# Influenza Updates

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

@WHOCCFluMelb

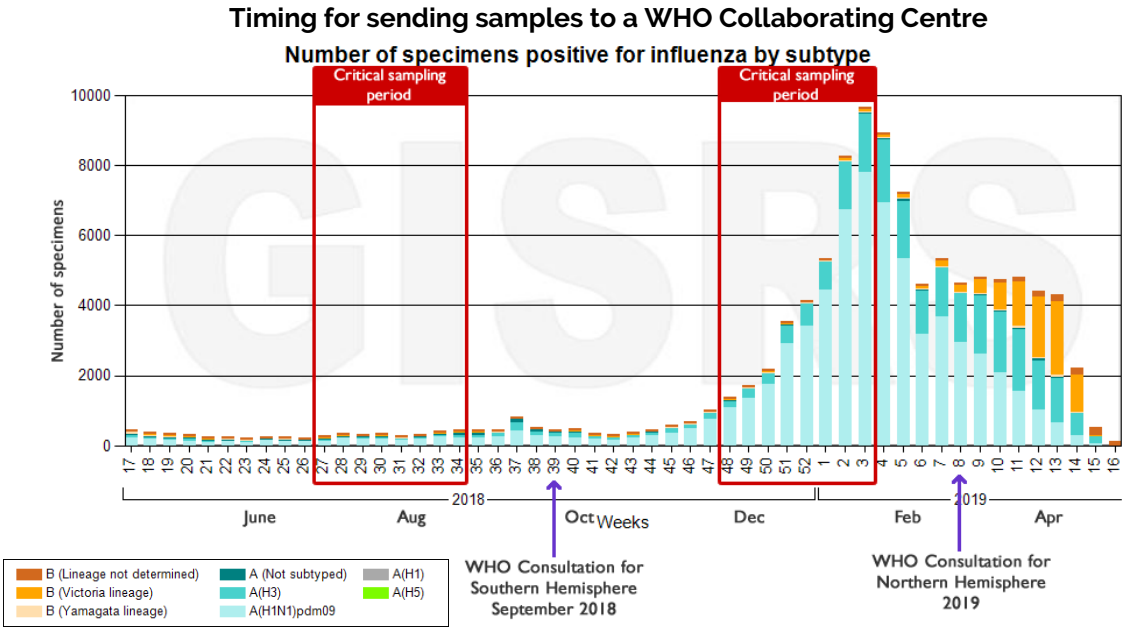
Volume 8, Issue 1, May 2019

## Preparation for the upcoming influenza season

The first few months of 2019 has seen unusually elevated levels of inter-seasonal influenza in most parts of Australia, and as such we been receiving a higher number of samples than usual for this time of year. We do not yet know whether this year's influenza season will be particularly severe in Australia or other countries with a similar seasonality. Nevertheless, with winter and/or the influenza season approaching over the next few month in many countries, we 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 2019.

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*.




*Circulation of influenza viruses, Western Pacific Region of WHO*
*Figure adapted from FluNet: http://www.who.int/influenza/gisrs_laboratory/flunet/en/*

WHO Collaborating Centre for Reference and Research on Influenza VIDRL

Doherty Institute

THE UNIVERSITY OF MELBOURNE

The Royal Melbourne Hospital

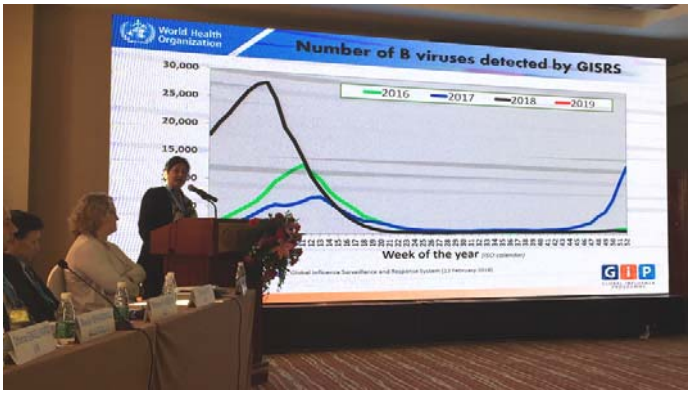
A joint venture between The University of Melbourne and The Royal Melbourne Hospital

