Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

Influenza Vaccine Manufacturing

Industry Perspective for 2022-23 Northern Hemisphere Influenza Vaccine Supply

Vaccines and Related Biological Products

Advisory Committee

07 March 2023

Elisabeth Neumeier

(GlaxoSmithKline on behalf of 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 GSK, Sanofi, AstraZeneca and Seqirus.

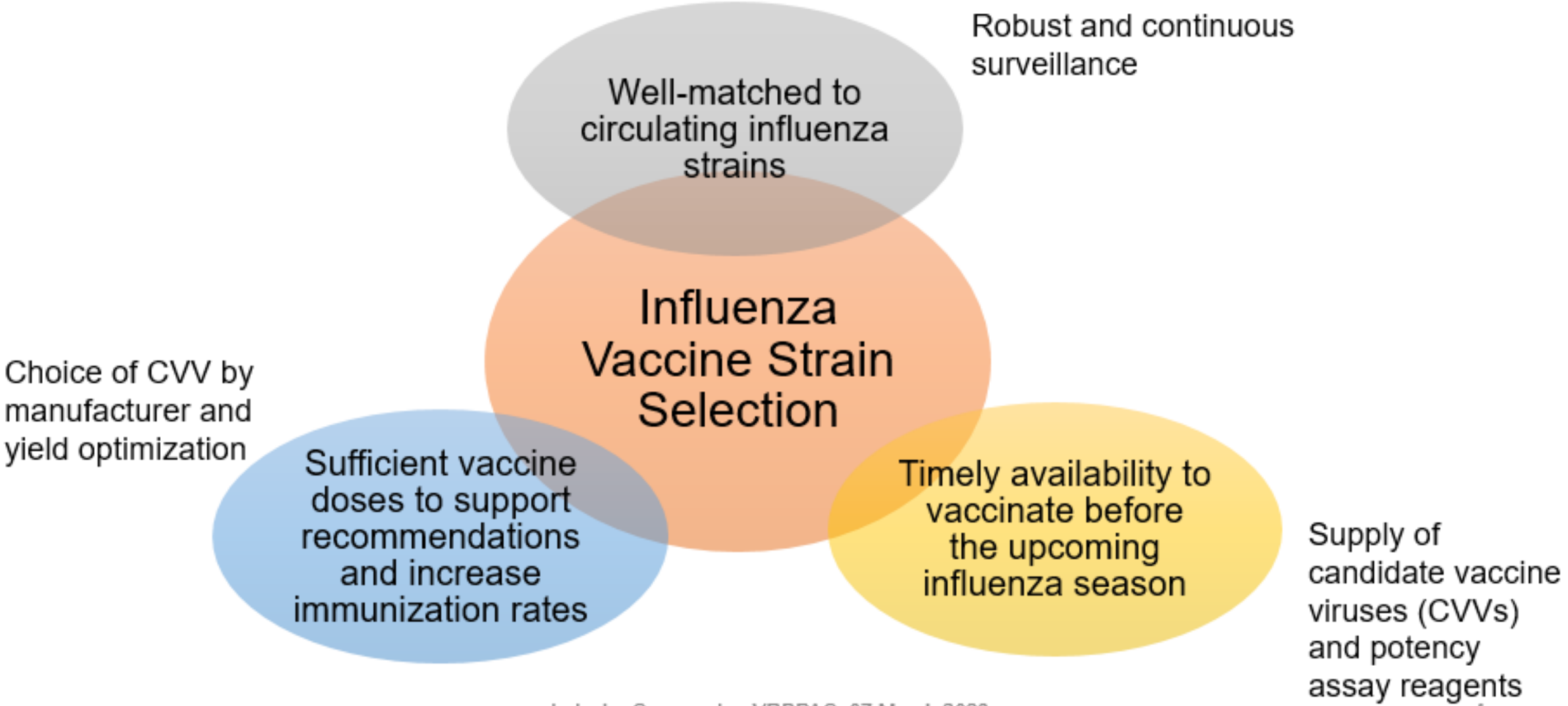
Presenter Disclosure Statement

- I am an employee of GlaxoSmithKline and own shares in the company

Key Messages

- Key components of a successful vaccination campaign
- Influenza Surveillance during and after COVID-19 pandemic
- Strain changes and reagent supply for NH 2022/23 season
- Overview of NH 2022/23 manufacturing campaign
- Impact of the Nagoya Protocol on seasonal influenza vaccine manufacturing
- Avian influenza update

