Recommended composition of influenza virus vaccines for use in the 2022 southern hemisphere influenza season

September 2021

WHO convenes technical consultations[1] in February and September each year to recommend viruses for inclusion in influenza vaccines[2] for the northern and southern hemisphere influenza seasons, respectively. This recommendation relates to the influenza vaccines for use in the southern hemisphere 2022 influenza season. A recommendation will be made in February 2022 relating to vaccines that will be used for the northern hemisphere 2022-2023 influenza season. For countries in tropical and subtropical regions, WHO recommendations for influenza vaccine composition (northern hemisphere or southern hemisphere) are available on the WHO Global Influenza Programme website[3].

Seasonal influenza activity

Greatly reduced numbers of influenza viruses were available for characterisation during the 01 February to 31 August 2021 time-period than in previous years. SARS-CoV-2 mitigation strategies including travel restrictions, use of personal protective equipment and social-distancing measures in several countries contributed to decreased influenza activity. Furthermore, public health and laboratory responses to the COVID-19 pandemic, caused by SARS-CoV-2, may have led to reduced influenza surveillance and/or reporting activities in some countries.

From February through August 2021, very low levels of influenza were reported in all regions, including from countries in the temperate zone of the southern hemisphere. During this period, influenza A(H1N1)pdm09, A(H3N2) and influenza B viruses circulated, although the proportions of the viruses circulating varied among reporting countries.

In the temperate zone of the northern hemisphere, influenza activity remained well below inter-seasonal norms with very low-level detections of influenza A and/or B viruses in most reporting countries. There were only sporadic detections of influenza A and B viruses in Europe with a predominance of influenza A viruses. Of the influenza A viruses where subtyping was performed, A(H1N1)pdm09 was detected more frequently than A(H3N2). Influenza virus detections were reported mainly by Denmark, Norway, Sweden, and the United Kingdom of Great Britain and Northern Ireland. In Asia, the proportions of influenza A and B viruses detected differed among reporting countries. In China, Pakistan, Qatar and Saudi Arabia, influenza B was predominant, while in the Democratic People's Republic of Korea, influenza A was predominant with A(H1N1)pdm09 and A(H3N2) viruses detected in almost equal proportions. Of the influenza B viruses in Asia where lineage was determined, the great majority belonged to the B/Victoria/2/87 lineage. In North America, equal proportions of influenza A and B viruses were reported. In Africa, Egypt reported influenza A(H3N2) and influenza B activity from April to July, with a predominance of A(H3N2) viruses. In other regions of the temperate zone of the northern hemisphere, there was little or no influenza activity reported during this period.

Influenza activity in tropical and subtropical countries was generally very low in comparison to influenza seasons prior to the COVID-19 pandemic. While influenza A and B were reported in varying

[1] https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/candidate-vaccine-viruses
[2] https://apps.who.int/gb/pip/pdf_files/Fluvaccvirusselection.pdf
[3] https://www.who.int/teams/global-influenza-programme/vaccines/vaccine-in-tropics-and-subtropics

proportions by countries in Africa and Asia, there was an overall predominance of influenza A viruses. In east African countries, there was a predominance of influenza A(H3N2), followed by influenza B and A(H1N1)pdm09, with the majority of these detections reported by Ethiopia, Kenya and United Republic of Tanzania. In central and west African countries, most influenza detections were reported by Cameroon, Côte d'Ivoire and Ghana, where A(H1N1)pdm09 dominated though A(H3N2) and influenza B also circulated. In the tropical countries of south and south-east Asia, influenza A(H3N2) was predominant in India, Lao People's Democratic Republic, Nepal, the Philippines, Thailand and Timor-Leste while influenza B predominated in Bangladesh. Of the influenza B viruses in Africa and Asia where lineage was determined, all belonged to the B/Victoria/2/87 lineage. Very few detections of influenza A and B viruses were reported from the tropical countries of Central America and the Caribbean, with a predominance of influenza B viruses and, where lineage was determined, all but one were B/Victoria/2/87 lineage. The majority of influenza detections from the Caribbean region were reported by Haiti. In other tropical and subtropical countries, there was little or no influenza activity reported.

