Preparation for the upcoming influenza season

Winter and the influenza season is fast approaching over the next few months across many southern hemisphere countries. In fact, in Australia, the 2022 influenza season has started earlier than usual, with a big increase in cases in April and early May. Most of these cases are influenza A(H3N2), along with many A(H1N1)pdm09 infections seen in children. This means that any sample you are able to send to us will be vital in our continued surveillance efforts.

With this in mind, 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.

Figure adapted from FluNet: https://apps.who.int/flumart/Default?ReportNo=3&WHORegion=
Recommendations for Northern Hemisphere 2022-2023 vaccine announced

The WHO Consultation on the Composition of Influenza Vaccines for the northern hemisphere 2022-2023 was held as a hybrid Consultation on 25 February 2022. Following the Consultation, WHO made the following recommendation:

It is recommended that *quadrivalent* vaccines for use in the 2022-2023 northern hemisphere influenza season contain the following:

**Egg-based:**
- an A/Victoria/2570/2019 (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:**
- an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;
- an A/Darwin/6/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

The composition of trivalent influenza vaccines is recommended to include the A(H1N1)pdm09, A(H3N2), and the B Victoria lineage viruses.

The recommendations for the northern hemisphere 2022-2023 vaccine remain the same as the recommendations for the 2022 southern hemisphere vaccine. More details about the most recent recommendations can be found [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.

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.
Featured Research Articles

‘Influenza virus infection history shapes antibody responses to influenza infection’

And

‘Opposing effects of prior infection versus prior vaccination on vaccine immunogenicity against influenza A(H3N2) viruses’

Featuring Annette Fox, Sheena Sullivan, Kanta Subbarao, Ian Barr, Louise Carolan, Vivian Leung, Ryan Tseng, and Arseniy Khvorov from the Centre

Two studies on immune responses elicited from influenza vaccination were published in February.

The first article, published in Nature Medicine, showed that individuals who had prior exposure to influenza infection were likely to produce a better immune response when given the seasonal influenza vaccine. The study cohort for this nine year longitudinal study was established in Vietnam in collaboration with Oxford University and the National Institute of Hygiene and Epidemiology, Vietnam.

Both studies were predominantly led by Dr Annette Fox, in collaboration with A/Prof Sheena Sullivan.
‘Resurgence of avian influenza virus’

This Science Perspective article written by Dr Michelle Wille and Deputy Director Ian Barr outlines the facets to the resurgence of H5N1 avian influenza virus.

Since October 2021, there have been >3000 outbreaks of avian influenza lineage 2.3.4.4 H5N1, including both outbreaks in poultry and wild birds. In North America, for example, ~35 million birds have been culled since November 2021 when the first cases were recorded. In wild birds, there have been devastating outbreaks with thousands dying in mass mortality events. For example, the end of 2021 saw 8,000–10,000 Eurasian Cranes (Grus grus) die in Israel. Between November 2021 – March 2022, approximately 20% of Barnacle Geese (Branta leucopsis) died in the UK, and there is an ongoing outbreak in breeding Great Skuas (Stercorarius skua) due to this disease. Human cases of avian influenza are also of concern. While the risk for human transmission is low, this risk is higher for people who are in contact with poultry. To date, there have been cases in China, Laos, Russia, Nigeria, the UK, and the USA, for people who fall into this category.

Overall, H5Nx avian influenza is a One Health problem, that can likely only be solved with a One Health solution.

‘Australia as a global sink for the genetic diversity of avian influenza A virus’

Tying in with the above publication, this new study featuring Dr Michelle Wille has investigated how or if avian influenza viruses move between Australia and the northern hemisphere, how these viruses move within Australia, and whether the evolutionary genetics of Australian viruses are consistent with patterns from the northern hemisphere.

The study found that, while introductions of avian influenza from Asia and North America do occur, they are infrequent in many viral subtypes. Incursions were more common in subtypes detected as infrequent in duck populations, which highlights the important role of long distance migratory shorebirds in viral introductions. We found that virus exportation events from Australia were rare, with only a single instance. Essentially, viruses are introduced to Australia, then circulate and become extinct within Australia, suggesting that this country is a global sink for avian influenza diversity. Within Australia, virus movement is most common between adjacent states, with no clear movement corridors or directions.

Critically, this is the first holistic analysis of avian influenza genomes across Australia, comprising more than 300 unique genomes recovered from all states and most territories. This project relied on collaboration between national, state and university laboratories and research groups working together as part of the National Avian Influenza Wild Bird Program.

Building COVID-19 diagnostic capacity in the Solomon Islands

A recent article by the Peter Doherty Institute for Infection and Immunity covered the work that Prof Patrick Reading and Jean Moselen had done in the Solomon Islands to assist with strengthening molecular testing for SARS-CoV-2.

They were predominantly based at the National Referral Hospital molecular laboratory in Honiara.

This work was funded by the Department of Foreign Affairs and Trade Indo-Pacific Centre for Health Security through the COMBAT-AMR project.

To read the full article, please click here.

Upcoming meetings and conferences

The 11th OPTIONS meeting for the Control of INFLUENZA will be held this year on 26-29 September in Belfast, UK as a hybrid meeting. The abstract deadline has been extended until 25 May 2022, and early bird registration will close on 28 June 2022.

For more information, and to register for the event, please click here.

The 2022 NRL Asian Summit will be held this year on 23-24 May as a virtual event. The two day meeting will include regional speakers focusing on topics as they relate to quality in testing and provide a forum for interactive discussion by delegates.

