Update on Influenza B/Yamagata Surveillance

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WHO’s Global Influenza Surveillance and Response System (GISRS)

The mission of GISRS is to protect people from the threat of influenza by continuously functioning as a:

- Global mechanism of surveillance, preparedness and response for seasonal, pandemic and zoonotic influenza
- Global platform for monitoring influenza epidemiology and disease
- Global alert for novel influenza viruses and other respiratory pathogens
WHO’s Global Influenza Surveillance and Response System (GISRS)

152 WHO National Influenza Centers in 129 Member States

- GISRS National Influenza Centers (NICs)
  - Collect respiratory specimens from established networks of physicians, health care centers or other sentinel sites, and/or they solicit influenza virus-positive samples
  - Perform initial influenza virus detection, typing and subtyping
    - CDC develops and manufactures assays which are distributed by IRR
  - Share a subset of representative influenza virus specimens and/or isolates with WHO CCs for antigenic and genetic characterization and creation of candidate vaccine viruses
  - Report to WHO RespiMart
    - epidemiological information FluID
    - laboratory results to FluNet

- 7 WHO Collaborating Centers for Influenza
- 4 Essential Reference Laboratories
- 12 WHO H5 Reference Laboratories
FluNet data can be delineated by surveillance site type

• **Sentinel** – Sentinel surveillance systems collect high-quality data in a timely manner, systematically and routinely from sentinel surveillance sites representative of the population under surveillance. Case definition (ILI, SARI, ARI) and populations differ by country (e.g., only certain age groups, health-care workers, hospitalized)

• **Non-sentinel** – Data reported in this category may include outbreak investigation, universal testing, testing at point of care or other systems apart from sentinel surveillance

• **Type not defined** – These data may include sentinel or non-sentinel surveillance sources or both

The level of information reported to FluNet depends on the country and the laboratory where testing occurs

• Rapid tests only determine influenza A or B

• Large clinical and hospital laboratories often only determine influenza A or B, with some assays also determining influenza A subtype

• A higher proportion of viruses from sentinel surveillance will include influenza A and B subtyping results
WHO GISRS

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Types of Assays for B/lineage at NIC:

• Serology Based
  • CDC WHO Kit
    • anti-B/Vic and anti-B/Yam goat antiserum – created by WHO CC Atlanta available in CDC IRR
    • 52 countries recently ordered kits
  • HI Assay–anti-B/Vic and anti-B/Yam ferret antiserum provided by WHO CCs

• Molecular Based
  • CDC RT-PCR B Lineage Assay RUO - created by WHO CC Atlanta available in CDC IRR
    • 104 countries recently ordered kits
  • Other RT-PCR assays
  • Sequencing (sanger or NGS) – clinical specimens or viral isolates

GISRS NICs also submit specimens to WHO CCs for virus characterization

• Using the above methods B lineage is attempted for all viruses received
  • WHO CC have confirmed ZERO circulating B/Yamagata lineage viruses collected after March 2020
    • Those reported as B/Yamagata were determined to be incorrectly lineage reports, negative for influenza or B/Yamagata component of LAIV

Non-sentinel surveillance may use different assays than those listed above.
• Influenza B/Yamagata lineage viruses were the predominant B/lineage circulating during the 2017-18 Northern Hemisphere and 2018 Southern Hemisphere seasons
• 2018-2019 Northern Hemisphere had much less B activity overall and B/Victoria lineage viruses predominated
• 2019 Southern Hemisphere showed regional differences in B/lineage circulation with B/Yamagata mainly circulating in South America
• 2019-20 Northern Hemisphere season began with an early B/Victoria lineage peak, followed by A(H1N1)pdm09
• COVID-19 Pandemic and its mitigation saw a drop in influenza virus detection and circulation
WHO GISRS Influenza Surveillance
September 2020- August 2023

- GISRS NICs continued influenza surveillance during the COVID-19 Pandemic
- Influenza continued to be detected but without seasonal peaks in epidemics until late 2021
- All influenza B activity due to B/Victoria lineage
- February 1 – August 31, 2023
- 1/3 of all viruses detected by GISRS were influenza B
- Parts of Northern Hemisphere saw second peak of activity due to B/Victoria and A(H1N1)pdm09 viruses
- Southern Hemisphere 2023 season co-circulation of B/Victoria and A(H1N1)pdm09 viruses
Countries reporting influenza B detections to FluNet February 1- August 31, 2023
All Types of Surveillance

