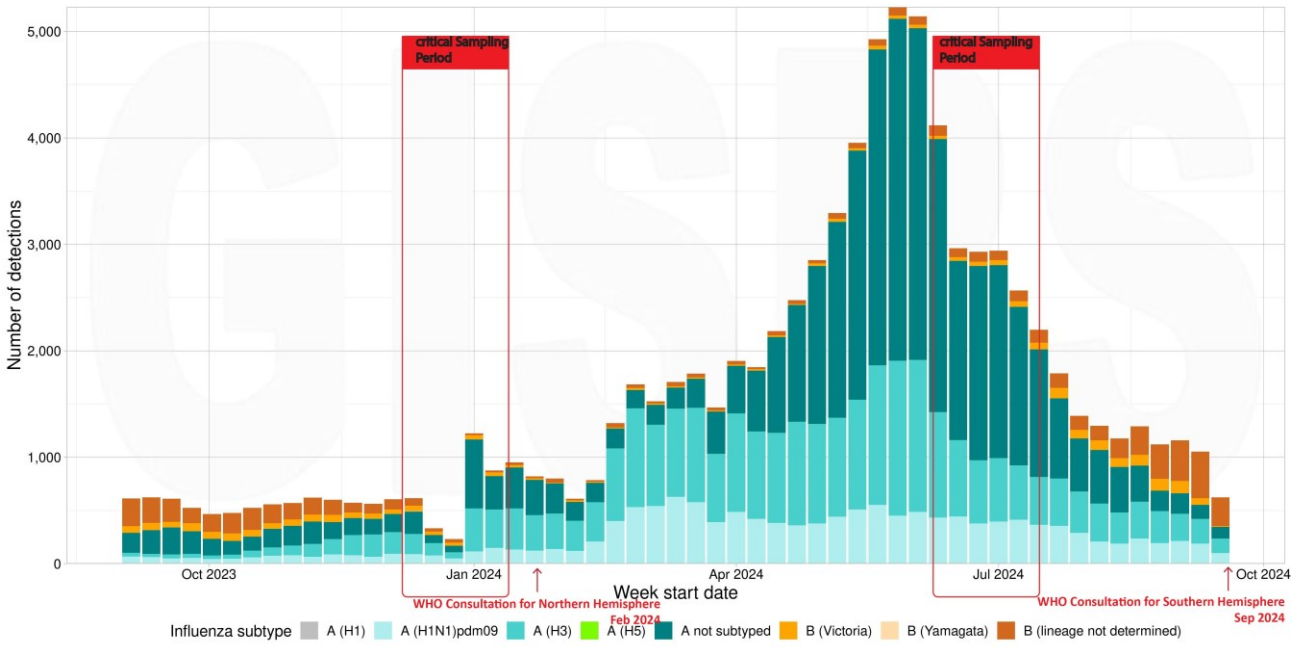


Figure adapted from FluNet: https://app.powerbi.com/view?r=eyJrIjoiZTkyODcyOTEtZjA5YS00ZmI0LWFkZGUtODIxNGI5OTE3YjM0IiwidCI6ImY2MTBjMGI3LWJkMjQtNGIzOS04MTBiLTNkYzI4MGFmYjU5MCIsImMiOjh9

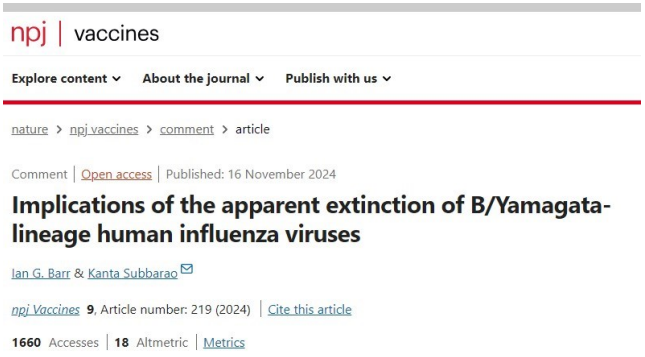
We encourage you to send samples in a timely manner, as soon as possible after collection. Please avoid sending your samples in large batches collected over long periods, as up-to-date data for the current influenza season are the most useful for WHO GISRS surveillance and vaccine formulation.