Registration details and the full program can be accessed here.

Farewell and good luck

It is with sadness but good wishes that we announce the departure of two staff members from the Centre. We thank Gen and Ryan for their significant contributions to the Centre, and wish them all the very best for their future.

Ms Genevieve O’Neill had been a Medical Scientist with the Centre Epidemiology team for around 9 months. She has now taken on a role as an Epidemiologist in Lismore.

Dr Ryan Tseng had been a Post-Doctoral researcher with Dr Annette Fox’s research group for around 2 years. He has now taken on a position with Oxford Nanopore.
Recent activities at the Centre (1 January — 30 April 2022)

Below is a summary of surveillance activities at the Centre during this current reporting period. We have seen a significant rise in influenza activity compared to this time in 2021. We anticipate that the next few months will continue to be busy as the southern hemisphere influenza season returns.

Samples received: The Centre received 1338 influenza samples from the laboratories and institutions listed below during the period 1 January—30 April 2022.

AUSTRALIA: Canberra Hospital, 4Cyte Pathology, Westmead Hospital, John Hunter Hospital, Royal Darwin Hospital, QLD Health Forensic and Scientific Services (QHFSS), SA Pathology, Royal Hobart Hospital, Alfred Hospital, Austin Pathology, Australian Clinical Labs, Dorevitch Pathology Heidelberg, Eastern Health Pathology, Monash Medical Centre, Royal Children’s Hospital Molecular Microbiology Department (Bio21), Royal Melbourne Hospital, St Vincent’s Hospital, VIDRL, PathWest Laboratory Medicine (QEII)

FJI: Center for Communicable Disease Control
INDIA: National Institute of Virology
PHILIPPINES: Research Institute for Tropical Medicine
SINGAPORE: National Public Health Laboratory
SRI LANKA: Medical Research Institute
TIMOR-LESTE: Laboratório Nacional da Saúde

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 2022, 3 A(H1N1)pdm09 and 3 A(H3N2) viruses were successfully isolated in eggs at the Centre.
Recent activities at the Centre (1 January — 30 April 2022) continued

**Antigenic analysis**
212 viruses analysed by haemagglutination inhibition (HI) assay

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

**Sequencing**
282 viruses analysed
- 127 HA genes
- 82 NA genes
- 64 MP genes
- 55 NS genes

<table>
<thead>
<tr>
<th>Country of submitting laboratory</th>
<th>No. of viruses analysed by HI assay*</th>
<th>No. of viruses tested by NAI assay*</th>
<th>No. of viruses sequenced by NGS or Sanger sequencing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A(H1N1)pdm09</td>
<td>A(H3N2)</td>
<td>B lineage</td>
</tr>
<tr>
<td>Australia</td>
<td>35</td>
<td>186</td>
<td>2</td>
</tr>
<tr>
<td>Fiji</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>3</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Philippines</td>
<td>5</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Singapore</td>
<td>3</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timor-Leste</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>38</strong></td>
<td><strong>223</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>

* 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 April 2022

The data below are results for viruses collected or sampled between 1 January and 30 April 2022 that have been analysed at the Centre as of 3 May 2022.

**Virus types/subtypes**

The type and subtype/lineage of 631 viruses have been determined.

- 10.5% A(H1N1)pdm09
- 52.6% A(H3N2)
- 0.2% B/Victoria

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**Subtypes of viruses analysed**

<table>
<thead>
<tr>
<th>Region of submitting laboratory</th>
<th>No. samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>South East Asia</td>
<td>5</td>
</tr>
<tr>
<td>South Pacific Region</td>
<td>10</td>
</tr>
</tbody>
</table>

**Legend**

- A H1pdm09
- A H3
- A unsubtyped
- A mixed subtype
- B Vic
- B Yam
- B lineage undetermined
- Mixed type
- Untyped

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**Australasia**

<table>
<thead>
<tr>
<th>No. samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
</tr>
</tbody>
</table>

**Legend**

- A H1pdm09
- A H3
- A unsubtyped
- A mixed subtype
- B Vic
- B Yam
- B lineage undetermined
- Mixed type A/B
- Untyped
- C

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*Subtypes and lineages are based on analysis of the HA and in some cases confirmed by genetic analysis of NA.*
Viruses were identified as low-reactors if their titre against reference antiserum was at least 8-fold lower than the titre of the reference virus. All A(H1N1)pdm09 and B/Victoria viruses were antigenically similar to their respective reference strains. A small proportion (3.9%) of A (H3N2) viruses were low reactors to the reference strain, A/Darwin/6/2021.

*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 of the haemagglutinin (HA) gene

Phylogenetic analysis shows the majority cluster in the 3c.2a1b.2a.2 clade
Antiviral drug susceptibility testing:
187 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).

<table>
<thead>
<tr>
<th>Type/subtype/lineage</th>
<th>Oseltamivir</th>
<th>Peramivir</th>
<th>Laninamivir</th>
<th>Zanamivir</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal inhibition</td>
<td>Reduced inhibition</td>
<td>Highly reduced inhibition</td>
<td>Normal inhibition</td>
</tr>
<tr>
<td>A(H1N1)pdm09</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>171</td>
<td>171</td>
<td>171</td>
<td>171</td>
</tr>
<tr>
<td>B/Victoria</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>187</strong></td>
<td><strong>187</strong></td>
<td><strong>187</strong></td>
<td><strong>187</strong></td>
</tr>
</tbody>
</table>

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.