## Recommendations for Northern Hemisphere 2019-2020 vaccine announced

The WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2019-2020 was held in Beijing, China on 18-20 February 2019. Following the Consultation, WHO made the following recommendation:

> *It is recommended that egg based quadrivalent vaccines for use in the 2019-2020 northern hemisphere influenza season contain the following:*
>
> - *an A/Brisbane/02/2018 (H1N1)pdm09-like virus;*
> - *an A/Kansas/14/2017 (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 the influenza B virus component of trivalent vaccines for use in the 2019-2020 northern hemisphere influenza season be a B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage.*
>
> *** The recommended A(H3N2) component was announced on 21 March 2019.*

The recommendation 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 2019). The change in the recommended A(H1N1)pdm09 component was based on differences in the response of recent circulating viruses to human post-vaccination sera compared to the cell- and egg-grown viruses of the previous A(H1N1)pdm09 vaccine strain.




*Centre director Kanta Subbarao presents data at the WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2019-2020.*

The recommendation for the A(H3N2) component of the vaccine was postponed by one month—such a delay is very unusual and has only happened once in the previous 20 years. The delay was due to the continual rapid evolution of circulating A(H3N2) viruses, and in particular a recent increase in the proportion of one group of antigenically distinct A(H3N2) viruses circulating in some countries. Postponing the recommendation enabled more time to monitor circulating viruses and characterise potential vaccine viruses. Ultimately, the recommended A(H3N2) component was changed due to differences in the antigenic properties of recently circulating viruses compared to the previous A(H3N2) vaccine strain.

### Contribution of National Influenza Centres to the vaccine

We thank everyone who sent us influenza samples in 2-3 months prior to the Consultation. Your viruses provided essential data on recently circulating strains and helped to inform the choice of recommended vaccine strains.

We are especially pleased that the newly recommended A(H1N1)pdm09 virus, **A/Brisbane/02/2018**, was originally submitted to our Centre by the Queensland Health Forensic and Scientific Services. This is in addition to **B/Phuket/3073/2013**, which was first included in the WHO vaccine recommendation in September 2014 and previously sent to the Centre by the Thai National Influenza Centre (Bangkok, Thailand) in 2013.

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.

## Australian Influenza Symposium and Australian Respiratory Virology Meeting

SAVE THE DATE: The 13th Australian Influenza Symposium will be held on 28–29 October 2019, followed by the Australian Respiratory Virology Meeting on 30th October. Both meetings will be held at the Queensland University of Technology, Brisbane.

An invitation to register and further details will be emailed to the symposium mailing list in coming months. If you have attended either of these meetings in the past you will be on the mailing list. If your contact details have changed or if you wish to be added to the mailing list, please register your details here. Details will also be provided on the Centre website: http://www.influenzacentre.org/news_symposium.htm

## 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 Chris, Rob and Aeron for their invaluable contributions to the Centre and the global influenza surveillance community over many years, and wish them all the very best for the future.

**Mr Chris Durrant** retired from his position as laboratory manager in June 2018 after 51 years' continuous service at the Centre and its predecessor at the Commonwealth Serum Laboratories (CSL). Chris was an integral member of the Centre's laboratory team and his longstanding knowledge of the Centre's processes and history will be missed.

**Mr Robert Shaw** retired from his position as Head of Antigenic Analysis in March 2019 after 29 years at the Centre. Rob joined the Centre two years prior to its designation as a WHO Collaborating Centre, and oversaw antigenic analyses of viruses for surveillance and vaccine development purposes.