Successful influenza vaccination campaigns: A balancing act



Influenza detections by subtype in the United States reported to FluNet

- Circulation of influenza viruses has returned to and exceeded pre-2020 levels
- Pattern of influenza circulation is still unusual (two peaks in 2021-22 season; early and very high peak in 2022-23 season)

NH 2022/23 Season Strain Recommendation

On 03 Mar 2022 the VRBPAC committee recommended that the quadrivalent formulation of influenza vaccines for the U.S. 2022/23 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-like virus (B/Victoria lineage)
- a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

Cell or recombinant based

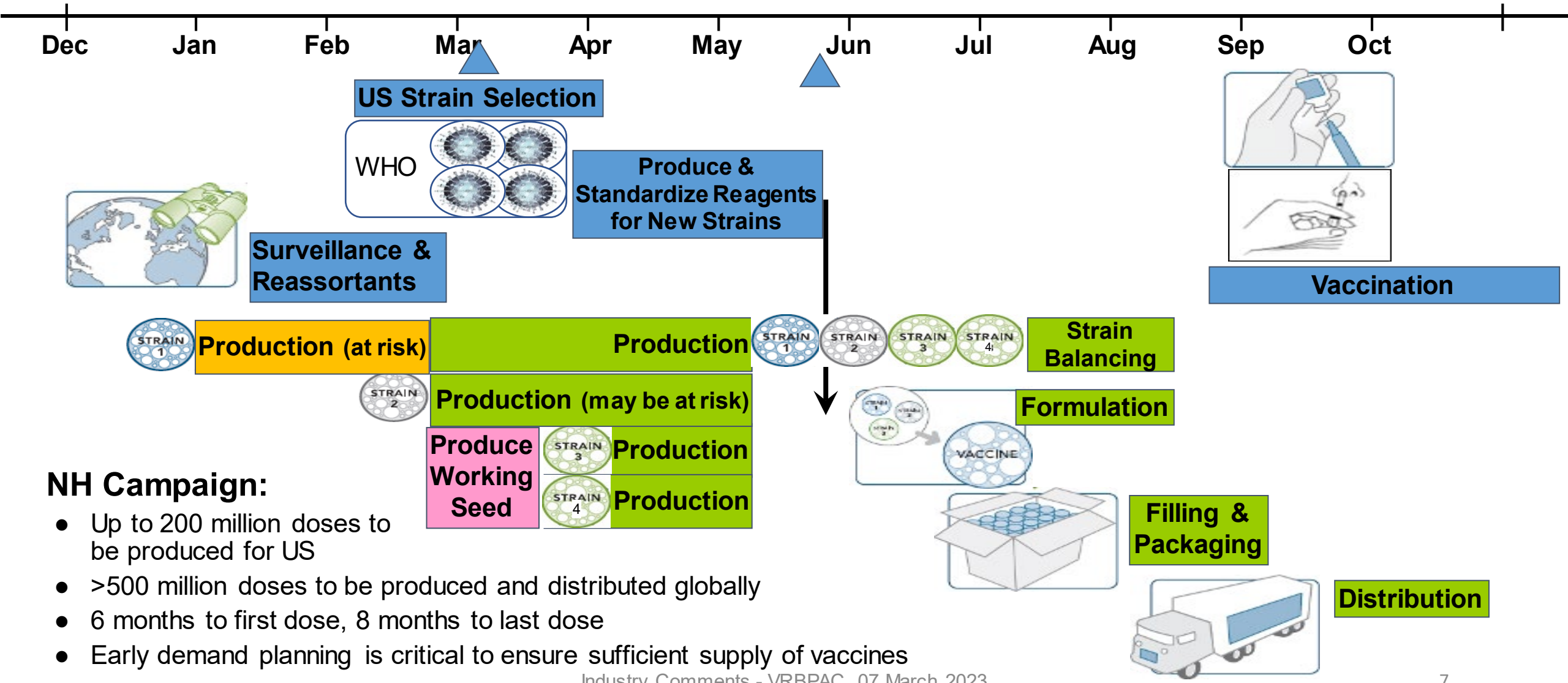
- an A/Wisconsin/588/2019 (H1N1) pdm09-like virus
- an A/Darwin/6/2021 (H3N2)-like virus
- a B/Austria/1359417/2021-like virus (B/Victoria lineage)
- a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

