Vaccines and Related Biological Products Advisory Committee March 3, 2022 Meeting Presentation

Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please 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 2021-22 Northern Hemisphere Influenza Vaccine Supply

Vaccines and Related Biological Products Advisory Committee

03 March 2022

Beverly Taylor

(Seqirus 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 Seqirus, GSK, Sanofi, and AstraZeneca.

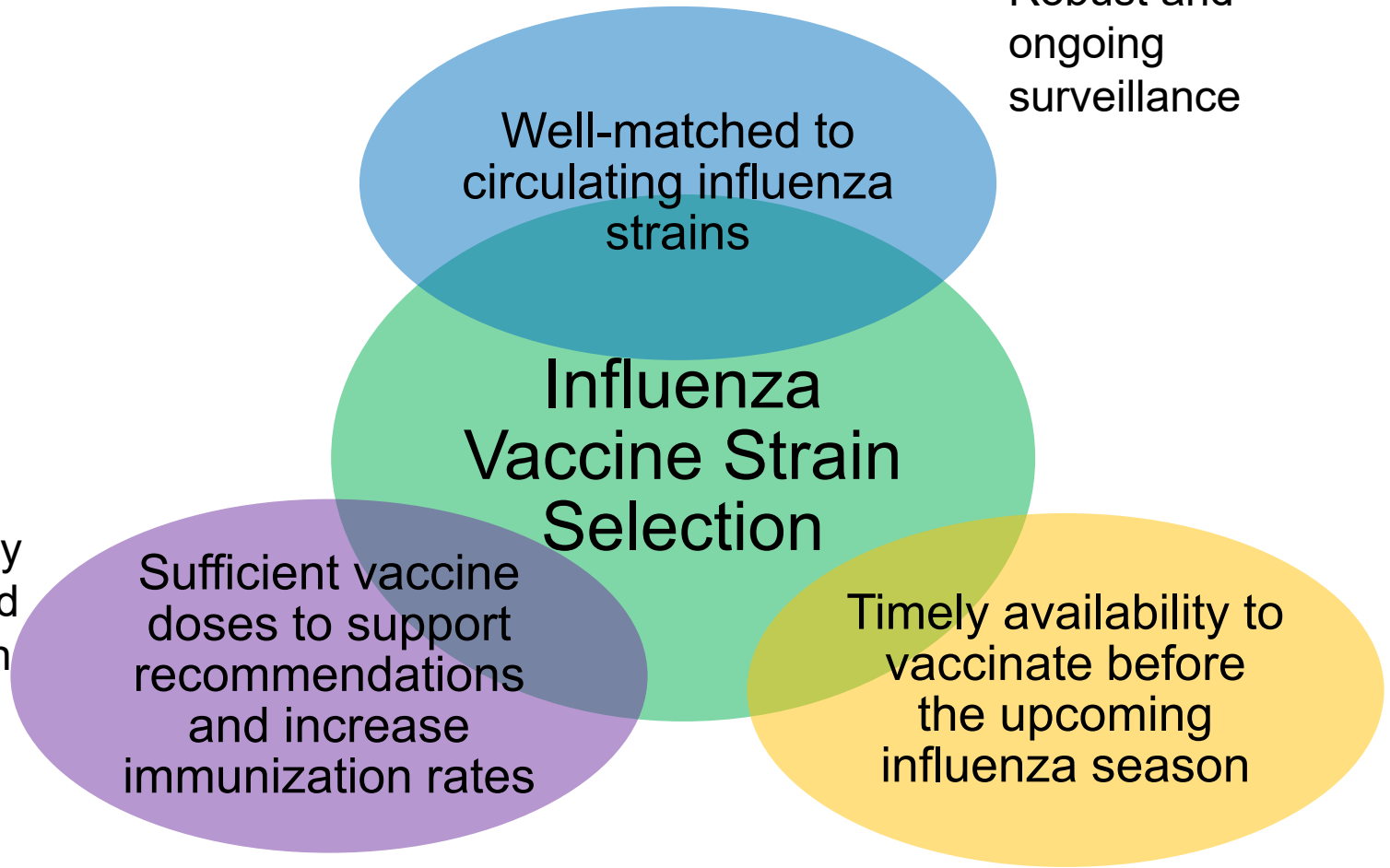
Presenter Disclosure Statement

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

Key Messages

- Key components of a successful vaccination campaign
- Influenza Surveillance during COVID-19 pandemic
- Strain changes and reagent supply for NH 2021/22 season
- Overview of manufacturing campaign timelines
- Continued challenges due to COVID-19
- Nagoya Protocol update