Featured Research Articles

'Implications of the apparent extinction of B/Yamagata-lineage human influenza viruses"

Featuring Deputy Director Ian Barr and former Director Kanta Subbarao

Published in November in NPJ Vaccines, this article discusses implications of the apparent extinction of B/Yamagata-lineage viruses on vaccine composition as well as the risk of re-introduction of B/Yamagata-lineage viruses into the human population.



Barr IG, Subbarao K. Implications of the apparent extinction of B/Yamagata-lineage human influenza viruses. NPJ Vaccines. 2024 Nov 16;9(1):219. doi: 10.1038/s41541-024-01010-y. PMID: 39550399; PMCID: PMC11569178.

"Influenza A(H5N1) Virus Clade 2.3.2.1a in Traveler Returning to Australia from India, 2024"

Featuring Yi-Mo Deng, Michelle Wille, Clyde Dapat, Olivia Lay, Heidi Peck and Ian Barr from the Centre.

Published in Emerging Infectious Diseases, this report provides details on Australia's first reported human case of a HPAI A(H5N1) virus clade 2.3.2.1a infection. The case was a 2.5-year-old patient who returned to Melbourne, Australia, from Kolkata, India. The patient developed severe influenza symptoms in India and was hospitalized upon arrival in Australia, requiring intensive care and mechanical ventilation. The virus identified was a reassortant, containing gene segments from clade 2.3.2.1a, 2.3.4.4b and wild bird low pathogenicity avian influenza viruses.

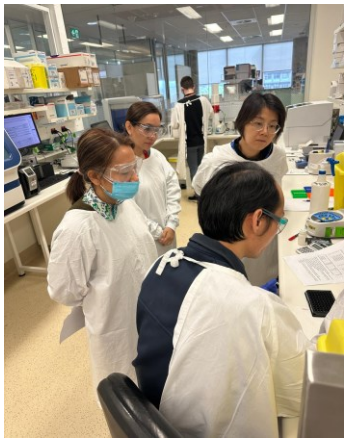
Deng YM, Wille M, Dapat C, Xie R, Lay O, Peck H, Daley AJ, Dhanasakeran V, Barr IG. Influenza A(H5N1) Virus Clade 2.3.2.1a in Traveler Returning to Australia from India, 2024. Emerg Infect Dis. 2024 Dec 3;31(1). doi: 10.3201/eid3101.241210. Epub ahead of print. PMID: 39625816.

Training at the Centre

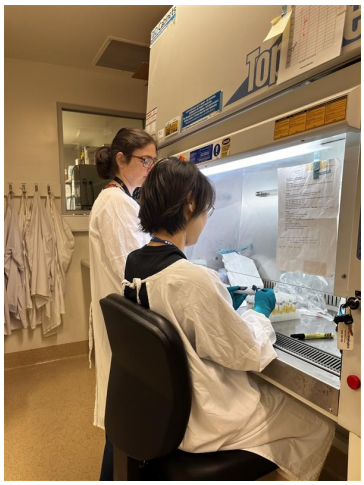
The Centre recently held training workshops for visiting scientists from the Philippines, Vietnam and China.

We welcomed **Vina Lea Arguellesa**, **Jonjee Calaor-Morin** and **Catherine Calzado-Dacasin** from the Research Institute of Tropical Medicine (RITM), Philippines from 4-11th October 2024. Training was conducted by Clyde Dapat, Xiaomin Dong, and Steven Edwards and covered topics such as NGS library preparation, ONT sequencing, quality assessment of sequence data, genome assembly of influenza and RSV, genome annotation and phylogenetic analyses.