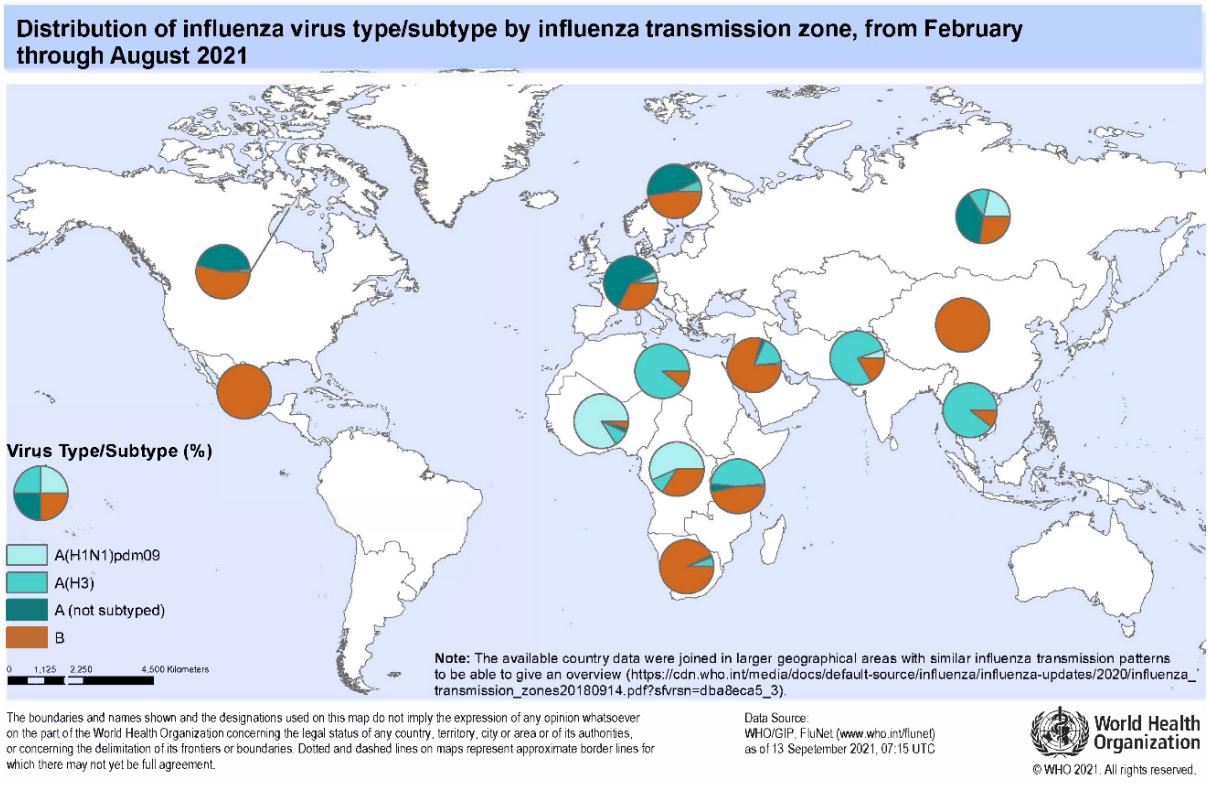
In the temperate zone of the southern hemisphere, very few influenza virus detections were reported and detection rates remained below seasonal epidemic thresholds despite testing being at usual or increased levels. In South Africa, both influenza A and B viruses were reported with a predominance of influenza B. Of the influenza B viruses where lineage was determined, only B/Victoria/2/87 lineage viruses were detected. There was little or no influenza activity reported in other countries.

Influenza A

Globally, influenza A viruses were detected in more countries than influenza B viruses. Influenza A(H1N1)pdm09 and A(H3N2) viruses were reported in most regions. In Africa, proportions of influenza A(H1N1)pdm09 and A(H3N2) varied among reporting countries. In east and north African countries, A(H3N2) was predominant while in central and west African countries, A(H1N1)pdm09 was dominant. In Asia, A(H3N2) viruses were predominant, and in south-east Asian countries it was the only influenza A subtype reported. In Europe, both A(H1N1)pdm09 and A(H3N2) viruses circulated with a predominance of A(H1N1)pdm09. In North America, equal proportions of influenza A(H1N1)pdm09 and A(H3N2) viruses were detected.

Influenza B

Globally, influenza B virus detections outnumbered those of influenza A during this period. Influenza B viruses predominated in Africa (United Republic of Tanzania, Ethiopia, Kenya, Madagascar and South Africa), Asia (Bangladesh, China, Oman, Pakistan, Qatar and Saudi Arabia), Europe (Sweden and the Russian Federation) and the Caribbean (Haiti). China reported the great majority of these detections. Where influenza B virus lineage was determined, nearly all were B/Victoria/2/87 lineage viruses with very few B/Yamagata/16/88 lineage viruses reported globally. None of the B/Yamagata/16/88 lineage viruses were available for characterisation.



