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Influenza Vaccine Manufacturing

Industry Perspective: 2023-2024 and 2024-2025 Northern Hemisphere Influenza Seasons

Vaccines and Related Biological Products Advisory Committee

05 March 2024

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Informed by consultation with Influenza Vaccine Manufacturers

The FDA CBER requested this annual summary of information from influenza vaccine manufacturers supplying the U.S., for purposes of a general presentation to the VRBPAC. This summary has been prepared from a variety of public sources, and was reviewed by AstraZeneca, CSL Seqirus, GSK, and Sanofi.

Presenter Disclosure Statement

I am an employee of Sanofi and own shares in the company.

Key Messages / Agenda Items

- NH 2023-2024 seasonal vaccine was distributed with strain change of H1N1 pdm09-like virus.
- Since the COVID-19 pandemic, US influenza vaccine demand and coverage rates have declined amid vaccine supply surplus; special care required for communication bearing in mind TIV transition.
- Industry aligned with multiple stakeholders globally and worked closely with CBER on regulatory submissions to enable transition from QIV to TIV; in addition, operational and commercial preparations are progressing.
- Industry has or will have the necessary CBER approval for TIV distribution in the US for the NH 2024-2025 season with agreed timing.
- Concerns continue with the impact of the Nagoya Protocol on seasonal and pandemic influenza vaccine manufacturing.

On 24th Feb 2023, WHO recommended some updates to the quadrivalent formulation of influenza vaccines for the NH 2023-2024 influenza season

Influenza Vaccine Composition Recommendations

The recommendation was that influenza vaccines should contain the following:

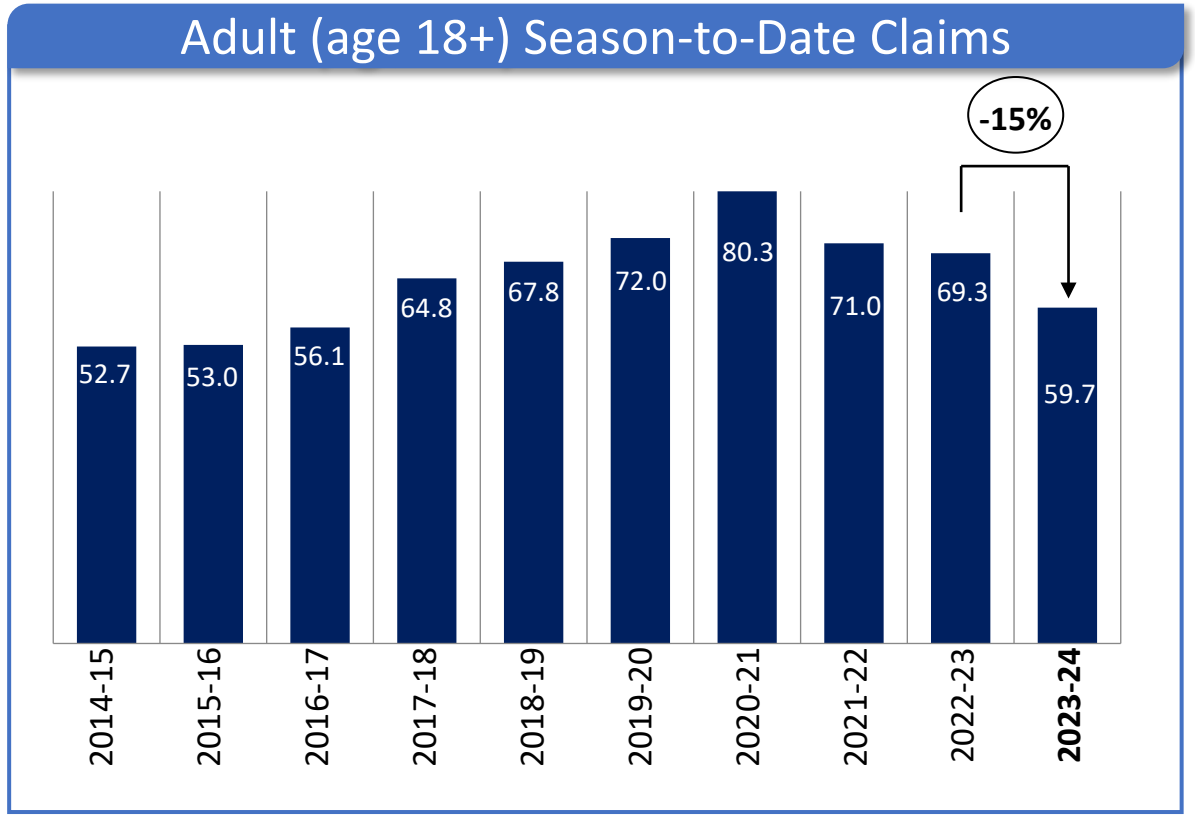
- **If egg-based:**
  - A/Victoria/4897/2022 (H1N1) pdm09-like virus
  - A/Darwin/9/2021 (H3N2)-like virus
  - B/Austria/1359417/2021-like virus (B/Victoria lineage)
  - B/Phuket/3073/2013-like virus (B/Yamagata lineage)
- **If cell or recombinant-based:**
  - A/Wisconsin/67/2022 (H1N1) pdm09-like virus
  - A/Darwin/6/2021 (H3N2)-like virus
  - B/Austria/1359417/2021-like virus (B/Victoria lineage)
  - B/Phuket/3073/2013-like virus (B/Yamagata lineage)