We welcomed **Thu Ngoc Nguyen** and **Minh Hang Duong** from the Pasteur Institute, Ho Chi Minh City, Vietnam from 4-17th October 2024. Training was conducted by Heidi Peck, Malet Aban and Leah Gillespie and covered topics such as mammalian cell culture, influenza virus isolation and influenza virus serology.



We welcomed **Dr Zhaomin Feng** from the Institute for Infectious Disease and Endemic Disease Control at Beijing CDC, from 20th October - 19th November 2024. Training was coordinated by Yi-Mo Deng and focussed on RSV genomic surveillance.



We welcomed **Min He** from Nanjing CDC, from 07th October – 20th December 2024. Training was conducted by Yi-Mo Deng, Michelle Wille Clyde Dapat, Xiaomin Dong, and Steven Edwards, and covered topics including NGS, phylogenetic analyses, bioinformatics, serological analysis of influenza viruses and detection of avian influenza viruses.

Highlights from the 17th Bi-regional Meeting of National Influenza Centres and Influenza Surveillance for WHO's South-East Asia and Western Pacific Regions| 20 – 22 Nov 2024

The 17th Bi-regional meeting was held in Manilla and attended by Clyde Dapat, Jessica Miller, Ian Barr, Patrick Reading, and Yi-Mo Deng from the Centre. Key highlights from the meeting include discussion of:

- Strengths and weaknesses of surveillance systems for influenza and other respiratory viruses, as well as National Influenza Centre (NIC) capabilities, in different countries. Progress made in imple-menting the expanded Global Influenza Surveillance and Response System (eGISRS) at the country level, were also highlighted.

- The scope of the revised NIC Terms of references (TORs) and the provisions under the Nagoya protocol were clarified, highlighting material and non-material benefits.

- There was consensus on the need to enhance surveillance capacity for seasonal and zoonotic influenza, as well as preparedness for potential future pandemics. It was agreed that continued collaboration among institutions and stakeholders working on Influenza and other respiratory viruses was critical

- Other resources such as the WHO online PISA (Pandemic Influenza Severity Assess-ment), the International Reagent Resource were highlighted

- The Nagoya Protocol and its implications for NICs and influenza vaccine development were also discussed

Recent activities at the Centre (1 January— 30 November 2024)

Below is a summary of surveillance activities at the Centre during this current reporting period. The Southern Hemisphere influenza season in 2024 has been especially busy for us, with high levels of influenza cases 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 12,761 influenza samples from the laboratories and institutions listed below during the period 1 January — 30 November 2024.

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), Princess Alexandra Hospital, SA Pathology, Hobart Pathology, Royal Hobart Hospital, Australian Clinical Labs (Geelong), Alfred Hospital, Australian Clinical Labs, Austin Pathology, Melbourne Pathology, Monash Medical Centre, Royal Children's Hospital, Royal Melbourne Hospital, St Vincent's Hospital, VIDRL, PathWest QEII Medical Centre

BRUNEI: RIPAS Hospital

CAMBODIA: Institut Pasteur du Cambodge

COOK ISLANDS: Te Marae Ora Ministry of Health

FIJI: Center for Communicable Disease Control

INDIA: National Institute of Virology

INDONESIA: Balai Besar Laboratorium Biologi Kesehatan

MALAYSIA: Institute for Medical Research, National Public Health Laboratory, University of Malaya

NEPAL: National Public Health Laboratory

NEW CALEDONIA: Centre Hospitalier de Nouvelle Calédonie

NEW ZEALAND: Institute of Environmental Science and Research

PAPUA NEW GUNIEA: Institute of Medical Research

PHILIPPINES: Research Institute for Tropical Medicine

SAMOA: Tupua Tamases Meaole Hospital

SINGAPORE: National Public Health Laboratory

SOLOMON ISLANDS: National Referral Laboratory

SOUTH AFRICA: National Institute for Communicable Diseases

SRI LANKA: Medical Research Institute

TAHITI: Institut Louis Malarde

THAILAND: Thai National Influenza Center

TIMOR-LESTE: Laboratório Nacional de Saúde

TONGA: Laboratory Service Viola Hospital Tongatapu

Isolation of viruses in eggs:

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January — 30 November 2024, 15 A(H1N1)pdm09, 4 B/Victoria and 16 A(H3N2) viruses were successfully isolated in eggs at the Centre.

