Recommended composition of influenza virus vaccines for use in the 2024-2025 northern hemisphere influenza season

February 2024

WHO convenes technical consultations\(^1\) in February and September each year to recommend viruses for inclusion in influenza vaccines\(^2\) for the northern hemisphere (NH) and southern hemisphere (SH) influenza seasons, respectively. This recommendation relates to the influenza vaccines for use in the NH 2024-2025 influenza season. A recommendation will be made in September 2024 relating to vaccines that will be used for the SH 2025 influenza season. WHO guidance for choosing between the northern and southern hemisphere formulations for countries in tropical and subtropical regions is available on the WHO Global Influenza Programme website\(^3\).

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\(^4\).

Seasonal influenza activity

From September 2023 through January 2024, influenza activity was reported in all transmission zones and overall activity was similar compared to the same reporting period in 2023. The predominant viruses varied among zones and between countries.

In Africa, influenza A and B viruses co-circulated, with predominance of influenza A and roughly equal circulation of A(H1N1)pdm09 and A(H3N2) across the continent. In Northern Africa, influenza activity increased through the current reporting period, with a predominance of A(H1N1)pdm09 viruses. In Eastern Africa, influenza A predominated, with primarily A(H3N2) viruses detected; however, there were more influenza B/Victoria/2/87 (B/Victoria) lineage viruses detected at the start of the reporting period. In Middle Africa, while overall detections remained low, there was an increase in activity with a peak in November; influenza A(H1N1)pdm09, A(H3N2), and B/Victoria lineage viruses co-circulated. In Southern Africa, influenza activity remained low throughout the reporting period, with a predominance of B/Victoria lineage viruses. In Western Africa, influenza activity peaked in September with mostly A(H1N1)pdm09 viruses detected.

In Asia, influenza virus detections peaked in December. Most detections were reported from Eastern Asia with predominance of influenza A(H3N2) viruses, followed by mostly B/Victoria lineage viruses since mid-January. In South-East Asia, influenza detections remained relatively stable throughout the reporting period and influenza A(H1N1)pdm09, A(H3N2) and B/Victoria lineage viruses co-circulated. In Southern Asia, activity peaked in mid-October with A(H1N1)pdm09 viruses representing the majority of detections. In Central Asia, detections were low during the first half of the reporting period but activity increased and peaked in mid-December with A(H3N2) viruses most commonly detected. In Western Asia, there was an overall increase in influenza detections through November with co-circulation of A(H1N1)pdm09, A(H3N2) and B/Victoria lineage viruses.

In Europe, influenza activity increased over the reporting period; influenza A predominated with co-circulation of A(H1N1)pdm09 and A(H3N2) viruses. In Northern Europe, similar proportions of influenza A(H1N1)pdm09 and A(H3N2) viruses were detected, in South West Europe A(H1N1)pdm09

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viruses predominated, while in Eastern Europe mostly influenza A(H3N2) viruses were detected. Influenza B/Victoria lineage viruses were mostly detected in January in Eastern Europe but throughout the reporting period in South West Europe and Northern Europe.

**In the Americas**, influenza activity varied by transmission zone. In North America, activity remained elevated with a predominance of A(H1N1)pdm09 viruses. In Central America and the Caribbean, influenza activity increased starting in November and remained elevated in January; most detections were A(H1N1)pdm09 viruses. In Tropical South America, influenza B/Victoria lineage viruses predominated at the start of the reporting period, but as activity increased into December and January, influenza A became the predominant circulating type with equal proportions of A(H1N1)pdm09 and A(H3N2) viruses detected. In Temperate South America, influenza activity was low during the reporting period; influenza A and B viruses co-circulated, with a predominance of B/Victoria lineage viruses.

**In Oceania**, influenza detections were at a decline from seasonal activity at the start of the reporting period and continued to decline. There was co-circulation of influenza A(H1N1)pdm09 and A(H3N2) viruses during the reporting period with some detections of influenza B/Victoria lineage viruses.

**Influenza A**

Globally, influenza A virus detections outnumbered those of influenza B. Influenza A(H1N1)pdm09 and A(H3N2) viruses were reported in all transmission zones, although the predominating subtype varied. A(H1N1)pdm09 viruses were detected more frequently in the Americas and South Asia. A(H1N1)pdm09 and A(H3N2) viruses co-circulated in West Asia and A(H3N2) viruses predominated elsewhere in Asia. Europe and Africa reported similar proportions of influenza A(H1N1)pdm09 and A(H3N2) viruses with some variation among transmission zones. A predominance of A(H3N2) viruses was reported in Oceania towards the end of the reporting period.