180th VRBPAC Votes

- At the 180th meeting on 7th March 2023 of the Vaccines and Related Biological Products Advisory Committee, recommendations were made on the selection of strains to be included in the influenza virus vaccines for the 2023 – 2024 influenza season.
- Four voting questions were asked for inclusion of specific strains for:
  - A (H1N1)
  - A (H3N2)
  - B/Victoria lineage
  - B/Yamagata lineage
- Each voting result confirmed inclusion of all four strains recommended by the WHO.

The H1N1 pdm09-like viruses above represent changes from both the NH2022-2023 and SH2023 seasons.

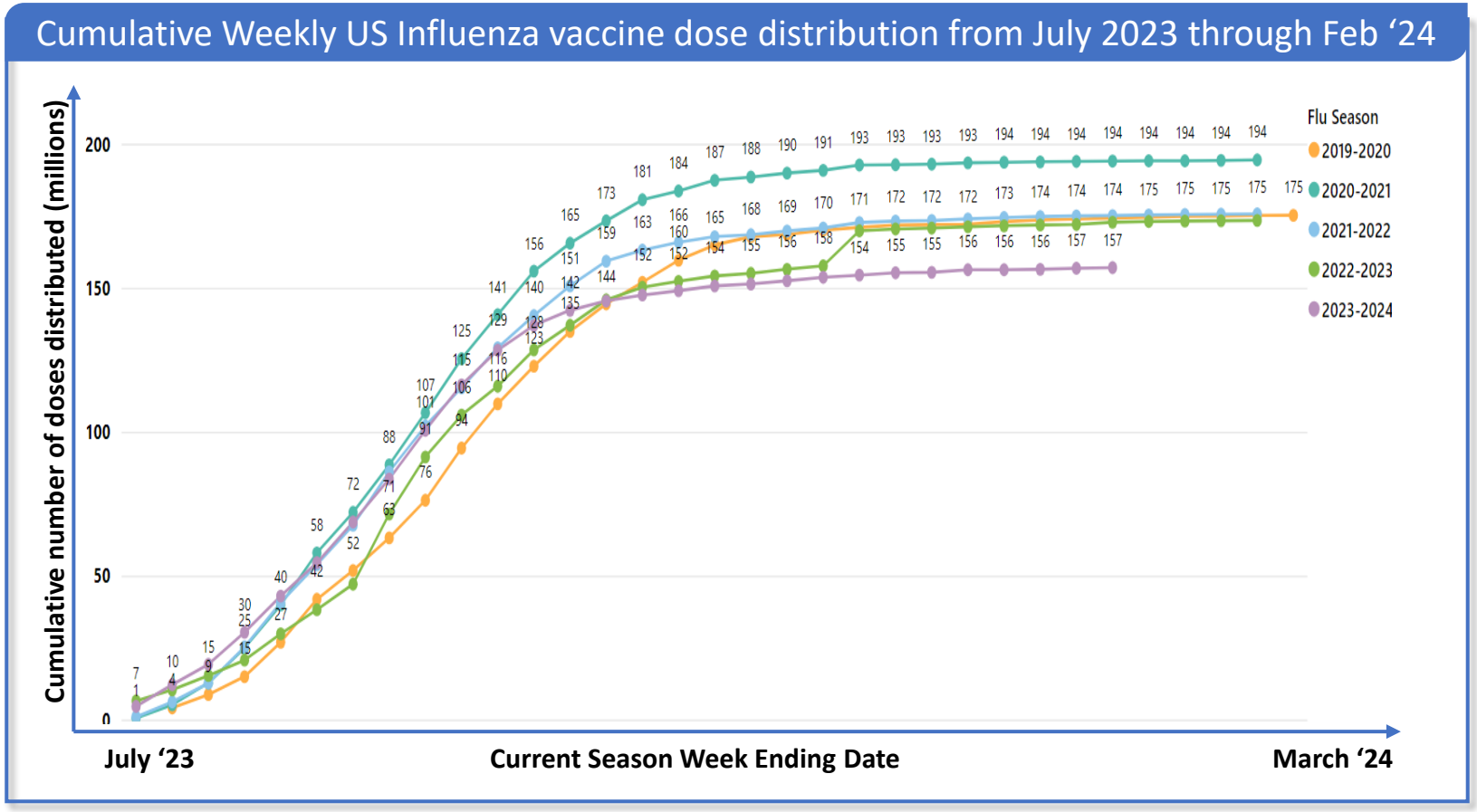
Since the COVID-19 pandemic, US Influenza vaccine coverage rates have declined amid vaccine supply surplus