Successful influenza vaccination campaigns: A balancing act



Robust and ongoing surveillance

Choice of CVV by manufacturer and yield optimization

Supply of candidate vaccine viruses (CVVs) and potency assay reagents

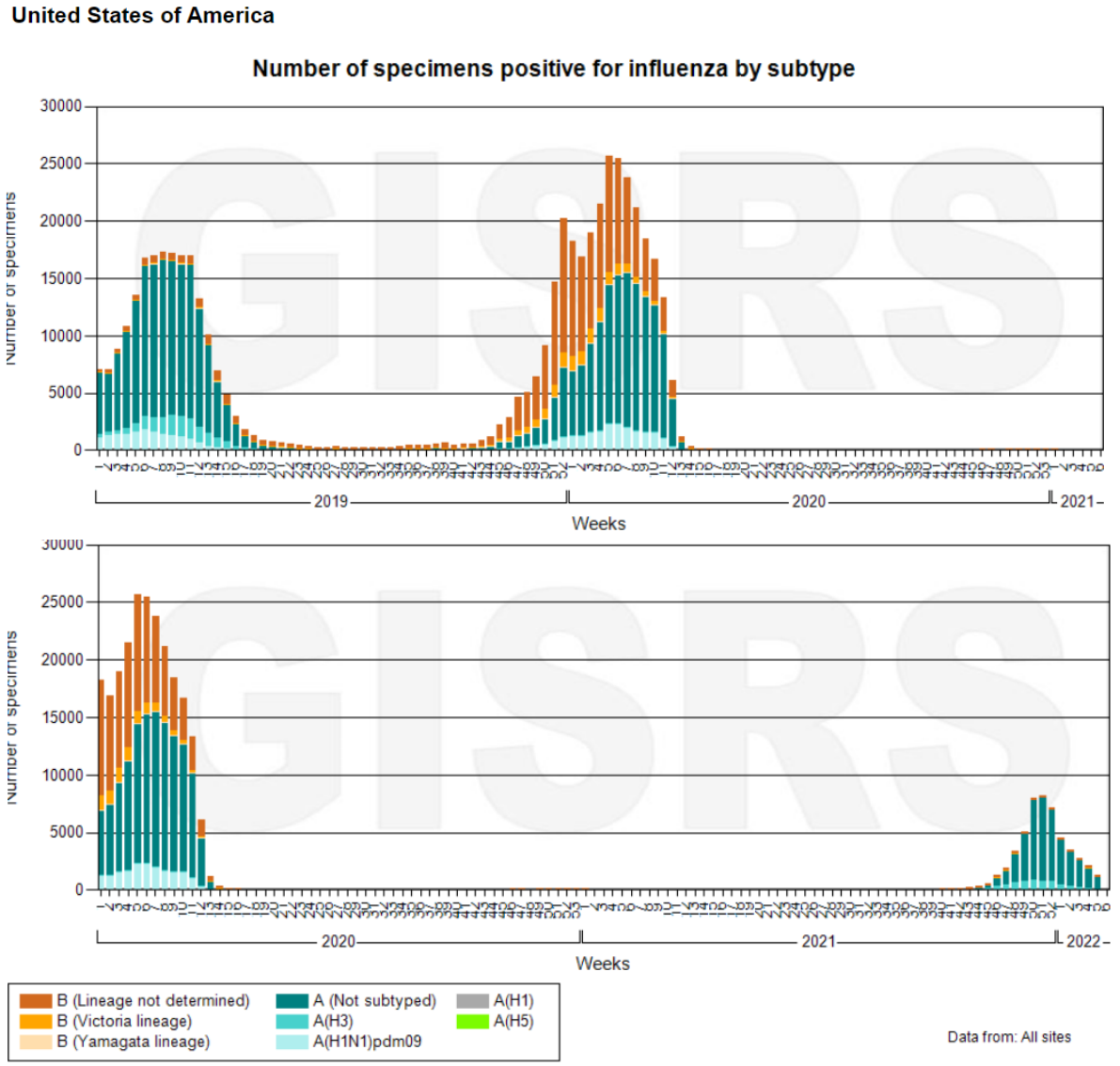
US Surveillance 2019/20 vs 2020/21

- Circulation of influenza viruses was extremely low from about week 12, 2020 until late 2021