Detailed information by country of the extent of seasonal influenza activity and type/subtype of viruses worldwide is available on the WHO website: https://www.who.int/tools/flunet

Antigenic and genetic characteristics of recent seasonal influenza viruses, human serology and antiviral susceptibility

Influenza A(H1N1)pdm09 viruses

A(H1N1)pdm09 viruses that have circulated since September 2020 have haemagglutinin (HA) genes that belong to phylogenetic clades 6B.1A5 and 6B.1A7, with the vast majority clustering within subclade 6B.1A5A, characterised by HA1 amino acid substitutions N129D, T185I and N260D. Subclade 6B.1A5A (**5A**) has further diverged into two major groups defined by HA amino acid substitutions: **5A1** (formerly 5A-187A), characterised by D187A and Q189E (located in HA antigenic site Sb) and **5A2** (formerly 5A-156K) defined by K130N, N156K (located in antigenic site Sa), L161I, V250A in HA1 and E179D in HA2 (E506D). Viruses belonging to both groups have circulated during 2020-2021. Since February 2021, **5A1** viruses had predominated but **5A2** viruses have been detected recently in India and in travellers returning to Australia from India.

The antigenic characteristics of A(H1N1)pdm09 viruses were assessed with post-infection ferret antisera in haemagglutination inhibition (HI) assays. However, only a limited number of viruses with collection dates after January 2021 were available for antigenic analysis. Results showed that **5A1** viruses were well recognised by antisera raised against the 2020-2021 northern hemisphere vaccine viruses (egg-propagated A/Guangdong-Maonan/SWL1536/2019 and cell culture-propagated A/Hawaii/70/2019). However, **5A2** viruses were poorly recognised by these antisera. Antisera raised against the 2021 southern hemisphere vaccine viruses (egg-propagated A/Victoria/2570/2019 and cell culture-propagated A/Wisconsin/588/2019) recognised **5A2** viruses well, but showed poor recognition of **5A1**, and 6B.1A7 viruses, which retain N156 in HA1.

Human serology studies used 15 serum panels, from children (6 months to 17 years), adults (18-64 years) and older adults (≥65 years) who had received egg-based quadrivalent inactivated vaccines (standard, high dose or with adjuvant) or cell culture-based quadrivalent inactivated vaccine. Egg-based vaccine formulations for the northern hemisphere in 2020-2021 (NH 2020-21: 13 serum panels) contained antigens from A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like, A/Hong Kong/2671/2019 (H3N2)-like, B/Washington/02/2019-like (B/Victoria lineage) and B/Phuket/3073/2013-like (B/Yamagata lineage) viruses. Cell culture-based NH 2020-21 vaccines contained A/Hawaii/70/2019 (H1N1)pdm09-like and A/Hong Kong/45/2019 (H3N2)-like virus antigens as well as the required influenza B components. The vaccine formulations for the southern hemisphere in 2021 (SH 2021: 2 serum panels) contained a change in the A(H1N1)pdm09 component. The egg- and cell culture-based vaccines contained A/Victoria/2570/2019 (H1N1)pdm09-like and A/Wisconsin/588/2019 (H1N1)pdm09-like viruses, respectively.

In serum panels from recipients of NH 2020-21 vaccines, when compared to titres against cell culture-propagated A/Hawaii/70/2019 (H1N1)pdm09-like **5A1** vaccine viruses, post-vaccination HI geometric mean titres (GMTs) against cell culture-propagated **5A2** viruses were significantly reduced in almost all serum panels. GMTs against most cell culture-propagated **5A1** viruses were not significantly reduced. In serum panels from recipients of SH 2021 vaccines, when compared to titres against cell culture-propagated A/Wisconsin/588/2019 (H1N1)pdm09-like **5A2** vaccine viruses, post-vaccination HI GMTs against the majority of recent **5A1** and **5A2** cell culture-propagated viruses were not significantly reduced.

Of 133 A(H1N1)pdm09 viruses collected after January 2021 and examined by genetic or phenotypic analysis, none showed evidence of reduced inhibition by neuraminidase inhibitors. Of 124 A(H1N1)pdm09 viruses analysed, one had a PA amino acid substitution (E23K) associated with reduced susceptibility to the endonuclease inhibitor baloxavir.