- Influenza vaccine demand has **declined each year** since the peak of the 2020-21 pandemic.
- This has been seen consistently **across all age and risk groups**.
- **Demand in 2023-24 lower** than pre-pandemic year of 2019-20.
- There is **consistently a supply surplus** of influenza vaccines for the US.

Data Source: IQVIA National Pharmacy Claims Report; Medical (as of 01/13/2024) and Retail (as of 01/13/2024)
**IQVIA national claims at CPT code level. IQVIA doesn't capture claims from Public, Kaiser, VA, LTC, FQHCs, Hospital and Non-AMA affiliated Physicians.

US Influenza vaccine dose distribution has declined in response to lower coverage rates

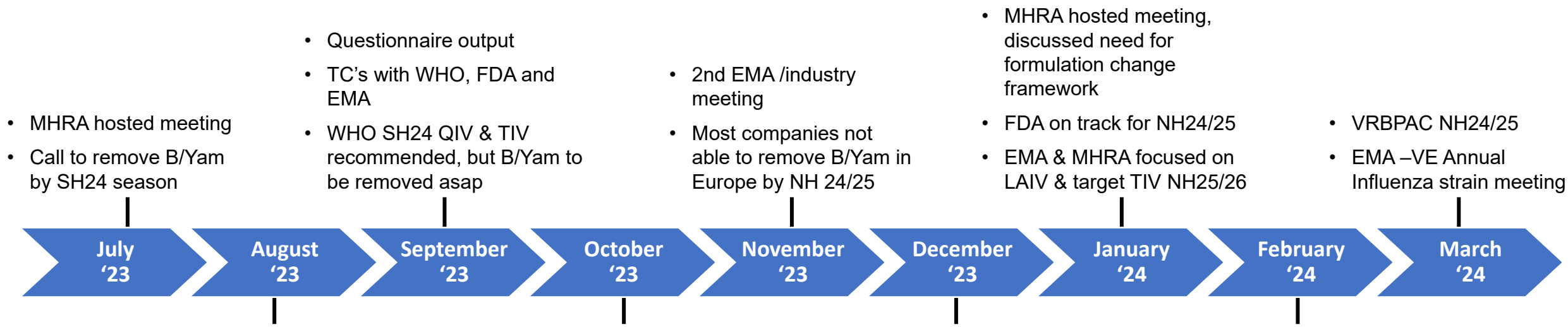


- US market has been **oversupplied and demand has consistently decreased** since the NH 2020-2021 COVID-19 pandemic season.
- In NH 2023-2024, demand has **declined by 37 million doses** vs. NH 2020-2021[1].

https://www.cdc.gov/flu/fluvaxview/dashboard/vaccination-doses-distributed.html (accessed 14 February 2024)

[1] CDC FluVaxView Seasonal Influenza Vaccine Supply for the U.S. 2023-2024 Influenza Season | CD

The Vaccines Industry aligned with multiple stakeholders globally and worked closely with CBER to enable the transition from QIV to TIV