Map made from data available at GIP FLUNET PowerBI
Virus Detections by B lineage reported to FluNet
All Types of Surveillance

1 B/Yamagata reported (non-sentinel surveillance)
1 February 2023 through 31 August 2023

Data source: GIP FLUNET PowerBI
Virus Detections by subtype reported to FluNet Sentinel Surveillance

No B/Yamagata detected in GISRS sentinel surveillance
1 February 2023 through 31 August 2023

Data source: GIP FLUNET PowerBI
WHO GISRS Influenza B/Lineage Reports
February 1 – August 31, 2023

- 99,453 influenza B viruses detected in 139 countries
- 15,878 influenza B viruses had results from B/lineage assays reported to FluNet from all surveillance types
  - 15 initial reports to GISRS as B/Yamagata underwent confirmation by WHO CCs and WHO Global Influenza Programme
    - 13 were confirmed as B/Victoria Lineage or negative for influenza and their FluNet records were updated accordingly
    - 2 did not have specimens available for confirmation testing at a WHO CC (one was not reported to FluNet). These specimens did not yield viral isolates or sequence data.
- All influenza B viruses received by WHO CCs were B/Victoria lineage
- Genomic surveillance of influenza B viruses found only genet segments derived from circulating B/Victoria lineage
- This data supports that B/Yamagata viruses are extremely rare and not responsible for recent epidemics
- The majority of B/Yamagata reports are due to an incorrect lineage determination

As of 31 August 2023
WHO vaccine recommendations for the Southern Hemisphere 2024

It is recommended that vaccines licensed for use in the 2024 southern hemisphere influenza season contain the following:

**Trivalent:** Egg-based Vaccines
- an A/Victoria/4897/2022 (H1N1)pdm09-like virus antigen*;
- an A/Thailand/8/2022 (H3N2)-like virus antigen**; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

**Trivalent:** Cell- or recombinant-based Vaccines
- an A/Wisconsin/67/2022 (H1N1)pdm09-like virus antigen*;
- an A/Massachusetts/18/2022 (H3N2)-like virus antigen**; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus antigen.

**Quadrivalent:** egg- or cell culture- or recombinant-based vaccines
- Above 3 components; and a B/Phuket/3073/2013 (B/Yamagata lineage)-like antigen.
  * Different from that recommended for the 2023 southern hemisphere season but the same as the NH 2023-24 recommendation.
  ** Different from that recommended for the 2023 southern hemisphere season and from NH 2023-24 recommendation.

WHO recommendation and technical reports available on the WHO web site: [https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations](https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations)
WHO Vaccine Recommendations Summary

• The absence of confirmed detection of naturally occurring B/Yamagata lineage viruses is indicative of very low risk of infection by B/Yamagata lineage viruses.

• While influenza vaccines are safe and effective, the manufacture and use of inactivated and live attenuated vaccines containing B/Yamagata lineage viruses pose a theoretical risk of reintroduction of B/Yamagata lineage virus into the population. This risk can be mitigated by the removal of B/Yamagata lineage viruses from the vaccines.

• It was the opinion of the WHO influenza vaccine composition advisory committee that the inclusion of a B/Yamagata antigen as a component of influenza vaccines is no longer warranted, and every effort should be made to exclude this component as soon as practically possible.

• The committee recognizes that national or regional authorities are responsible for approving the composition and formulation of vaccines used in each country and should consider the use & relative benefit(s) of trivalent or quadrivalent influenza vaccines.
Ongoing Influenza B Surveillance

- GISRS laboratories will continue to be supported by CDC for influenza testing, typing and influenza A/B subtyping through reagents available in IRR
- GISRS laboratories and WHO CCs will continue to perform B/lineage testing
  - Any reports of B/Yamagata viruses will be confirmed by WHO CCs
- For the 2023-2024 season, US public health labs will continue to perform assays to determine B/lineage— all B/Yamagata detections will be sent to CDC for confirmation.
- All US specimens with RT-PCR results of a mix of influenza A and B will also be sent to CDC for confirmation. The majority of previous results of A/B mixtures were from individual vaccinated with LAIV.
Support and Disclaimer

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