Influenza A(H3N2) viruses

Phylogenetic analysis of the HA gene of A(H3N2) viruses collected from February through August 2021 showed the vast majority fell into genetic clade 3C.2a1b with three subclades: 3C.2a1b.**1a** (also called T135K-A) with HA1 substitutions T135K (resulting in the loss of a glycosylation site), A138S, G186D, D190N, F193S and S198P; 3C.2a1b.**1b** (also called T135K-B) with HA1 substitutions T135K (resulting in the loss of a glycosylation site), S137F, A138S and F193S; and 3C.2a1b.**2a** (also called T131K-A) with HA1 substitutions K83E, Y94N and T131K. The **2a** HA genes continue to diversify and formed two subgroups referred to as **2a1**, with additional HA1 substitutions G186S, F193S, Y195F and S198P, and **2a2** with additional HA1 substitutions Y159N, T160I (resulting in the loss of a glycosylation site), L164Q, G186D, D190N, F193S and Y195F. **1a** viruses were detected in west African countries (Côte d'Ivoire, Ghana and Togo) as well as in Sweden and the Philippines. More recent **2a1** viruses were also detected in south-east Asia (Cambodia, Lao People's Democratic Republic, Thailand and Timor-Leste), Japan and Australia. **2a2** viruses, which represented the largest proportion during this period, were found in south Asia (India and Nepal), south-east Asia (Singapore and the Philippines), the Middle East (Qatar, Saudi Arabia and United Arab Emirates), east Africa (Kenya), Oceania (Australia and New Zealand), North America (the United States of America) and Europe (Belgium, Norway, the Russian Federation, Sweden and the Netherlands). Two viruses with clade 3C.3a HA genes were detected in this period in Australia and the Philippines.

Antigenic characterisation of A(H3N2) viruses was performed by HI and virus neutralization (VN) assays. Ferret antisera raised against cell culture-propagated A/Hong Kong/45/2019-like viruses (**1b**: e.g.

A/Darwin/726/2019), representing the cell/recombinant-based vaccine viruses for the NH 2020-21 and SH 2021 influenza seasons, recognised **1a** viruses well. Of the two new virus groups that have emerged, those in **2a1** were recognised less well and those in **2a2** were recognised poorly. Ferret antisera raised against egg-propagated A/Hong Kong/2671/2019-like viruses (**1b**), representing the egg-based vaccine viruses for the NH 2020-21 and SH 2021 influenza seasons, recognised all test viruses poorly.

In HI assays, viruses with HA genes belonging to 3C.2a1b subclades **1a** and **2a1** were recognised well by ferret antisera raised against cell culture-propagated A/Cambodia/e0826360/2020 (NH 2021-22 **2a1** vaccine virus) while **2a2** viruses were recognised less well (Table 1). Ferret antisera raised against egg-propagated A/Cambodia/e0826360/2020 showed a similar pattern. In contrast, ferret antisera raised against **2a2** viruses, such as cell culture-propagated A/Darwin/6/2021 or egg-propagated A/Darwin/9/2021, reacted well with **2a2** viruses but reacted poorly with **2a1**, **1a** and clade 3C.3a viruses (Table 1).