**Influenza B**

Globally, influenza B virus detections were lower than those of influenza A. However, influenza B viruses predominated in Temperate South America, Middle Africa and Southern Africa. All influenza B viruses where lineage was confirmed belonged to the B/Victoria lineage. No naturally occurring B/Yamagata/16/88 (B/Yamagata) lineage viruses were detected.

### Distribution of Influenza virus type/subtype by influenza transmission zone, between September 01 2023 and January 31 2024

![Map showing distribution of influenza virus type/subtype by transmission zone](image_url)

*Note: The available country data were placed in larger geographical areas with similar influenza patterns to be able to use an overview. Data source: Global Influenza Surveillance and Response System (GISRS) World Health Organization (WHO) Global Influenza Programme. (copyright 2024, all rights reserved).*
Zoonotic influenza

During the period from 26 September 2023 to 19 February 2024, sporadic zoonotic influenza cases were reported following exposure to infected birds and swine in most cases. Two cases of A(H5N6), four cases of A(H9N2) and one case of A(H10N5) were reported in China and eight cases of A(H5N1) were reported in Cambodia. Single cases of A(H1N1)v were reported in Brazil, Spain and Switzerland in this period. One case of A(H1N2)v was reported in the United Kingdom of Great Britain and Northern Ireland.

Genetic and antigenic characteristics of recent seasonal influenza viruses, human serology and antiviral susceptibility

Influenza A(H1N1)pdm09 viruses

Since September 2023, A(H1N1)pdm09 viruses circulated globally and predominated in most geographic regions. The haemagglutinin (HA) genes of viruses that were genetically characterized belonged to the 6B.1A.5a.2 clade. All viruses expressing clade 5a.2 HA genes have further diversified into designated subclades: the 6B.1A.5a.2a, with additional HA substitutions K54Q, A186T, Q189E, E224A, R259K and K308R; and the 6B.1A.5a.2a.1 subclade containing viruses expressing HA genes with additional substitutions P137S, K142R, D260E and T277A (e.g., A/Wisconsin/67/2022). Viruses from both subclades continued to circulate although their relative proportions differed among regions.

Within the 5a.2a subclade, several genetic groups were observed. A minor group with HA substitutions D94N and T216A predominated in Australia, Indonesia and New Zealand, and was detected in smaller proportions elsewhere. The largest group of 5a.2a viruses, defined by the HA substitution I418V, predominated in the Africa, Central America, Middle East, South-East Asia and some countries in Europe. Within the 5a.2a.1 subclade there were two main groups of viruses: one with T216A represented by A/Victoria/4897/2022, predominating in Canada, Japan, the Caribbean, the United States of America and some countries in Europe; and the other group represented by A/Wisconsin/67/2022, circulating in Brazil, Europe and South-East Asia.

The antigenic properties of A(H1N1)pdm09 viruses were assessed in haemagglutination inhibition (HI) assays with post-infection ferret antisera. HI results for viruses with collection dates since September 2023 showed that ferret antisera raised against cell culture-propagated A/Wisconsin/67/2022-like and egg-propagated A/Victoria/4897/2022-like viruses from the 5a.2a.1 subclade recognized viruses in both 5a.2a and 5a.2a.1 subclades well.

Human serology studies used 16 serum panels from children (6 months to 17 years), adults (18 to 64 years) and older adults (≥65 years) who had received egg-based quadrivalent inactivated (standard or adjuvanted), cell culture-propagated quadrivalent inactivated or recombinant HA quadrivalent vaccines with NH 2023-2024 influenza vaccine formulations. Egg-based vaccines contained A/Victoria/4897/2022 (H1N1)pdm09-like, A/Darwin/9/2021 (H3N2)-like, B/Austria/1359417/2021-like (B/Victoria lineage) and B/Phuket/3073/2013-like (B/Yamagata lineage) virus antigens. Cell culture-propagated and recombinant HA vaccines contained A/Wisconsin/67/2022 (H1N1)pdm09-like, A/Darwin/6/2021 (H3N2)-like, B/Austria/1359417/2021-like (B/Victoria lineage) and B/Phuket/3073/2013-like (B/Yamagata lineage) virus antigens.