**A/Prof Aeron Hurt** joined the Centre in 1999. As Head of Antiviral Drug Sensitivity, Aeron oversaw the establishment of routine testing of viruses for sensitivity to antiviral drugs for surveillance purposes since 2001. He also established a research group with interests in Antivirals and Animal Influenza Viruses. Aeron leaves the Centre in July 2019 to take up his new position as Principal International Medical Director – Influenza, at Roche in Switzerland.

## Upcoming meetings and conferences

Staff from our Centre will be attending and presenting posters and talks at the following meetings during 2019. Please contact us if you would like to meet us at any of these meetings.

**Australasian Ornithological Conference**
3–5 July 2019; Darwin, Australia
*https://www.aocdarwin.com/*
This conference provides a forum for the exchange of information and ideas between avian-based researchers and conservationists throughout the Australasian region. The conference will include a symposium on disease in birds, including avian influenza.

**Options X for the Control of Influenza**
28 August –1 September 2019; Singapore
*https://2019.isirv.org/*
This conference is held every 3-4 years and is the largest international conference focusing exclusively on influenza prevention, control and treatment, including seasonal influenza and pandemic preparedness.

**Communicable Diseases Control Conference 2019**
19–21 November 2019; Canberra, Australia
*https://www.phaa.net.au/events/event/communicable-diseases-control-conference-2019*
This theme of year's conference is *Controlling communicable diseases – mobilising evidence, action and partnerships*. This will include emergence or re-emergence of infectious agents, complex outbreaks, resistant microorganisms, genomics, and effective interventions, along with high rates of disease in rural and remote Australia.

**Australasian Virology Society (ASV10)**
2–5 December 2019; Queenstown, New Zealand *https://avs.org.au/avs-meetings/avs10-2019/*
This conference is held biennially to discuss recent advancements in virology and to facilitate the ongoing collaboration of virology professionals.

## Recent activity at the Centre (1 January — 30 April 2019)

Below is a summary of surveillance activities at the Centre from 1 January to 30 April. We have been especially busy for this time of year due to unusually elevated levels of influenza activity in Australia during the Southern Hemisphere summer. We anticipate that the next few months will continue to be busy as the Southern Hemisphere influenza season commences.

**Samples received**

The Centre received 2546 influenza samples from the laboratories and institutions listed below during the period 1 January—30 April 2019 .

AUSTRALIA: Canberra Hospital, Westmead Hospital, John Hunter Hospital, Lismore Base Hospital, Prince of Wales Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services, Sullivan Nicolaides Pathology, SA Pathology, Hobart Pathology, Royal Children's Hospital, Alfred Hospital, Monash Medical Center, Royal Children's Hospital Molecular Microbiology Department, Royal Melbourne Hospital, VIDRL, PathWest QEII Medical Centre