Table 1: Antigenic Analysis of A(H3N2) Viruses – HI Assay

			Reference Ferret Antisera							
			CELL	EGG	CELL	EGG	CELL	QMC*	EGG	
			Darwin/ 726	Hong Kong/2671	Cambodia/ e0826360	Cambodia/ e0826360	Darwin/6	Darwin/ 11	Darwin/ 9	
Reference Antigens	**Passage**	**Clade**	**3C.2a1b. 1b**		**3C.2a1b. 2a1**		**3C.2a1b. 2a2**			**Collection Dates**
A/Darwin/726/2019	SIAT2	3C.2a1b.1b	**640**	40	160	<40	<40	<40	<40	
A/Hong Kong/2671/2019	E9	3C.2a1b.1b	1280	**640**	80	160	80	80	160	
A/Cambodia/e0826360/2020	SIAT2	3C.2a1b. 2a1	40	<40	**320**	40	<40	40	80	
A/Cambodia/e0826360/2020	E5	3C.2a1b. 2a1	40	40	160	**320**	160	40	160	
A/Darwin/6/2021	SIAT2	3C.2a1b. 2a2	<40	<40	40	80	**640**	160	160	
A/Darwin/11/2021	QMC2	3C.2a1b. 2a2	40	<40	160	80	640	**160**	160	
A/Darwin/9/2021	E4	3C.2a1b. 2a2	40	<40	160	160	640	320	**320**	
Test Antigens										
A/Philippines/1/2021	SIAT1	3C.2a1b.1a	320	<40	160	<40	<40	<40	<40	14-05-21
A/Philippines/8/2021	SIAT1	3C.2a1b.1a	320	<40	160	<40	<40	<40	<40	13-07-21
A/Yamagata/1/2021	SIAT1	3C.2a1b.2a1	40	<40	320	40	<40	40	80	09-02-21
A/Darwin/17/2021	SIAT1	3C.2a1b.2a2	<40	<40	40	80	640	160	160	11-08-21
A/Darwin/18/2021	SIAT1	3C.2a1b.2a2	<40	<40	40	80	1280	160	160	11-08-21
A/Darwin/19/2021	SIAT1	3C.2a1b.2a2	<40	<40	40	80	1280	160	160	11-08-21
A/Darwin/23/2021	SIAT1	3C.2a1b.2a2	<40	<40	<40	40	320	80	80	12-08-21
A/Darwin/24/2021	SIAT1	3C.2a1b.2a2	<40	<40	40	80	320	160	160	12-08-21
A/Nepal/NPWR-05637/2021	SIAT1	3C.2a1b.2a2	80	40	160	160	320	160	320	08-04-21
A/Philippines/4/2021	SIAT1	3C.2a1b.2a2	<40	<40	160	80	640	160	160	24-06-21
A/Victoria/5/2021	SIAT2	3C.2a1b.2a2	<40	<40	40	80	320	160	160	11-08-21
A/Philippines/6/2021	SIAT1	3C.3a	<40	<40	40	<40	80	40	40	05-07-21

*Qualified Manufacturing Cell line (MDCK33016PF)

Human serology studies were conducted with serum panels as described above using HI and VN assays. When compared to titres against cell culture-propagated A/Hong Kong/45/2019-like vaccine viruses, post-vaccination GMTs of most serum panels were significantly reduced against the majority of cell culture-propagated **2a1** and **2a2** viruses. Reductions were less pronounced for **1a** and clade 3C.3a viruses.

Of 105 A(H3N2) viruses collected after January 2021 and examined by genetic or phenotypic analysis, none showed evidence of reduced inhibition by neuraminidase inhibitors. Of 125 A(H3N2) viruses collected in this period, none showed evidence of reduced susceptibility to baloxavir.

Influenza B viruses

Globally, influenza B viruses of the B/Victoria/2/87 lineage accounted for 60% of the viruses typed during the period February through August 2021. No B/Yamagata/16/88 lineage viruses have been confirmed after March 2020.

HA gene sequences of characterised B/Victoria lineage viruses belonged to clade 1A, nearly all belonging to subclade 1A.3 (also called 1A(△3)B) which share a three amino acid deletion in HA1 (positions 162-164) and the substitution K136E. Viruses with HA genes encoding further substitutions of N150K, G184E, N197D (resulting in the loss of a glycosylation site) and R279K in HA1 have predominated (group 1A.**3a**), with two main subgroups having emerged. One subgroup had additional HA1 substitutions V220M and P241Q (**3a1**) which was seen almost exclusively in China, and the other had HA1 substitutions A127T, P144L and K203R (**3a2**) which was seen in Asia, Africa, Oceania, Europe and North America. While **3a1** viruses predominated in China earlier in 2021, the number and the proportion of **3a2** viruses have increased steadily over recent months to become predominant. **3a2** viruses have shown further genetic divergence with additional HA1 amino acid substitutions identified in viruses from certain geographic locations.

Post-infection ferret antisera raised against both cell culture- and egg-propagated B/Washington/02/2019-like (1A.3) viruses recognised **3a** viruses poorly. Antisera raised against B/Sichuan-Jingyang/12048/2019-like viruses (**3a1**) inhibited viruses in this subgroup well but inhibited **3a2** viruses less well. Antisera raised against B/Austria/1359417/2021-like viruses (**3a2**) inhibited viruses from this subgroup well but inhibited **3a1** viruses less well and B/Washington/02/2019-like viruses poorly (Table 2).