Recent activities at the Centre (1 January— 30 November 2024) continued

Antigenic analysis
4366 viruses analysed by haemagglutination inhibition (HI)

Antiviral drug susceptibility
3378 viruses analysed by neuraminidase inhibition (NAI)

Sequencing
3600 viruses analysed
3599 HA genes
3599 NA genes
3439 MP genes
472 NS genes

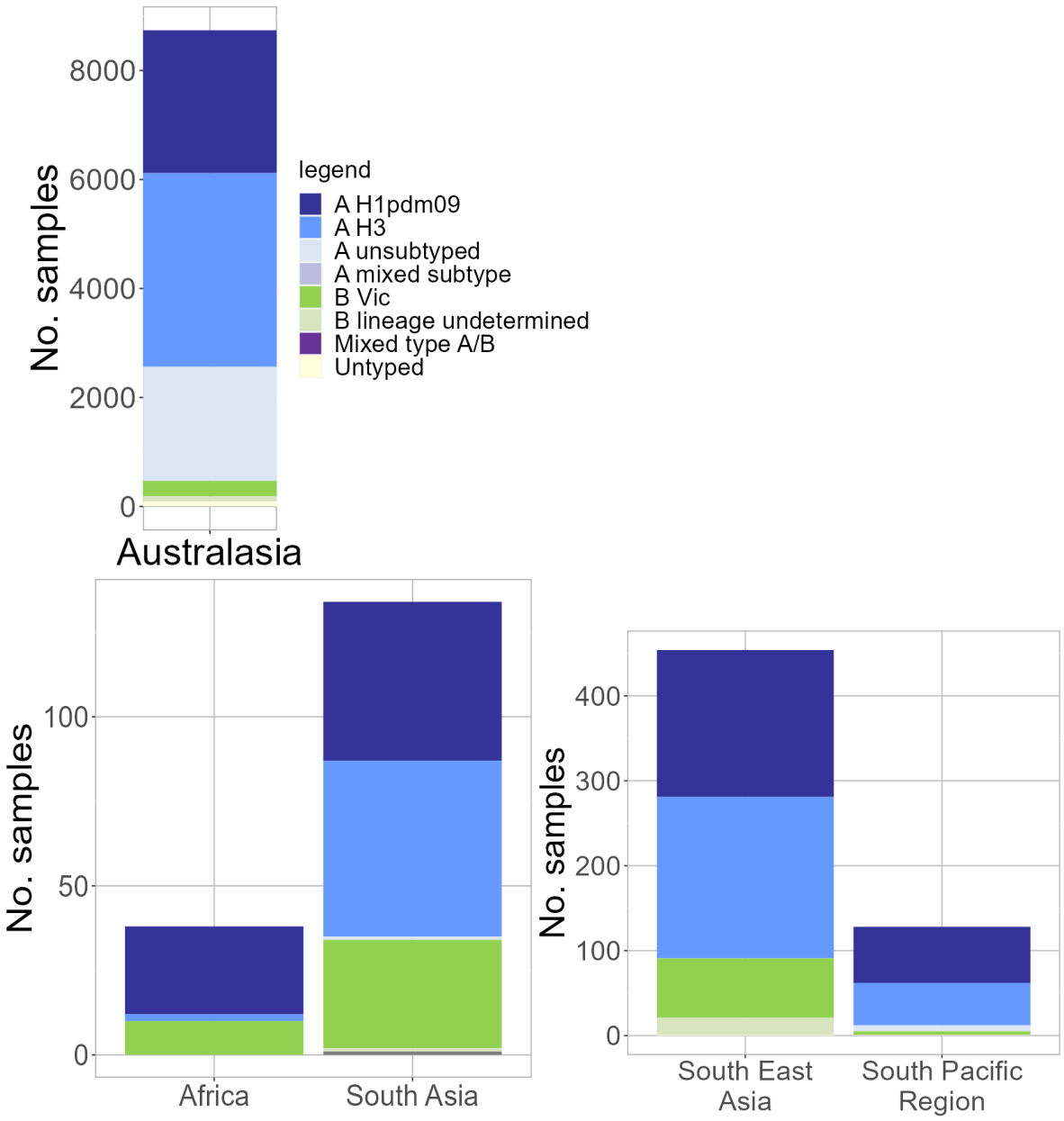
Country of submitting laboratory	No. of viruses analysed by HI assay*			No. of viruses tested by NAI assay*			No. of viruses sequenced by NGS						
	A(H1N1)pdm09	A(H3N2)	B/Victoria	A(H1N1)pdm09	A(H3N2)	B/Victoria	A(H1N1)pdm09	A(H3N2)	B/Victoria	A(5N1)	A unsubtyped	B lineage undetermined	Untyped
Australia	1530	1723	165	1047	1143	112	1127	1646	217	2	13		
Brunei	9	49	3	10	72	7	12	40	16			1	1