For trivalent influenza vaccines, the committee recommended that the A(H1N1) pdm09, A(H3N2) and B/Victoria lineage viruses recommended above for the quadrivalent vaccines be used.

Two strain changes from NH 2021/2022 season

Both strains have been a component of the SH 2022 influenza vaccine
→ CVVs and reagents were readily available

Annual Influenza Vaccine Manufacturing Timeline for US Supply



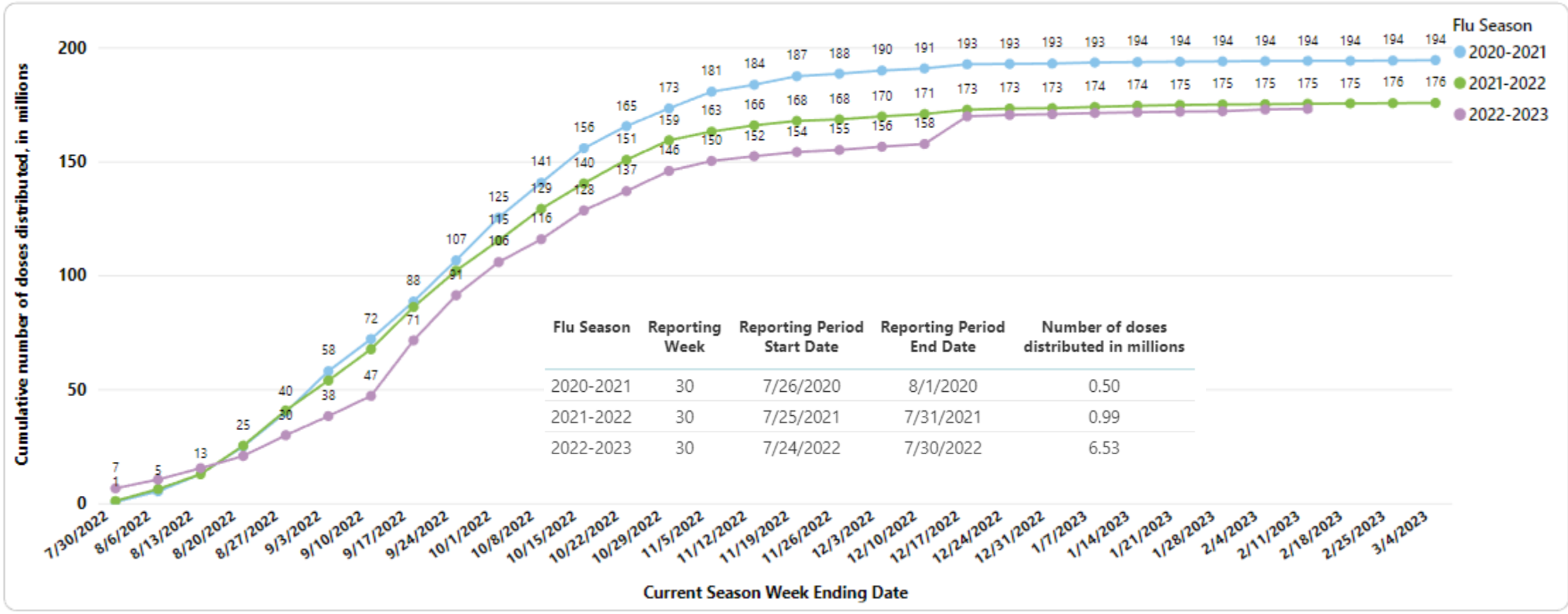
NH Campaign:

- Up to 200 million doses to be produced for US
- >500 million doses to be produced and distributed globally
- 6 months to first dose, 8 months to last dose
- Early demand planning is critical to ensure sufficient supply of vaccines

It takes teamwork to get Influenza Vaccine across the finish line

Relay race analogy	First runner is at full speed	CCs, ERLs, HYR labs full speed
	Receiving runner starts running before handoff	Manufacturers start producing at-risk
	Receiving runner is at full speed at handoff	Manufacturers ready for new strains and formulation
	Strong planning and communication	Bi-weekly WHO-Industry teleconferences and CFWG Influenza Hub
Additional challenges for influenza	Multiple batons	CVVs, Reagents, Vaccine types
	Multiple providers	CCs, ERLs, HYR labs
	Hurdles for NH 2022/23 manufacturing campaign	**Two strain changes A(H1N1)pdm and A(H3N2); CVVs and reagents readily available** **Nagoya Protocol: no issues**
	Outlook to NH 2023/24	**New A(H1N1) CVV and reagents** **Nagoya Protocol: no issues expected**

US Influenza Vaccine Distribution: cumulative number of doses distributed



Flu Season	Reporting Week	Reporting Period Start Date	Reporting Period End Date	Number of doses distributed in millions
2020-2021	30	7/26/2020	8/1/2020	0.50
2021-2022	30	7/25/2021	7/31/2021	0.99
2022-2023	30	7/24/2022	7/30/2022	6.53

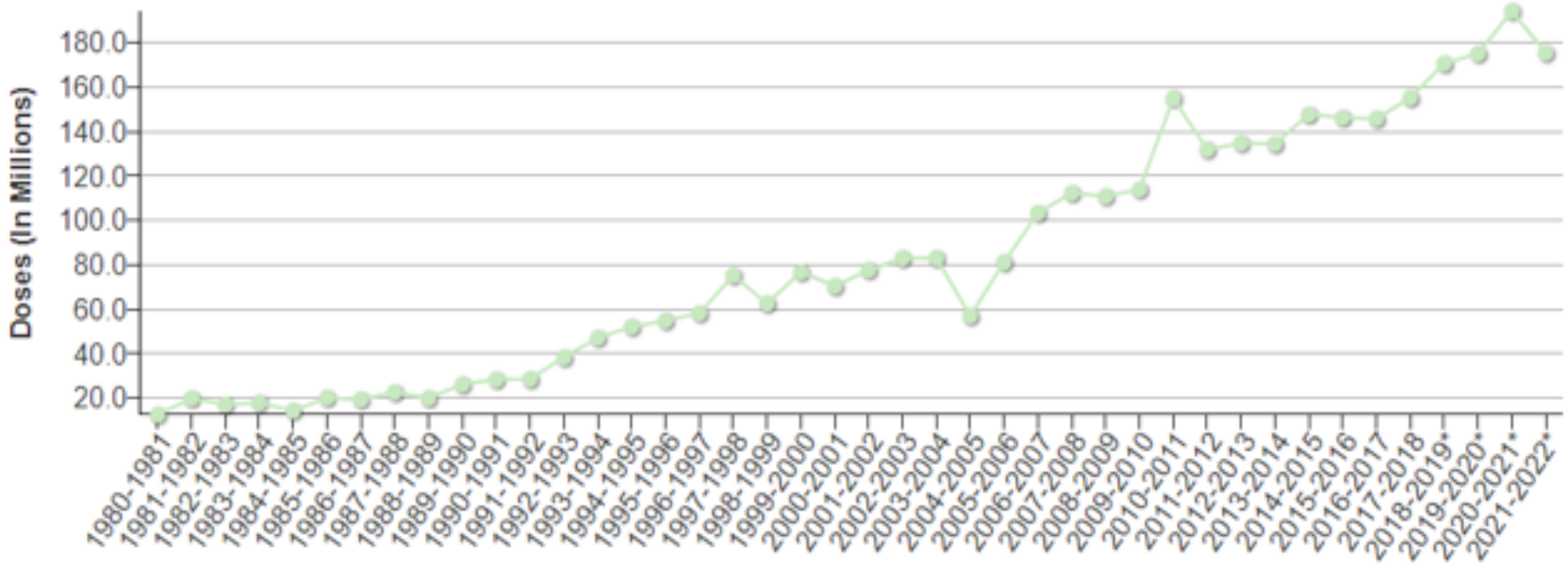
CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Influenza Vaccine Doses Distributed in the United States, By Season