Recent A(H1N1)pdm09 viruses with HA genes from subclades 5a.2a and 5a.2a.1 were analysed in HI assays using these human serum panels. When compared to the responses to cell culture-propagated A/Wisconsin/67/2022 (H1N1)pdm09-like vaccine reference viruses, post-vaccination geometric mean titres (GMTs) were not significantly reduced for most recently circulating viruses.
Of 2089 A(H1N1)pdm09 virus clinical samples and isolates that were examined for neuraminidase inhibitor (NAI) susceptibility by genetic and/or phenotypic analyses, 22 viruses showed evidence of reduced susceptibility to NAIs. Seven had NA substitution H275Y, one had H275Y, I223V and S247N, and 14 had I223V and S247N. Nine of these 22 viruses were tested in phenotypic assays and showed reduced or highly reduced inhibition by NAIs.

Of 1656 A(H1N1)pdm09 viruses examined by genetic and/or phenotypic analyses, one had the PA substitution Y24H and showed evidence of reduced susceptibility to the endonuclease inhibitor baloxavir marboxil.

**Influenza A(H3N2) viruses**

Phylogenetic analysis of the HA gene of A(H3N2) viruses showed that viruses belonging to clade 3C.2a1b.2a.2 predominated in all geographic regions and have evolved into multiple subclades. Since September 2023, the vast majority of viruses detected within this clade belonged to 2a.3a.1 with further diversification into several subclades. Viruses with HA substitutions N122D (loss of putative glycosylation site) and K276E predominated in Europe, North America, Oceania and West and South Asia. Another subclade of viruses with HA substitutions I25V, V347M and I418V was detected globally and predominated in Africa, East Asia and South America. A third virus subclade with the HA substitution V505I was detected in South and East Asia.

Generally, post-infection ferret antisera raised against cell culture-propagated A/Darwin/6/2021-like viruses and egg-propagated A/Darwin/9/2021-like viruses (subclade 2a), representing the vaccine viruses for the NH 2023-2024 influenza season, recognized many recent clade 2 viruses well, but reduced reactivity was seen against some recent viruses expressing HA genes from 2a.3a.1 subclades. Ferret antisera raised against 2a.3a.1 viruses (e.g., cell-propagated A/Massachusetts/18/2022-like and egg-propagated A/Thailand/8/2022-like, representing the vaccine viruses for the SH 2024 influenza season) recognized the majority of recent viruses expressing HA genes from clade 2a.3a.1 well, however, some viruses within this clade were less well recognized by these antisera.

Human serology studies were conducted using the serum panels as described above by HI and virus neutralization (VN) assays with recent circulating A(H3N2) viruses with HA genes from 2a.3a.1, 2a.1b and 2b clades. When compared to titres against cell-propagated A/Darwin/6/2021-like vaccine reference viruses, post-vaccination HI or VN GMTs against some recent 2a.3a.1 viruses were significantly reduced with some serum panels.

Of 3046 influenza A(H3N2) viruses examined by genetic and/or phenotypic analyses, none showed evidence of reduced susceptibility to NAIs. Of 1450 A(H3N2) viruses examined by genetic and/or phenotypic analyses, four showed evidence of reduced susceptibility to the endonuclease inhibitor baloxavir marboxil. These four viruses had substitutions at position 38 in PA.

**Influenza B viruses**

Since September 2023, influenza B viruses were detected in all WHO regions and all those characterized belonged to the B/Victoria lineage. There have been no confirmed detections of circulating B/Yamagata lineage viruses after March 2020.

The HA genes of B/Victoria lineage viruses characterized during this period belonged to clade 1A.3a which share the HA substitutions N150K, G184E, N197D (resulting in the loss of a putative glycosylation site) and R279K. The 1A.3a HA diversified into two main subclades, one with additional HA substitutions V220M and P241Q (designated as 3a.1) and the other with HA substitutions A127T, P144L and K203R (designated as 3a.2). Viruses with 3a.1 HA genes have continued to decline and only a few were detected in this period while viruses with 3a.2 HA genes have predominated globally. The 3a.2 HA genes have diversified further, with the majority sharing the substitution D197E.
Antigenic analysis showed that post-infection ferret antisera raised against B/Austria/1359417/2021-like viruses (3a.2) recognized the vast majority of viruses with 3a.2 HA genes well. The small number of viruses with clade 3a.1 HA genes were poorly recognized by these ferret antisera.

In human serology studies using the serum panels described above, post-vaccination HI GMTs against recent B/Victoria lineage viruses across the genetic diversity of clade 3a.2 were not significantly reduced when compared to titres against egg- or cell culture-propagated B/Austria/1359417/2021-like vaccine reference viruses. Serology studies were not performed for the B/Yamagata lineage virus.