Cambodia	35	13	30	34	32	29	32	28	23				
Cook Islands				6	2	0							
Fiji	13	8	0	15	8	0	15	5	0			1	
India	28	12	6	27	12	4	1	2	2				
Indonesia	0	4	2	3	4	2	2	3	2				
Malaysia	75	68	0	41	22	0	12	10	0			3	
Nepal	0	2	0	6	2	0	6	2	1				
New Caledonia	1	2	0	3	25	0	3	0	0				
New Zealand	80	42	9	103	90	9	43	32	9				
Papua New Guinea	6	0	4	6	15	7	0	0	7				
Philippines	6	40	26	6	42	21	5	29	13				
Samoa				11	1	0	9	3	0		1		
Singapore	79	66	43	80	66	42	3	1	0				
Solomon Islands							1	0	0				
South Africa	26	2	10	26	2	10	26	2	6				
Sri Lanka	11	1	5	12	10	5	30	42	14				
Tahiti	2	5	1	14	5	1	12	4	1				
Thailand	6	7	6	6	7	6	6	7	2				
Timor-Leste	17	77	0	19	77	0	13	38	0				
Tonga	11	0	0	11	0	0	13	0	0				
	1935	**2121**	**310**	**1486**	**1637**	**255**	**1371**	**1894**	**313**	**2**	**14**	**5**	**1**