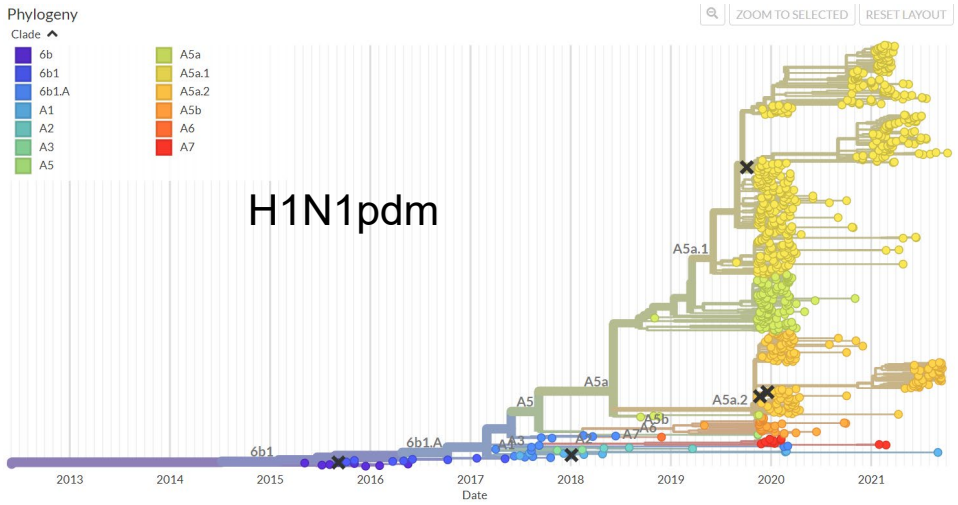
  e.g. Influenza positive samples 2020 vs 2021:

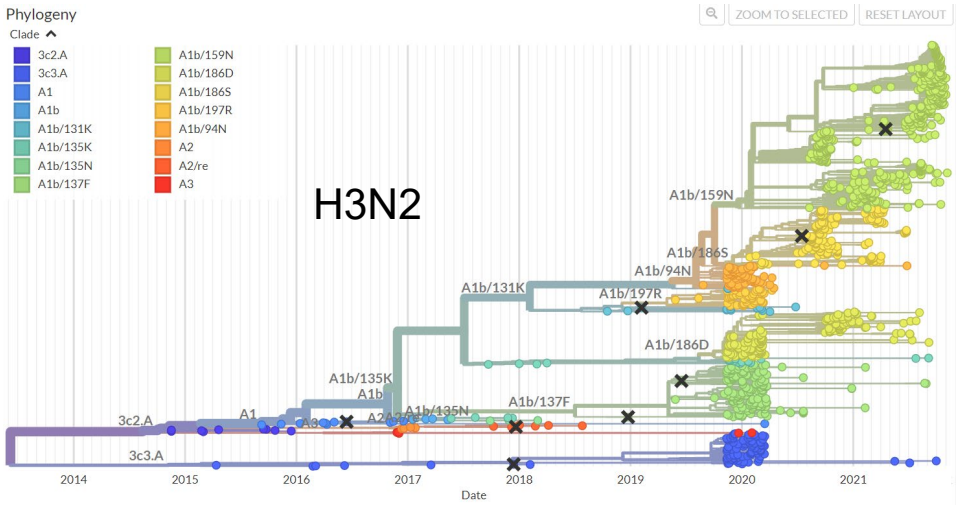
  - 2020 - wk 5 >25,000
  - 2021 - wk 5 <100

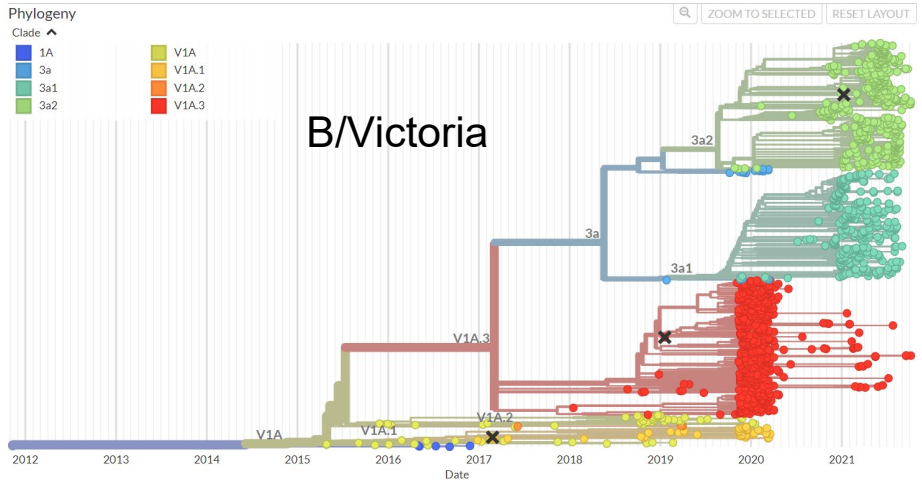
- However there were still pockets of activity in South East Asia and Africa and the antigenically distinct viruses were detected and a need to update the vaccine composition