- Manufacturers responded to increase in demand in NH 2020/21 season, >10% increase in doses vs 2019/20 season
- Demand for 2021/22 and 2022/23 NH season is returning to pre-COVID-19 volumes

- Flu vaccination uptake this season has been slower and lower overall than in previous seasons[1]

[1] CDC FluVaxView Influenza Vaccination Coverage for Persons 6 Months and Older | FluVaxView | Seasonal Influenza (Flu) | CDC



CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Source: Historical Reference of Seasonal Influenza Vaccine Doses Distributed | CDC

Summary of 2022-23 season

- Very high influenza peak early in the season
- Influenza vaccine was available early
- Vaccine demand was lower compared to previous year
- Flu vaccine provided substantial protection this season [1]

[1] CDC Flu News & Spotlights Flu Vaccine Provided Substantial Protection This Season | CDC

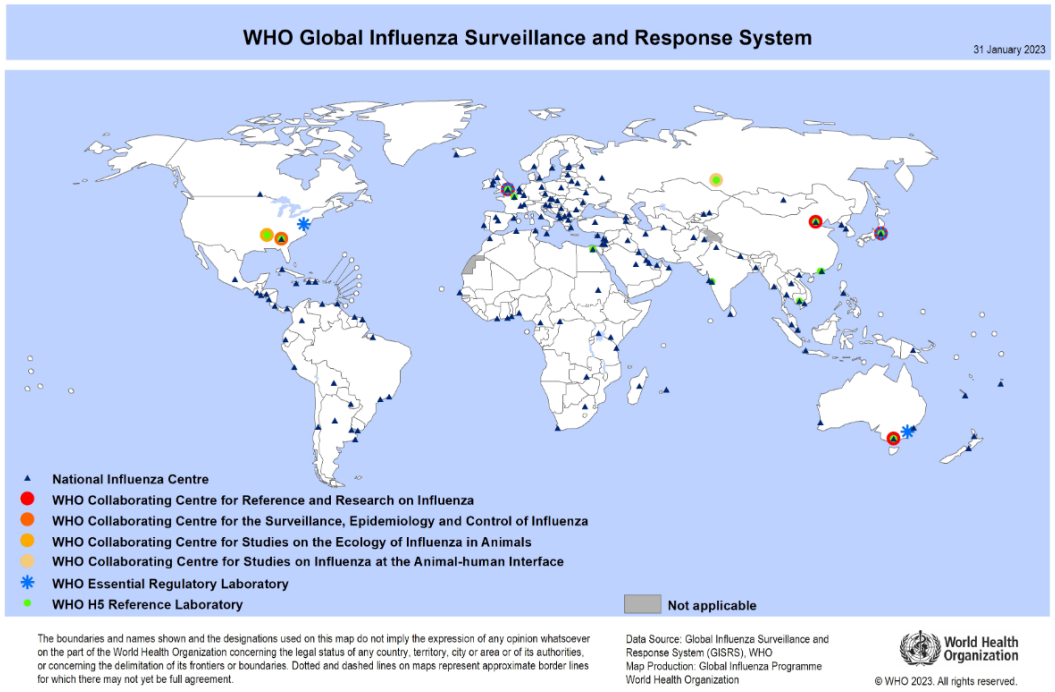
Nagoya Protocol: Impact on seasonal influenza