Surveillance update: Virus activity 1 January — 30 November 2024

The data below are results for viruses collected or sampled between 1 January and 30 November 2024 that have been analysed at the Centre as of 4 December 2024.

Virus types/subtypes*
The type and subtype/lineage of 7180 viruses have been determined.

30.9% A(H1N1)pdm09
40.5% A(H3N2)
4.2% B/Victoria



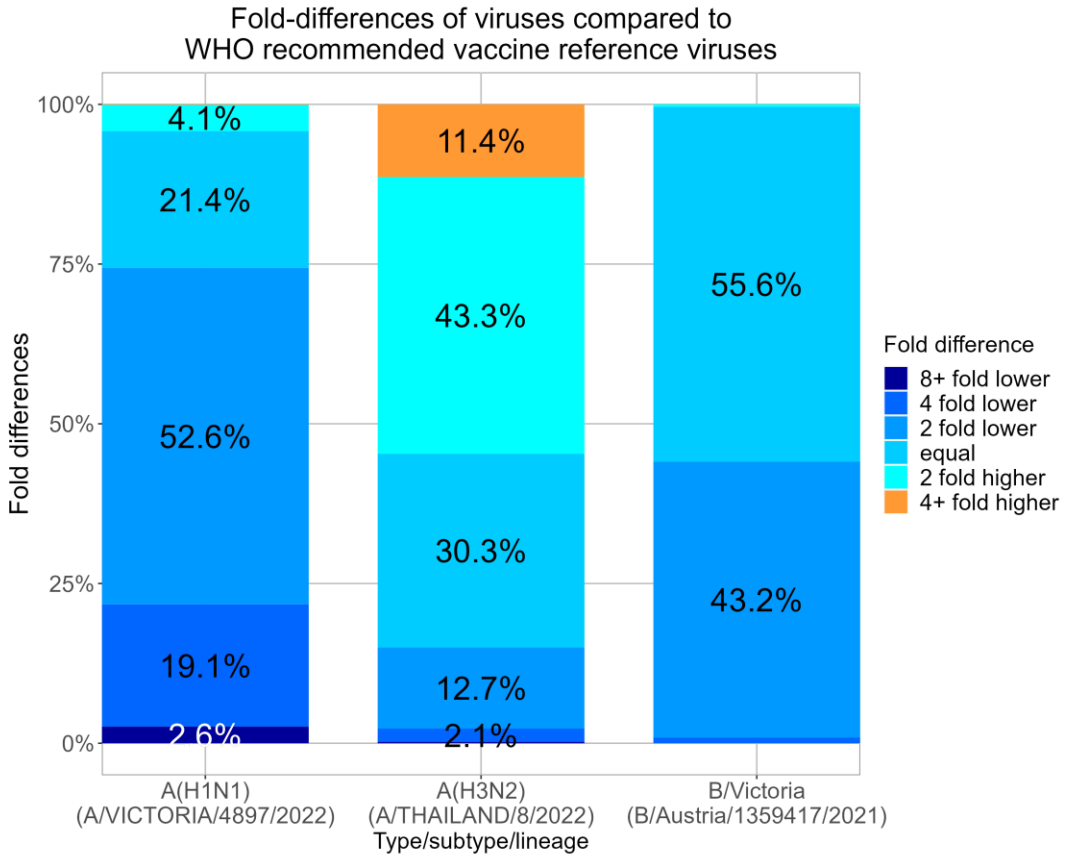
**Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