Of 1663 influenza B/Victoria lineage viruses examined by genetic and/or phenotypic analyses, four showed evidence of reduced or highly reduced susceptibility to NAIs. Three viruses had NA substitutions H134Y, H273N or D197N, respectively. One virus did not possess any mutations that were previously associated with reduced susceptibility to NAIs. Of 951 B/Victoria lineage viruses examined by genetic and/or phenotypic analyses, none showed evidence of reduced susceptibility to the endonuclease inhibitor baloxavir marboxil.

**Recommended composition of influenza virus vaccines for use in the 2024-2025 northern hemisphere influenza season**

Since September 2023, A(H1N1)pdm09 viruses circulated globally and predominated in most geographic regions. The haemagglutinin (HA) genes of viruses that were genetically characterized belonged to the 6B.1A.5a.2 clade, with further diversity within the subclades. Subclade 5a.2a viruses predominated in Europe, Oceania, the Middle East, Africa, South-East Asia, and Central America. Subclade 5a.2a.1 viruses within the group represented by A/Victoria/4897/2022 predominated in Europe, Japan, the Caribbean, and the United States of America, whereas viruses represented by A/Wisconsin/67/2022 predominated in Brazil, Europe and South-East Asia. Post-infection ferret antisera raised against the NH 2023-2024 and SH 2024 A(H1N1)pdm09 vaccine components (cell culture-propagated A/Wisconsin/67/2022 and egg-propagated A/Victoria/4897/2022) from the 5a.2a.1 subclade recognized 5a.2a and 5a.2a.1 viruses well. Post-vaccination GMTs were not reduced significantly for the most recently circulating A(H1N1)pdm09 viruses when compared to the responses to cell culture-propagated A/Wisconsin/67/2022 (H1N1)pdm09-like vaccine reference viruses.

The vast majority of A(H3N2) viruses collected since September 2023 have HA genes derived from subclade 2a.3a.1 (represented by A/Massachusetts/18/2022 and A/Thailand/8/2022) and have continued to diversify. Some recently circulating viruses showed reduced recognition by post-infection ferret antisera raised against NH 2023-2024 vaccine viruses, cell culture-propagated A/Darwin/6/2021 and egg-propagated A/Darwin/9/2021 (2a). Human serology assays showed that post-vaccination GMTs against A(H3N2) viruses with HA genes representing some genetic subgroups of 2a.3a.1 were significantly reduced in selected serum panels compared to titres against cell culture-propagated A/Darwin/6/2021-like vaccine reference viruses.

All circulating influenza B viruses characterized since September 2023 were of the B/Victoria lineage. The vast majority of recent viruses expressed HA genes belonging to subclade 3a.2 (i.e., 1A.3a.2). A few viruses belonging to clade 3a.1 were detected in China.Nearly all circulating viruses were recognized well by post-infection ferret antisera raised against cell culture- and egg-propagated B/Austria/1359417/2021-like vaccine reference viruses (3a.2). Human serology assays showed that post-vaccination GMTs against representative B/Victoria lineage viruses expressing 3a.2 HA genes were not significantly reduced compared to titres against cell culture-propagated B/Austria/1359417/2021-like vaccine reference viruses.
WHO convenes technical consultations each year to recommend viruses for inclusion in influenza vaccines. National or regional authorities are responsible for approving the composition and formulation of vaccines used in each country.

For trivalent vaccines for use in the 2024-2025 northern hemisphere influenza season, WHO recommends the following:

**Egg-based vaccines**

- an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- an A/Thailand/8/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

**Cell culture- or recombinant-based vaccines**

- an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- an A/Massachusetts/18/2022 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

There have been no confirmed naturally occurring B/Yamagata lineage virus detections after March 2020. Further to the WHO September 2023 recommendation, it remains the opinion of the WHO influenza vaccine composition advisory committee that the B/Yamagata lineage antigen should be excluded from influenza vaccines as it is no longer warranted. National or regional authorities should make decisions regarding the transition to trivalent influenza vaccines in their jurisdictions. Where quadrivalent vaccines are still used, the B/Yamagata lineage component remains unchanged from previous recommendations:

- a B/Phuket/3073/2013 (B/Yamagata 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. A list of reagents for vaccine standardization, including those for this recommendation, can also be found on the WHO website.