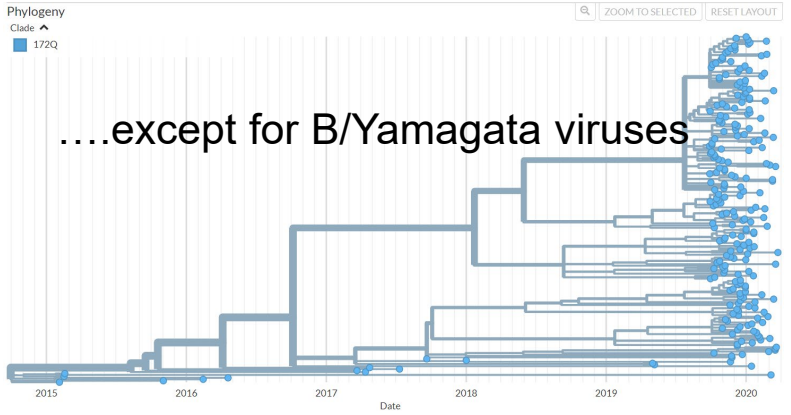


Continued to see viruses evolving…..









Graphic from Nextstrain using data from GISAID

NH 2021/22 Season Strain Recommendation

On 05 Mar 2021 the VRBPAC committee recommended that the quadrivalent formulation of influenza vaccines for the U.S. 2021/22 influenza season contain the following:

Egg based

- an A/Victoria/2570/2019 (H1N1) pdm09-like virus;
- an A/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019- 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/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019- 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 2020/2021 season

Supply of H1N1pdm Potency Reagents for 2021-22 Season

H1N1 pdm reagents			
ERL	**CVV**	**Egg/Cell/ Recombinant**	**Calibration date**
TGA	A/Victoria/2570/2019 IVR-215	Egg	24 Nov2020*
NIBSC	A/Victoria/2570/2019 IVR-215	Egg	15 Dec 2020*
CBER	A/Victoria/2570/2019 IVR-215	Egg	15 Dec 2020*
CBER	A/Delaware/55/2019	Cell	04 Feb 2021*
CBER	A/Wisconsin/588-2019	Recombinant	25 May 2021

* Calibrated for SH

CBER again confirmed they would accept TGA and NIBSC reagents for testing of egg based vaccines provided manufacturers specified which reagents they would use.

Supply of H3N2 Potency Reagents for 2021-22 Season

H3N2 reagents			
ERL	**CVV**	**Egg/Cell/ Recombinant**	**Calibration date**
TGA	A/Cambodia/e0826360/2020-like sheep antiserum (AS444)	All	27 May 2020
NIBSC	A/Cambodia/e0826360/2020 IVR-224	Egg	01 Jun 2021
NIBSC	A/Tasmania/503/2020 IVR-221	Egg	01 Jun 2021
CBER	A/Tasmania/503/2020 IVR-221	Egg	26 May 2021
CBER	A/Tasmania/503/2020	Cell	28 May 2021
CBER	A/Tasmania/503/2020*	Recombinant	26 May 2021