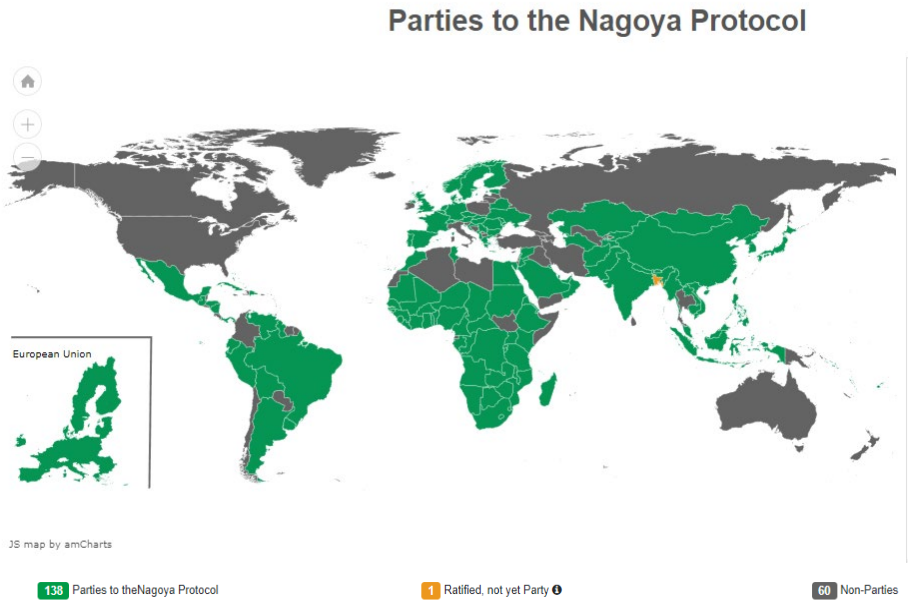
- The Nagoya Protocol (NP) on Access and Benefit Sharing (ABS) is an international treaty, supplementary to the Convention on Biological Diversity (CBD), which was adopted in 2010 with the objective of fair and equitable sharing of benefits arising from the utilization of genetic resources (GR), thereby contributing to the conservation and sustainable use of biodiversity.
- An increasing number of countries have enacted Nagoya Protocol/National ABS legislation, and in many cases genetic sequence data (GSD) are included within scope.

Convention on Biological Diversity

Nagoya Protocol: Impact on seasonal influenza

- Most National Influenza Centres (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



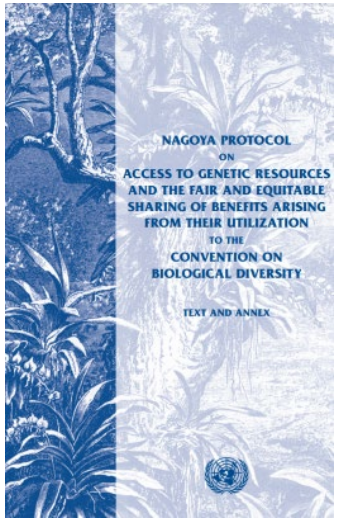


[ABSCH | Access and Benefit-Sharing Clearing-House (cbd.int)]

Nagoya Protocol and ABS Legislation

- The **sharing of pathogens and their associated information must be fast, easy and legally certain**. In recent years, national Nagoya (NP) or other access and benefit sharing (ABS) legislation, requiring bilateral negotiations, has created significant bureaucratic hurdles which make this increasingly difficult to achieve.
- There are more than 100 distinct ABS laws around the world which potentially impose legal requirements for benefit sharing that companies must navigate in return for access to pathogens
- Although the NP recognizes the importance of public health, only 12 countries out of 137 that have ABS rules have included a public health emergency provision.
- This has weakened legal certainty in access to pathogens samples and sequences, with negative consequences seen in the sharing of a number of viruses, including seasonal influenza,
- In the case of influenza viruses, since 2018, vaccine manufacturers have seen delays ranging from 3 weeks to 9 months before being able to access ~40 important influenza samples.