Table 2: Antigenic Analysis of B/Victoria Lineage Viruses – HI assay

			Reference Ferret Antisera					
			CELL	CELL	EGG	CELL	EGG	
			B/Washington/02/2019	B/Sichuan-Jingyang/12048/2019		B/Austria/1359417/2021		
Reference Antigens	Passage	Clade/Subgroup	1A.3	1A.3a1		1A.3a2		Collection Dates
B/Washington/02/2019	MDCK4	1A.3	**160**	160	80	40	20	
B/Sichuan-Jingyang/12048/2019	MDCK3	1A.3a1	80	**1280**	1280	160	160	
B/Sichuan-Jingyang/12048/2019	E3	1A.3a1	80	>2560	**>2560**	160	320	
B/Austria/1359417/2021	MDCK7	1A.3a2	80	640	640	**1280**	>2560	
B/Austria/1359417/2021	E3	1A.3a2	80	320	640	1280	**>2560**	
Test Antigens								
B/Hubei-Wujiagang/1299/2021	MDCK3	1A.3a1	80	>2560	1280	160	160	2021-03-18
B/Henan-Shanyang/37/2021	MDCK3	1A.3a1	80	>2560	1280	160	320	2021-03-29
B/Fujian-Zhangpu/34/2021	MDCK3	1A.3a1	80	>2560	1280	160	320	2021-03-22
B/Cote d'Ivoire/1063/2020	MDCK5	1A.3a2	40	640	320	640	1280	2021-01-25
B/Singapore/WUH4855/2021	MDCK1	1A.3a2	40	320	640	640	1280	2021-06-20
B/Gansu-Baiyin/1281/2021	MDCK3	1A.3a2	<20	320	640	640	1280	2021-04-13
B/Henan-Xigong/1118/2021	MDCK3	1A.3a2	40	640	640	1280	>2560	2021-02-17
B/Gansu-Chengguan/1515/2021	MDCK3	1A.3a2	<20	320	640	1280	640	2021-03-30
B/Singapore/WUH4618/2021	MDCK1	1A.3a2	40	640	640	1280	>2560	2021-06-18
B/Victoria/2/2021	MDCK1	1A.3a2	80	640	640	1280	>2560	2021-07-08
B/Philippines/6/2021	MDCK1	1A.3a2	40	640	640	1280	>2560	2021-06-14
B/Philippines/8/2021	MDCK1	1A.3a2	80	640	320	1280	1280	2021-07-05

Serum panels from recipients of both NH 2020-2021 and SH 2021 vaccines described above, with one additional NH 2020-2021 serum panel from children, were used in human serology studies of B/Victoria lineage viruses. When compared to titres against cell culture-propagated B/Washington/02/2019-like vaccine virus, post-vaccination HI GMTs against some cell culture-propagated **3a1** viruses were significantly reduced. With the exception of sera from older adults, reductions in titres to many **3a2** viruses were observed in most other serum panels.

B/Yamagata lineage viruses with collection dates after March 2021 were not available for characterisation and no serology studies were performed.

Of 1047 influenza B/Victoria lineage viruses collected after January 2021 and examined by genetic or phenotypic analysis, none showed evidence of reduced inhibition by neuraminidase inhibitors. Of 617 B/Victoria lineage viruses collected in this period, none showed evidence of reduced susceptibility to baloxavir.

Recommended composition of influenza virus vaccines for use in the 2022 southern hemisphere influenza season

Influenza A(H1N1)pdm09 viruses collected in the period February through August 2021 had HA genes that fell into two groups, 6B.1A**5A1** and 6B.1A**5A2**. Of these, 6B.1A**5A1** viruses had predominated since February 2021, and 6B.1A**5A2** viruses have been detected recently. Ferret antisera raised against the SH 2021 vaccine viruses (egg-propagated A/Victoria/2570/2019 and cell culture-propagated A/Wisconsin/588/2019) inhibited 6B.1A**5A1** viruses poorly, but 6B.1A**5A2** viruses well. Human serology assays showed no significant reduction of post-vaccination GMTs against recently circulating 6B.1A**5A1** and 6B.1A**5A2** viruses.

Most A(H3N2) viruses collected in the period February through August 2021 had HA genes that belonged to genetic groups 3C.2a1b.**2a1** and 3C.2a1b.**2a2**. The majority of recently circulating viruses were 3C.2a1b.**2a2** and were poorly recognised by ferret antisera raised against cell- and egg- propagated reference viruses representing the A(H3N2) vaccine components of the SH 2021 influenza season. However, ferret antisera raised against 3C.2a1b.**2a2** viruses, such as cell culture-propagated A/Darwin/6/2021 or egg-propagated A/Darwin/9/2021, inhibited 3C.2a1b.**2a2** test viruses well. Human serology assays showed post-vaccination GMTs were significantly reduced against circulating 3C.2a1b.**2a1** and 3C.2a1b.**2a2** viruses.