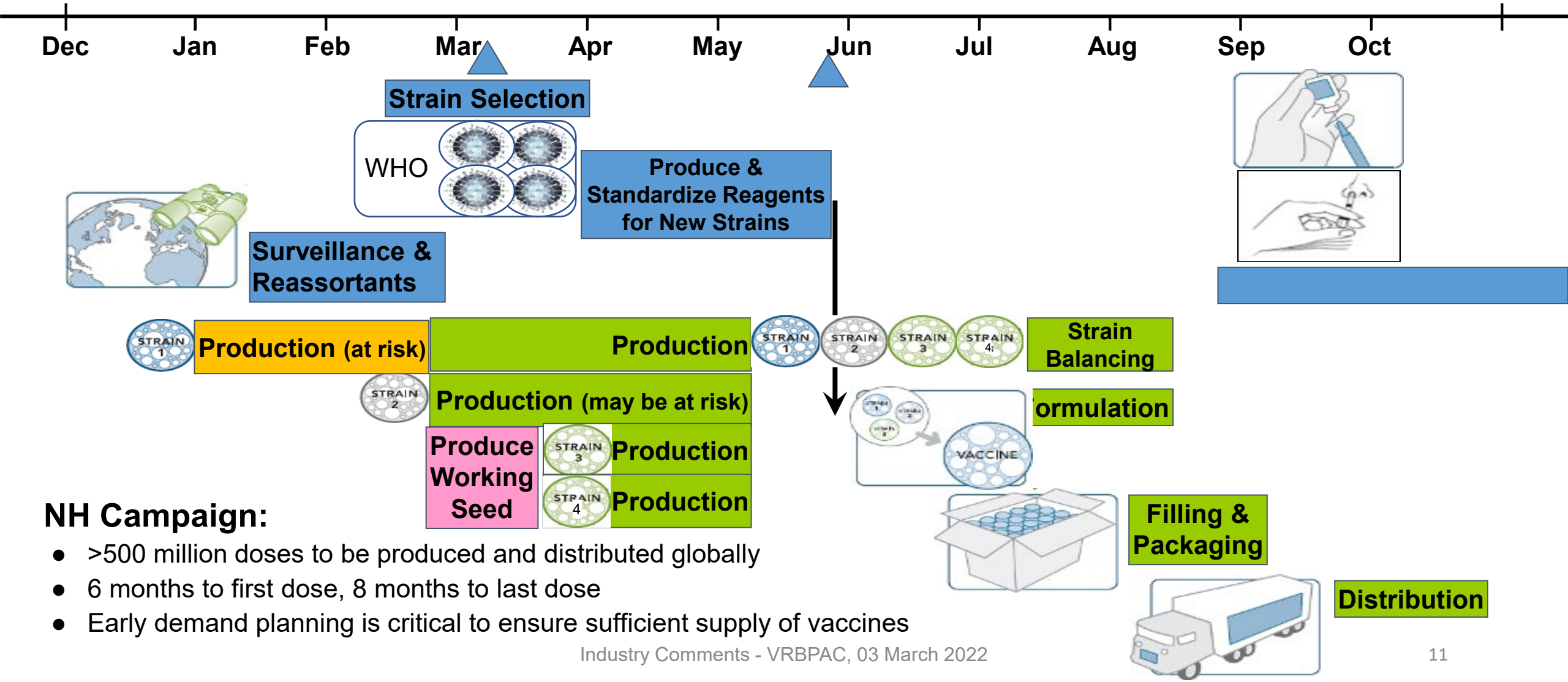
* Calibrated against TGA antiserum

Despite ongoing concerns about the reduced number of flights and issues with international couriers, ERL's prioritized calibration of reagents and the timing of the calibration values for reagents was similar to previous years

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 2021/22 manufacturing campaign	**Two strain changes A(H1N1)pdm and A(H3N2)** **Nagoya Protocol issues** **Challenges with materials and components supply** **Ongoing impact of COVID-19 Pandemic on transport and freight**