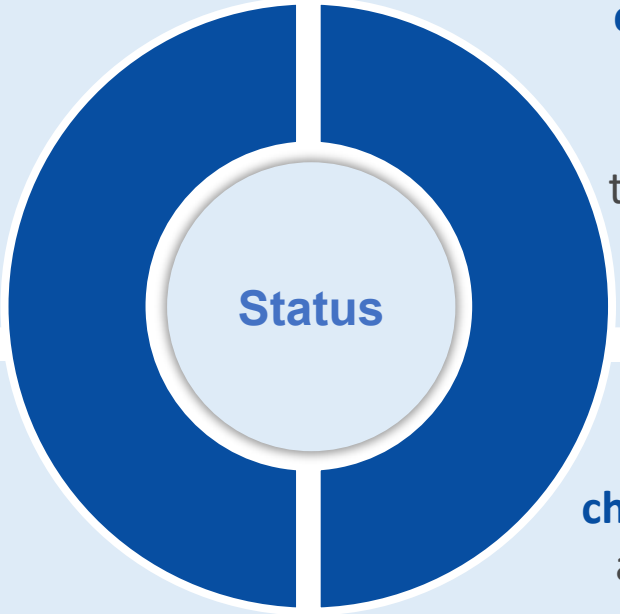
There are several challenges to be mindful of, when heading into the 2024-2025 NH season

- On 30 January 2023, WHO's report of their 2nd TC held 25 January 2023 provided an indication of the H1N1 human antisera data outcomes for that time frame, which **enabled manufacturers to prepare** for the composition of influenza vaccines for the NH 2023-2024 season.
  - This season the comparable WHO reports ahead of the NH 2024-2025 season **did not contain human antisera information**.
- Planning for the NH 2024-2025 season has been challenging due to the **shift to quickly remove the B/Yamagata virus strain** from all influenza vaccines.

All manufacturers are prepared to remove B/Yamagata from their influenza vaccines for the NH 2024-2025 season for the US

Industry **has or will have the necessary CBER approval for TIV distribution** in the US for the NH 2024-2025 season with agreed timing.

Industry worked **in close collaboration with CBER to rapidly submit regulatory files** related to manufacturing, CMC, quality, testing, and others in the transition from QIV to TIV.



Majority of ex-US countries will not transition to TIV for the NH 2024-2025 season; therefore, QIV will be distributed to those markets; **CBER release** will be required for some of these markets.

One of Industry next steps will be to **share a first draft for a formulation change framework** to include input from a broad selection of stakeholders and organizations based on B/Yamagata lessons learned; **workshop planned for the WHO CC, ERL & Industry meeting in July**.

Concerns continue with the impact of the Nagoya Protocol on seasonal and pandemic influenza vaccine manufacturing

- **The sharing of pathogens and their associated information must be fast, easy, and legally certain.** In recent years, national Nagoya Protocol (NP) or other Access and Benefit Sharing (ABS) legislation has made this increasingly difficult to achieve.

- National Influenza Centers (NICs) continue to supply influenza viruses under the agreed Terms of Reference as part of the global influenza surveillance and response system (GISRS), however there is often a **lack of legal clarity if the viruses can be used for vaccine manufacturing and research**.

- Since 2018, supply of **~40 influenza viruses to companies has been impacted**.

- In recent years, to avoid delays and complexity in an already tight seasonal manufacturing schedule, the focus has been on **using viruses from countries with a track record of timely approvals** for use of viruses or no requirements for negotiation.

- This adds an **extra step and level of complexity for manufacturers** each season, due to having to check the legislation status in each country supplying a candidate vaccine virus (CVV).

- The impact is not only on seasonal influenza; the **supply of pre-pandemic avian viruses can also be impacted** as they are not covered by the WHO Pandemic Influenza Preparedness (PIP) Framework.

Here are today's key takeaways

NH 2023-2024 seasonal vaccines contained H1N1 pdm09-like viruses that **changed both from the NH2022-2023 and SH2023 seasons**.

The Industry is working to address coverage and confidence issues in collaboration with CDC, 3rd party organizations (e.g., NAIIS (National Adult Immunization and Influenza Summit) and other interested parties.

Since the COVID-19 pandemic, **US influenza vaccine demand and coverage rates have declined** amid vaccine supply surplus; special care required for communication bearing in mind TIV transition.

Industry aligned with multiple stakeholders globally and worked closely with CBER to transition from QIV to TIV.

Industry has or will have the **necessary CBER approval for TIV distribution** in the US for the NH 2024-2025 season with agreed timing.

The Influenza vaccine **formulation change framework first draft to be further developed** at next WHO CC, ERL, and Industry meeting in July.

Concerns of the impact of the Nagoya Protocol on seasonal and pandemic influenza vaccine manufacturing continue.

The focus has been on viruses from countries that can provide approvals for use rapidly, however for some seasons the options have been limited.

Thank you for your attention.