All influenza B viruses collected in the period February through August 2021 were of the B/Victoria/2/87 lineage. Most recent viruses belonged to the antigenically distinct 1A.**3a1** (V220M and P241Q) or 1A.**3a2** (A127T, P144L and K203R) groups, with the latter showing a wider geographic spread. The great majority of these viruses showed reductions in inhibition by post-infection ferret antisera raised against both cell culture- and egg-propagated 1A.3 viruses, such as the current vaccine virus B/Washington/02/2019. Post-infection ferret antisera raised to B/Austria/1359417/2021-like viruses (1A.**3a2**) inhibited viruses from this group well. Human serology assays showed significant reduction of post-vaccination GMTs against 1A.**3a1** and 1A.**3a2** viruses. No B/Yamagata lineage viruses were available for characterisation.

The WHO recommends that quadrivalent vaccines for use in the 2022 southern hemisphere influenza season contain the following:

Egg-based vaccines

- **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 vaccines

- **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 WHO recommends that trivalent vaccines for use in the 2022 southern hemisphere influenza season contain the following:

Egg-based vaccines

- **an A/Victoria/2570/2019 (H1N1)pdm09-like virus;**
- **an A/Darwin/9/2021 (H3N2)-like virus; and**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.**

Cell- or Recombinant-based vaccines

- **an A/Wisconsin/588/2019 (H1N1)pdm09-like virus;**
- **an A/Darwin/6/2021 (H3N2)-like virus; and**
- **a B/Austria/1359417/2021 (B/Victoria lineage)-like virus**

Lists of prototype viruses for egg-propagated, cell culture-propagated and recombinant-based vaccines together with candidate vaccine viruses (CVVs) suitable for use in human vaccine production are available on the WHO website [4]. A list of reagents for vaccine standardization, including those for this recommendation, can also be found on the WHO website.

National or regional authorities approve the composition and formulation of vaccines used in each country. National public health authorities are responsible for making recommendations regarding the use of the vaccine. WHO has published recommendations on the prevention of influenza[5].

CVVs (including reassortants) and reagents for use in the laboratory standardization of inactivated vaccines may be obtained from:

- Biotherapeutics Section, Laboratories Branch, Medical Devices and Product Quality Division, Therapeutic Goods Administration, P.O. Box 100, Woden, ACT, 2606, Australia (email: influenza.reagents@health.gov.au; website: http://www.tga.gov.au)
- Division of Virology, National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, United Kingdom of Great Britain and Northern Ireland

[4] https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/candidate-vaccine-viruses
[5] https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/

(fax: +441707641050, email: enquiries@nibsc.org),
website: http://www.nibsc.org/science_and_research/virology/influenza_resource_.aspx)

- Division of Biological Standards and Quality Control, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, Maryland, 20993, the United States of America (email: cbershippingrequests@fda.hhs.gov)
- Centre for Influenza and Respiratory Virus Research, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81425616156,
email: flu-vaccine@nih.go.jp)

Requests for reference viruses should be addressed to:

- WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, Peter Doherty Institute, 792 Elizabeth Street, Melbourne, Victoria 3000, Australia (fax: +61393429329, email: whoflu@influenzacentre.org, website: http://www.influenzacentre.org).
- WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81425616149 or +81425652498, email: whocc-flu@nih.go.jp).
- WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop H17-5, Atlanta, GA 30329, the United States of America (fax: +14046390080, email: influenzavirussurveillance@cdc.gov, website: http://www.cdc.gov/flu/)
- WHO Collaborating Centre for Reference and Research on Influenza, The Francis Crick Institute, 1 Midland Road, London NW1 1AT, United Kingdom of Great Britain and Northern Ireland (tel: +44 203 796 1520 or +44 203 796 2444, email: whocc@crick.ac.uk, website: http://www.crick.ac.uk/research/worldwideinfluenza-centre)
- WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Viral Disease Control and Prevention, China CDC, 155 Changbai Road, Changping District, 102206, Beijing, China. (tel: +86 10 5890 0851, fax: +86 10 5890 0851, email: whocc-china@cnic.org.cn, website: http://www.chinaivdc.cn/cnic/en)

WHO provides fortnightly updates [6] of global influenza activity. Other information about influenza surveillance can be found on the WHO Global Influenza Programme website[7].

Acknowledgements

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[6] https://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/influenza-updates
[7] https://www.who.int/teams/global-influenza-programme

Vaccine Effectiveness (GIVE) Collaboration for sharing estimates of influenza vaccine effectiveness on a confidential basis.