Annual Influenza Vaccine Manufacturing Timeline for US Supply

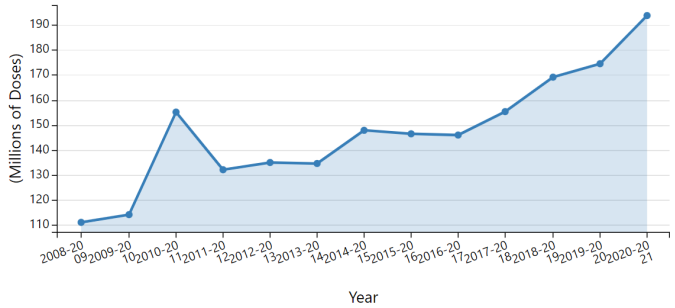


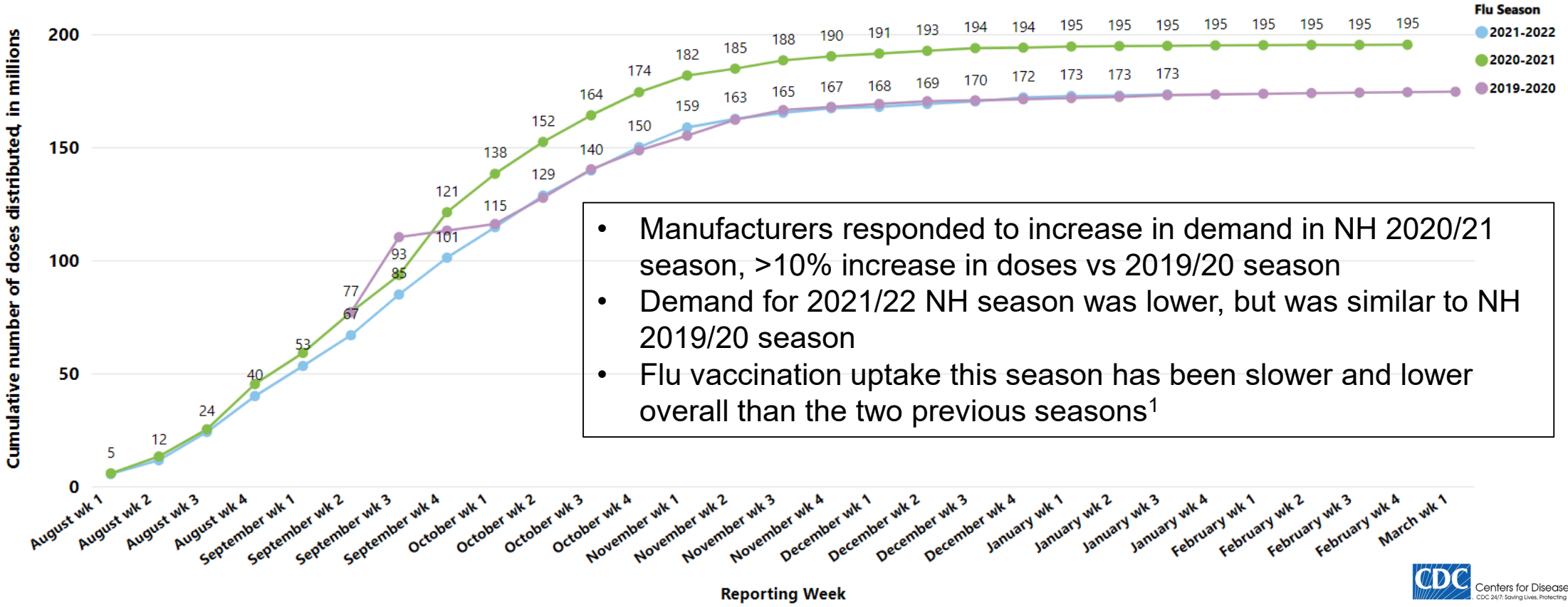
NH Campaign:

- >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

US Influenza Vaccine Distribution

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 NH season was lower, but was similar to NH 2019/20 season
- Flu vaccination uptake this season has been slower and lower overall than the two previous seasons[1]

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

[1]Summary of CDC update on US seasonal uptake Jan 20 - | National Adult and Influenza Immunization Summit (izsummitpartners.org)

Continued Challenges due to COVID-19

- Despite increased testing by National Influenza Centres, only low levels of influenza detected with main pockets of activity in China, SE Asia and parts of Africa
- Different viruses were isolated in different regions so difficult to predict which viruses would predominate in NH 2021/22 season
- Low number of available virus isolates for NH 2021/22 and SH 2022 manufacturing campaigns
- No genetic sequence data or physical samples received for B/Yamagata viruses in ~2 years
- Lack of clarity on Nagoya/ABS status of the limited number of available viruses
- Supply chain challenges and material shortages due to prioritization of materials for COVID-19 vaccines
- Slower and Reduced influenza vaccine uptake rates