BRUNEI: RIPAS Hospital

CAMBODIA: Institut Pasteur du Cambodge

MACAU: Public Health Laboratory

NEW CALEDONIA: Institut Pasteur

NEW ZEALAND: Institute of Environmental Science and Research

PHILIPPINES: Research Institute for Tropical Medicine

SINGAPORE: National Public Health Laboratory

SOLOMON ISLANDS: National Referral Hospital

SRI LANKA: Medical Research Institute

THAILAND: Thai National Influenza Center

| | **Antigenic analysis:** A total of 1470 influenza isolates were analysed by HI assay. | | | | | **Neuraminidase inhibitor susceptibility:** A total of 1376 influenza isolates were tested by neuraminidase inhibition (NAI) assay for susceptibility to oseltamivir, zanamivir, peramivir and laninamivr. | | | | | **Genetic analysis:** Sequencing was performed on 492 HA, 482 NA, 381 MP and 14 NS genes from 496 viruses by Sanger sequencing or Next Generation Sequencing (NGS) techniques. | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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) | A mixed subtype | B/Victoria | B/Yamagata | A(H1N1)pdm09 | A(H3N2) | A mixed subtyped | B/Victoria | B/Yamagata | A(H1N1)pdm09 | A(H3N2) | A mixed | B/Victoria | B/Yamagata | Mixed type A/B |
| Australia | 683 | 313 | 1 | 25 | 28 | 611 | 290 | 4 | 26 | 38 | 131 | 194 | 1 | 15 | 23 | 2 |
| Brunei | 5 | 5 | | 1 | | 5 | 1 | | 1 | 4 | 2 | | | 1 | | |
| Cambodia | 39 | 1 | | 6 | 21 | 39 | 1 | | 6 | 21 | 1 | | | 3 | 5 | |
| Fiji | | 11 | | 1 | 16 | | 13 | | | 16 | | 3 | | | 6 | |
| Macau SAR | 29 | 10 | | 1 | | 29 | 10 | | 1 | | 8 | 5 | | 1 | | |
| Malaysia | 30 | 24 | | 23 | 19 | 29 | 24 | | 22 | 19 | 7 | 3 | | 18 | 8 | |
| New Caledonia | 2 | | | | | | | | | | | | | | | |
| New Zealand | 12 | | | | | | | | | | | 2 | | | | |
| Philippines | 13 | 2 | | 17 | | 13 | 2 | | 17 | 2 | 5 | | | 3 | | |
| Singapore | 21 | 16 | | 8 | 10 | 21 | 16 | | 8 | 10 | | | | | | |
| Sri Lanka | 7 | 13 | | 14 | 4 | 7 | 13 | | 14 | 4 | 4 | 9 | | 12 | 1 | |
| Thailand | 16 | 15 | | 3 | 5 | 16 | 15 | | 3 | 5 | 8 | 7 | | 3 | 5 | |
| **Total** | 857 | 410 | 1 | 99 | 103 | 770 | 385 | 4 | 98 | 119 | 166 | 223 | 1 | 56 | 48 | 2 |

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

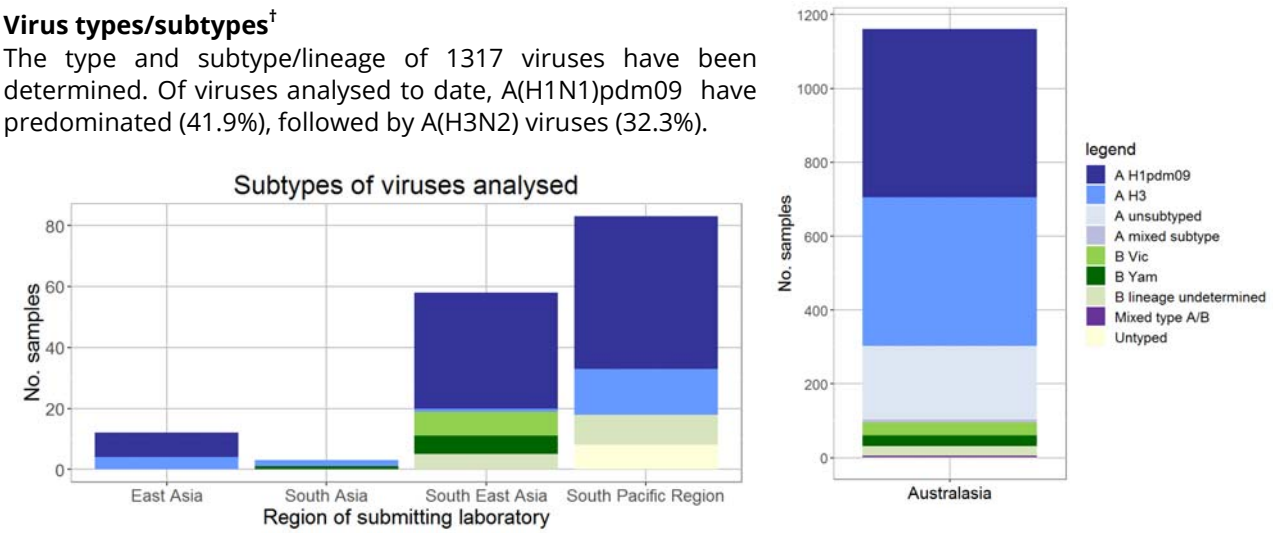
**Isolation of viruses in eggs**

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 January to 30 April 2019, 5 A(H1N1)pdm09, 8 A(H3N2) and 6 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 2019 that have been analysed at the Centre as of 7 May 2019.