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

- Therapeutic Goods Administration, P.O. Box 100, Woden, ACT, 2606, Australia (email: influenza.reagents@health.gov.au; website: [http://www.tga.gov.au](http://www.tga.gov.au))
- Medicines and Healthcare products Regulatory Agency (MHRA), Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG, United Kingdom of Great Britain and Northern Ireland (email: enquiries@nibsc.org) website: [http://www.nibsc.org/science_and_research/virology/influenza_resource.aspx](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, USA (email: cbshippingrequests@fda.hhs.gov)
- Research Centre for Influenza and Respiratory Viruses, National Institute of Infectious Diseases, 4-7-1 Gakuen, Musashi-Murayama, Tokyo 208-0011, Japan (email: flu-vaccine@nih.go.jp)

Requests for reference viruses should be addressed to:

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5 https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations
6 Description of the process of influenza vaccine virus selection and development available at: [http://www.who.int/gb/pitp/pdf_files/Fluvaccvirusselection.pdf](http://www.who.int/gb/pitp/pdf_files/Fluvaccvirusselection.pdf)
WHO provides fortnightly updates of global influenza activity. Other information about influenza surveillance can be found on the WHO Global Influenza Programme website.

Acknowledgements

The WHO recommendation on vaccine composition is based on the year-round work of the WHO Global Influenza Surveillance and Response System (GISRS). We thank the National Influenza Centres (NICs) of GISRS, and non-GISRS laboratories including the WOAH/FAO Network of Expertise on Animal Influenza (OFFLU), who contributed information, clinical specimens, viruses and associated data; WHO Collaborating Centres of GISRS for their in-depth characterization and comprehensive analysis of viruses; University of Cambridge for performing antigenic cartography and phylogenetic analysis; WHO Essential Regulatory Laboratories of GISRS for their complementary virus analyses and contributions from a regulatory perspective; and laboratories involved in the production of high growth/yield reassortants as candidate vaccine viruses. We also acknowledge the GISAID Global Data Science Initiative for the EpiFlu™ database and other sequence databases which were used to share gene sequences and associated information; modelling groups for virus fitness forecasting; and the Global Influenza 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 2024-2025 northern hemisphere influenza season was made through a WHO Consultation with relevant WHO Collaborating Centers 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 four years) financial or other interests relevant to the subject of work:

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10 https://www.who.int/teams/global-influenza-programme
<table>
<thead>
<tr>
<th>Institution</th>
<th>Representative</th>
<th>Personal interest</th>
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<tbody>
<tr>
<td>WHO ERL TGA Woden</td>
<td>Dr Pearl Bamford</td>
<td>None</td>
</tr>
<tr>
<td>WHO ERL NIBSC Potters Bar</td>
<td>Dr Othmar Engelhardt</td>
<td>All items declared and listed below belong to Dr Engelhardt’s Research Unit in the form of contract research and grants from: IFPMA, Innovative Medicines Initiative and PATH.</td>
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<tr>
<td>WHO CC and ERL NIID Tokyo</td>
<td>Dr Hideki Hasegawa</td>
<td>None</td>
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| WHO CC Atlanta | Dr Rebecca Kondor | Below item declared and listed below belong to Dr Kondor’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 for influenza vaccines. |
| WHO CC London | Dr Nicola Lewis | Following items were declared:  
  - Invited speaker and panel member on event organized by Seqirus. No payment received.  
  The items declared and listed below belong to Dr Lewis’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. |
| WHO CC Koltsovo | Dr Vasily Marchenko | None |
| WHO CC Melbourne | Dr Kanta Subbarao | All items declared and listed below belong to Dr Subbarao’s Research Unit:  
  - 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. |
| WHO CC Beijing | Dr Dayan Wang | None |
| WHO CC Memphis | Dr Richard Webby | Following items were declared:  
  - Participated in a Sanofi next generation influenza vaccine advisory panel, November 2022. No renumeration received.  
  - Participated in a Seqirus-sponsored session at Options XI for the Control of Influenza meeting in Belfast, September 2022. No renumeration for participation or travel received.  
  - Participated in Seqirus’ National Influenza Educational Webinar on Tuesday 22 March 2022 as a virtual speaker. Topic was on impact of COVID-19 on influenza activity. No renumeration received. |
Based on the WHO assessment, the interests declared by Drs Engelhardt, Kondor, Lewis, Subbarao, and Webby 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 Engelhardt, Kondor, Lewis, Subbarao, and Webby should continue to serve as Advisers.