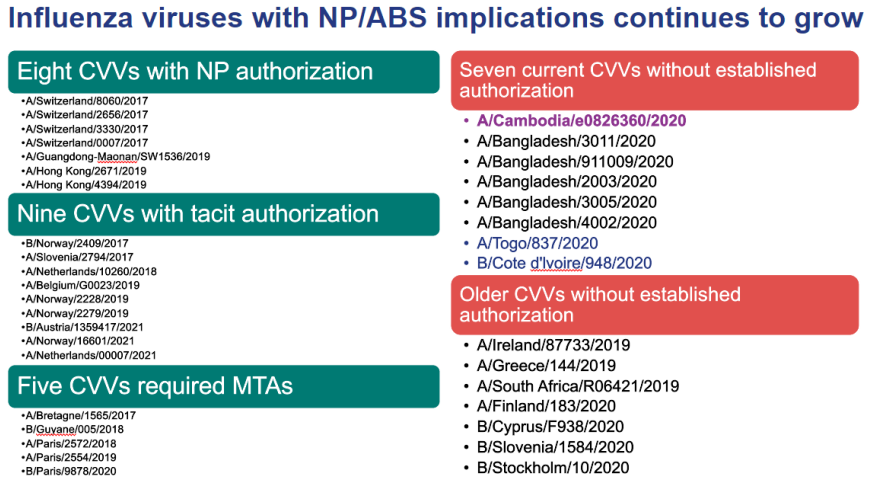
Nagoya Protocol - Background

- The Nagoya Protocol (NP) on Access and Benefit Sharing (ABS), an international treaty supplementary to the Convention on Biological Diversity (CBD), 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.
- Under the terms of the NP, GR may be accessed subject to the “prior informed consent” (PIC) of the country of origin and once “mutually agreed terms” (MAT) have been reached.
- It is the responsibility of each Party (country) to decide how to address pathogens as part of their implementing legislation, in many cases they have been included.
- To date, 134 countries have become a party to the NP, many of which have implemented ABS legislation which could potentially impact pathogen sharing or the use of digital sequence information (DSI) / genetic sequence data (GSD).
- Legislation differs in each country which poses challenges with interpretation of requirements.

Convention on Biological Diversity

Current situation and Impact on NH 2021/2022 Campaign

- An increasing number of countries have enacted Nagoya Protocol/National ABS legislation, and in many cases includes genetic sequence data (GSD) within scope.
- 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
- Since Sep 2018, > 30 influenza viruses impacted by national NP/ABS legislation incurring delays from 3 wks to several months before legal clarity obtained, in an increasing number of cases this is still outstanding.
- The delays in obtaining legal clarity on the ability to use the H3N2 virus from Cambodia for the NH 2021/22 season impacted:
  - Timing of decisions on which virus to use by manufactures
  - Whether critical reagents would be prepared and made available to manufacturers
  - Manufacturers ability to use the virus even though it had been listed on the WHO website for a month
  - Possibility of manufactured batches being discarded



- "Commercial use" eventually approved by Cambodia, but still no written confirmation that monetary benefits are not required

Poses an ongoing risk of impact to seasonal influenza vaccine supply including for the U.S. market

Nagoya Protocol impact on sharing of influenza viruses

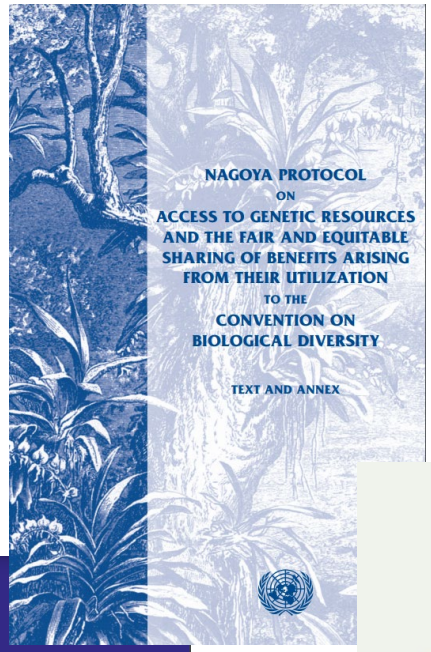
- There have been frequent questions regarding compliance with the Nagoya Protocol (NP) in the sharing of seasonal influenza viruses, with different stakeholders often facing similar issues
- Covingtons (Belgium) generated a report based on the responses from stakeholder interviews carried out in 2021 which included:
  - Current work processes in GISRS
  - Impact of NP/national ABS laws
  - Suggestions to overcome NP challenges
- The report was reviewed by a multi-stakeholder group at a meeting held at the National Institute for Biological Standards and Control (NIBSC) in the UK in July 2021, with the aim of finding a solution to the NP challenges. There was a general agreement to work towards a common approach to compliance with the NP and national ABS laws
- Next steps were discussed earlier this year at the January NIBSC meeting and include:
  - Continue communication with national authorities, particularly the Ministries of Health and Environment, on the benefits from GISRS, and how that fits with NP
  - Development of toolkit for NICs to use with NP National Focal Points
  - Use of a Seasonal Influenza Material Transfer Agreement (SIMTA)
  - Review of Terms of Reference for NICs