**Virus types/subtypes**[†]

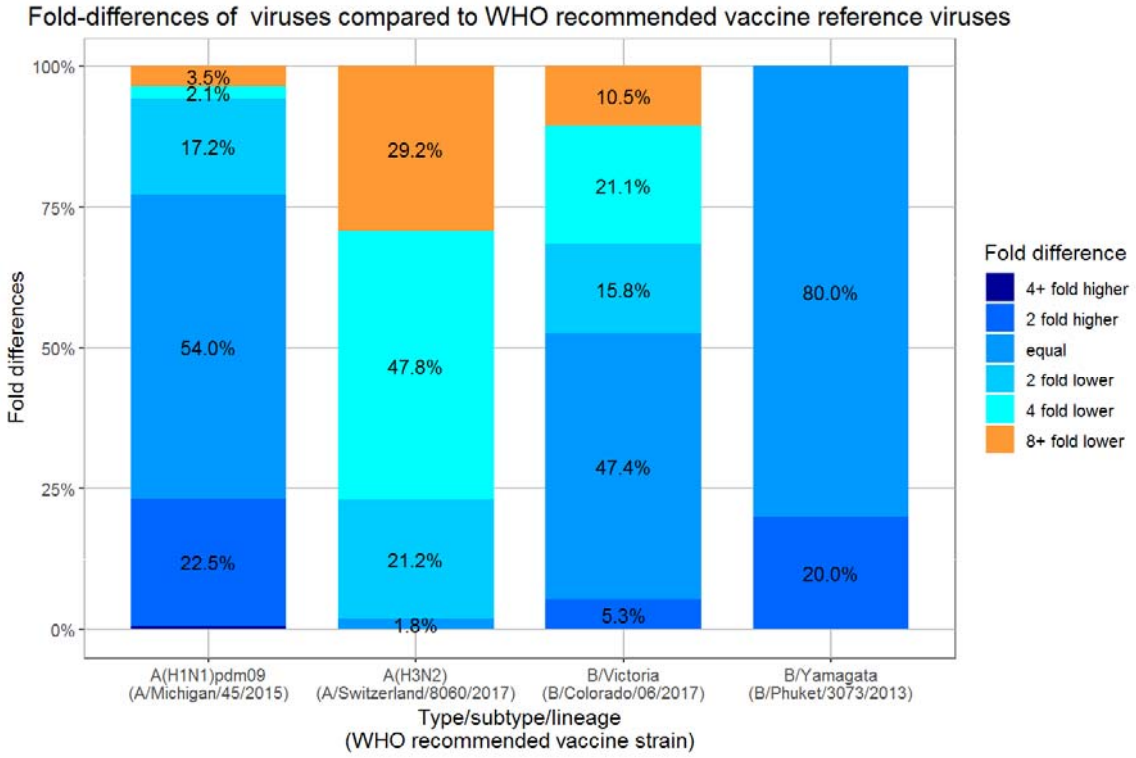
The type and subtype/lineage of 1317 viruses have been determined. Of viruses analysed to date, A(H1N1)pdm09 have predominated (41.9%), followed by A(H3N2) viruses (32.3%).




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

**Antigenic analysis**[†]

A total of 422 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 majority of viruses were antigenically similar to their respective 2019 Southern Hemisphere vaccine reference strains, however, a larger proportion of A(H3N2) viruses were low reactors to the A/Switerland/8060/2017 reference strain.