Annex 1

Declarations of interest

The WHO recommendation on the composition of influenza vaccines for use in the southern hemisphere 2022 influenza season was made through a WHO Consultation with relevant WHO Collaborating Centres on Influenza (CCs) and Essential Regulatory Laboratories (ERLs).

In accordance with WHO policy, Directors and experts of the relevant WHO CCs and ERLs, in their capacity as representatives of their respective institutions ("Advisers"), completed the WHO form for Declaration of Interests for WHO experts before being invited to the Consultation. At the start of the Consultation, the interests declared by the Advisers were disclosed to all participants.

The Advisers declared the following personal current or recent (within the past 4 years) financial or other interests relevant to the subject of work:

Institution	Representative	Personal interest
WHO ERL TGA Canberra	Dr Pearl Bamford	None
WHO ERL NIBSC London	Dr Othmar Engelhardt	All items declared and listed below belong to Dr Engelhardt's Research Unit in the form of contract research and grants from: IFPMA; WHO; Deptartment of Health, United Kingdom; European Commission; BARDA/HHS, USA; Innovative Medicines Initiative; PATH; Bill and Melinda Gates Foundation and MRC-AMED adhered to the Medicines and Healthcare Products Regulatory Agency of the United Kingdom Government Department of Health.
WHO CC Koltsovo	Dr Elena Gavrilova	None
WHO CC and ERL NIID Tokyo	Dr Hideki Hasegawa	None
WHO CC London	Dr John McCauley	Following items were declared: • Served on an organizing committee for an educational flu awareness meeting/symposium/teleconferences organized by Seqirus. No payment received. • Served as an advisor on antiviral drug (Baloxavir) and attended a meeting on new influenza inhibitors organized by Roche as part of an ISIRV Antiviral Group. No payment received. • Serving as an advisor on RNA vaccines to Pfizer. No payment received. • Serving as an advisor on carbohydrate-based diagnostics, including influenza to Iceni Diagnostics. No payment received.

		• Member of the advisory committee for the Global Influenza Hospital Surveillance Network. No payment received. • Participant in the Global Influenza Initiative by Sanofi Pasteur. No payment received. The items declared and listed below belong to Dr McCauley's Research Unit: • Received significant financial support for research activities on annual basis from IFPMA for isolation of influenza viruses in hens' eggs as potential vaccine strains for development as influenza vaccine strains for the period from July 2010- June 2021 • Daily expenses reimbursed by the European Medicines Agency for participation in the meeting on the outcome of Northern Hemisphere WHO Vaccine Selection Meeting to European Medicines Agency to provide advice for European Regulations for the vaccine.
WHO CC Melbourne	Dr Kanta Subbarao	All items declared and listed below belong to Dr Subbarao's Research Unit: • Received significant financial support for research activities CRADA from Seqirus for development of cell-based manufacturing technologies. Ceased 2019. • Received significant financial support for research activities from IFPMA for isolation of influenza viruses in hens' eggs as potential vaccine strains for development as influenza vaccine strains. Ceased 2019. • Received non-monetary support from Roche, GSK, Biocrvst and Romark with supply of antiviral drugs for use in antiviral drug sensitivity testing for surveillance and research purposes. Value not determined. • Received non-monetary support from CSL Limited/Seqirus in the form of Service Agreement for access to animal facilities and provision of some materials. Value not determined. Being co-owner with NIH of a patent: Influenza Hemagglutinin and Neuraminidase

		Variants, USA Patent Number: 7,504,109 B2, 17 March 2009. The patent ceased in 2018. No benefit generated or expected from it.
WHO CC Beijing	Dr Dayan Wang	None
WHO CC Memphis	Dr Richard Webby	None
WHO CC Atlanta	Dr David Wentworth	Below item declared and listed below belong to Dr Wentworth's Research Unit: • Received significant financial support for research activities (Collaborative research and development agreement (CRADA)) from Seqirus for development of cell-based manufacturing technologies. Being co-inventor with others and employers: • Intellectual Property in a patent on influenza reassortment and another on modified bat influenza viruses and their uses. Both are USA patents and are not licensed.
WHO ERL CBER Bethesda	Dr Zhiping Ye	None

Based on the WHO assessment, the interests declared by Drs McCauley, Subbarao, Engelhardt and Wentworth were determined not to present a conflict of interest with the objectives of the WHO consultation. Therefore it was concluded that with disclosure at the beginning of the consultation to all participants, Drs McCauley, Subbarao, Engelhardt and Wentworth should continue to serve as Advisers.