Surveillance update: Virus activity 1 January—30 November 2024 continued

Antigenic analysis*

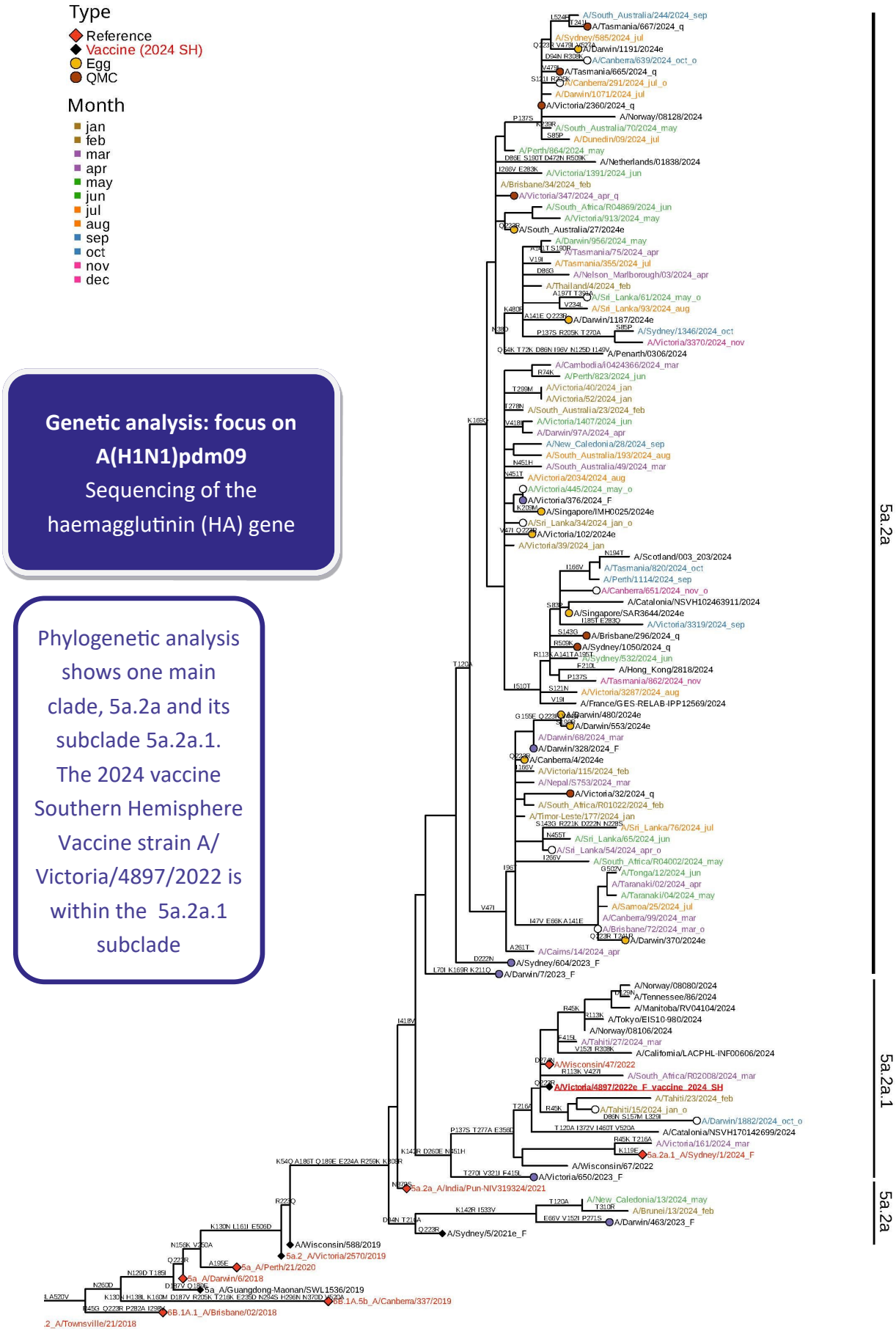
A total of 4366 viruses were tested using the haemagglutination inhibition (HI) assay.

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.*

Surveillance update: Virus activity 1 January—30 November 2024 continued



Genetic analysis: focus on A(H1N1)pdm09
Sequencing of the haemagglutinin (HA) gene

Phylogenetic analysis shows one main clade, 5a.2a and its subclade 5a.2a.1. The 2024 vaccine Southern Hemisphere Vaccine strain A/ Victoria/4897/2022 is within the 5a.2a.1 subclade

Surveillance update: Virus activity 1 January — 30 November 2024 continued

Antiviral drug susceptibility testing:
3076 viruses tested by neuraminidase inhibition (NAI) assay

Testing for susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir, and laninamivir showed that 11 viruses had highly reduced inhibition by Oseltamivir and Peramivir

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	1361	1	12	1362	1	11	1374	0	0	1374	0	0
A(H3N2)	1499	0	5	1504	0	0	1504	0	0	1499	5	0
B/Victoria	198	0	0	198	0	0	198	0	0	198	0	0
Total	**3058**	**1**	**17**	**3064**	**1**	**11**	**3076**	**0**	**0**	**3071**	**5**	**0**

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/VICTORIA/275/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/DARWIN/393A/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/DARWIN/478/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/DARWIN/486/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/SYDNEY/242/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/THAILAND/7/2024	Thailand	*	*	Normal Inhibition	Normal Inhibition

Viruses with highly reduced inhibition to one or more NAI continued

Type/subtype/lineage		Country of submitting laboratory	NAI(s) with highly reduced inhibition (marked with *)			
			Oseltamivir	Peramivir	Laninamivir	Zanamivir
A(H1N1)pdm09	A/PERTH/860/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/SOUTHAFRICA/ R04202/2024	South Africa	*	*	Normal Inhibition	Normal Inhibition
	A/SYDNEY/419B/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/SYDNEY/709/2024	Australia	*	*	Normal Inhibition	Normal Inhibition
	A/PERTH/1114/2024	Australia	*	*	Normal Inhibition	Normal Inhibition

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