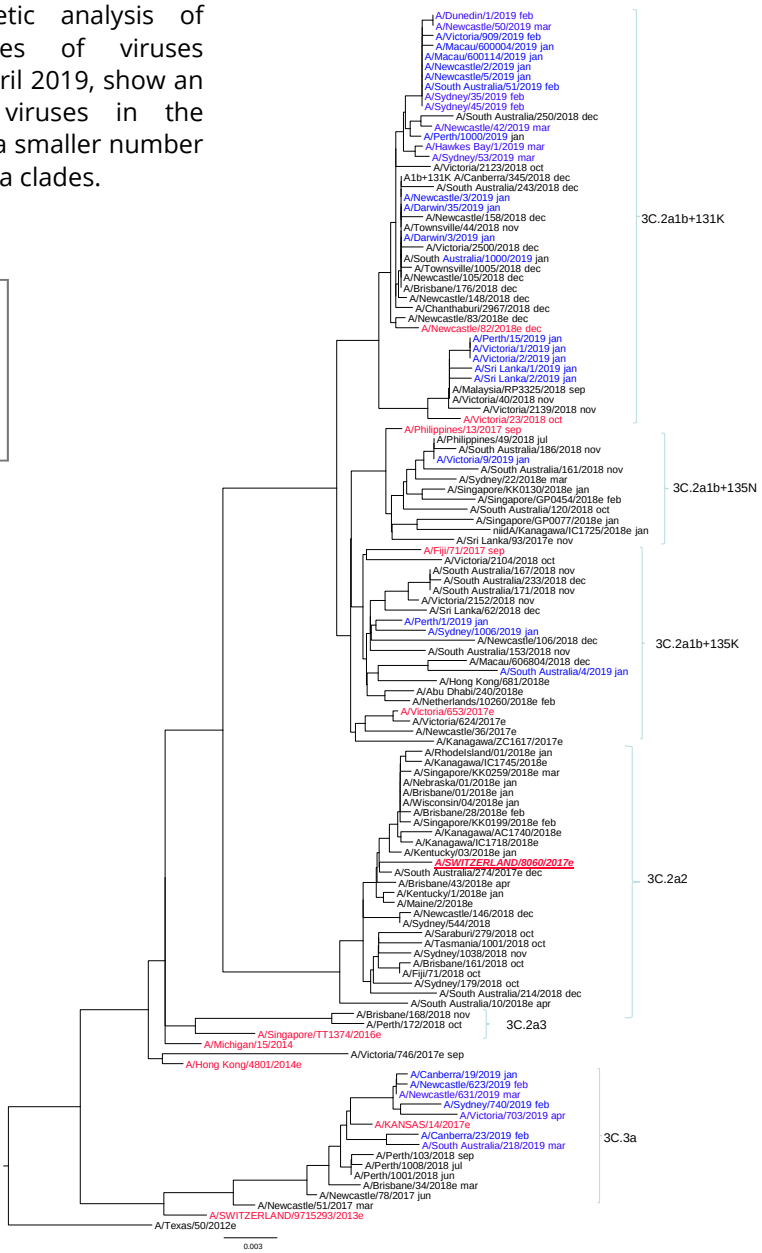



[†] *Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*

## Genetic analysis: focus on A(H3N2)

Sequencing and phylogenetic analysis of haemagglutinin (HA) genes of viruses circulating during January–April 2019, show an increasing proportion of viruses in the 3C.2a1b subclade, as well as a smaller number of viruses falling into the 3C.3a clades.

Legend
Reference strains
***CURRENT VACCINE STRAIN***
Viruses collected in 2019
} Brackets indicate clades
Scale bar represents 0.3% nucleotide sequence difference between viruses




## 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. Of 484 viruses tested, none showed highly reduced inhibition to any of the neuraminidase inhibitors.

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/subtype/ lineage† | No. viruses tested by NAI assay |
|---|---|
| A(H1N1)pdm09 | 248 |
| A(H3N2) | 195 |
| A mixed subtype | 2 |
| B/Victoria | 22 |
| B/Yamagata | 17 |

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



WHO Collaborating Centre for Reference and Research on Influenza
Peter Doherty Institute for Infection and Immunity
792 Elizabeth Street, Melbourne VIC 3000, Australia
ph: +61 3 9342 9300 Fax: +61 3 9342 9329
Email: whoflu@influenzacentre.org http://www.influenzacentre.org