Convention on Biological Diversity



Nagoya Protocol: Impact on seasonal influenza

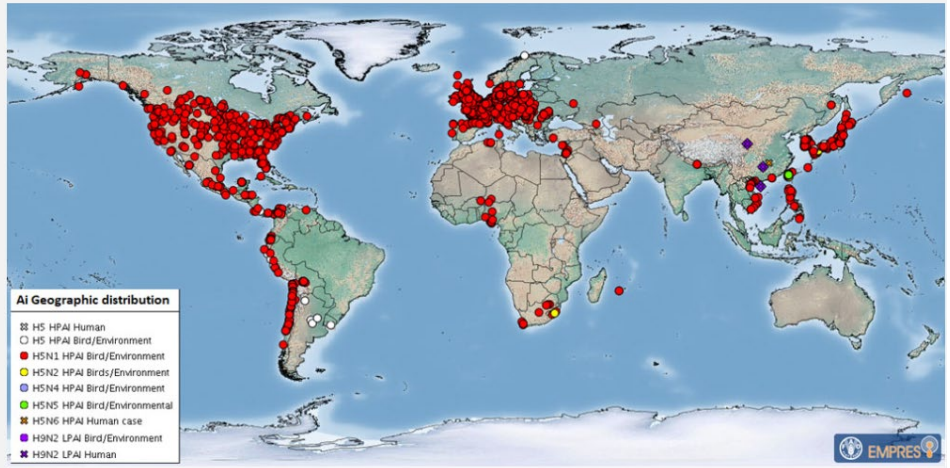
- Timely sharing of pathogen samples and information is essential for responding to potential epidemics and pandemics
- Inclusion of pathogens, including influenza, under national ABS legislation continues to cause delays and disruptions
  - Since Sep 2018, approximately 40 influenza viruses have been impacted by national NP/ABS legislation incurring delays from 3 weeks to several months before legal clarity obtained. In an increasing number of cases this is still outstanding.
- Legal certainty regarding the status of pathogen sharing is essential

Convention on Biological Diversity

Circulation of A(H5N1) avian influenza viruses in wild birds and poultry

- Since October 2021 an increasing number of outbreaks of avian influenza in wild birds and poultry has been reported worldwide with new geographic regions being impacted
- Infections in mammalian species have been reported with higher frequency
- The risk to human health is still considered to be low
- New CVVs that match recent antigenic variants are being prepared and made available to industry
- The response to a pandemic threat requires coordination among all stakeholders in the public and private sector

Map 1. *Global distribution of AIV with zoonotic potential* observed since 1 October 2022 (i.e. current wave)*



Note: Symbols may overlap for events in similar geographic locations.
* includes H5Nx, high pathogenicity avian influenza (HPAI) viruses.

Food and Agriculture Organization of the United Nations

Summary

- Two components of the NH2022/23 influenza vaccine were updated to match circulating viruses. CVV's and potency assay reagents were available early
- Approximately 173M influenza vaccine doses were supplied to the US market
- Vaccine demand was lower compared to previous year
- Flu vaccine provided substantial protection this season [1]
- Nagoya Protocol & ABS legislation is posing an increasing challenge and impacts ability to select & manufacture "best" vaccine strains
- Confidence in flu vaccination continues to be of great importance as flu circulation returns to pre-COVID-19 levels

[1] CDC Flu News & Spotlights Flu Vaccine Provided Substantial Protection This Season | CDC

Thank you for your attention