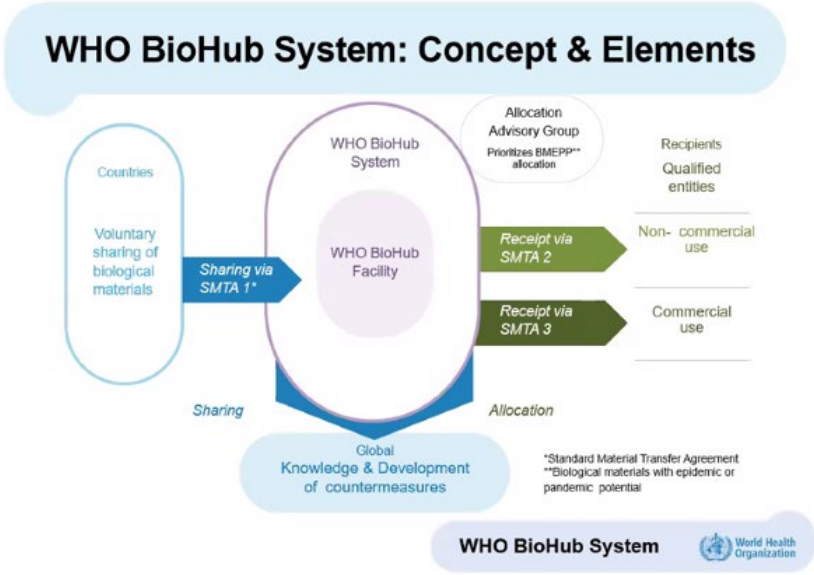
The Bedrock of Global Health Security…

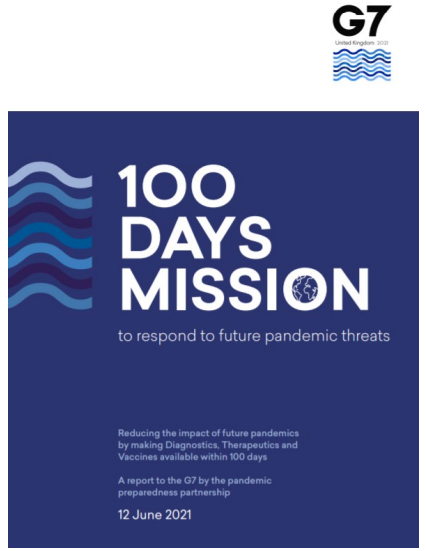
…is the Swift, certain, and unencumbered access to pathogens and their genetic information

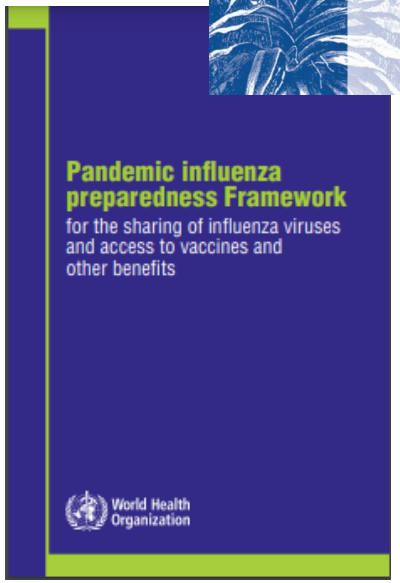
- **Pathogens know no borders**
- The **timely sharing of pathogen samples and information is essential** for responding to potential epidemics and pandemics.
- **Inclusion** of pathogens, including influenza, under national ABS legislation is **already causing significant delays/disruptions**.
- **Bilateral negotiation** of access and benefit-sharing contracts are lengthy and block any possibility of quickly responding to public health emergencies. Global alignment on ABS is essential to enable rapid responses to global health threats.
- **Legal certainty** regarding the status of pathogen sharing under ABS legislation is necessary; **clear exemption is the most effective** way forward.

Landscape complexity is increasing









Summary

- Despite extremely low circulation of influenza viruses, the virus continued to evolve which resulted in the vaccine composition being updated for the NH2021/22 season
- CVV's and potency assay reagents were supplied within normal timeframes
- Challenges due to COVID-19 continued, these included issues with supply of materials and components and with transport/freight
- Approximately 174M influenza vaccine doses were supplied to the US market, but vaccine uptake rates were slower and lower than the last two seasons[1]
- Influenza is a serious, yet often underestimated disease, for which vaccination is the best means of prevention
- Nagoya Protocol & ABS legislation is posing an increasing challenge and impacts ability to select & manufacture "best" vaccine strains
- The complexity of the ABS landscape is increasing with the WHO Biohub and a new pandemic instrument being developed, risking further delays in virus sharing.
- **Flu vaccination continues to be of great importance as flu circulation increases and international travel resumes**

[1]Summary of CDC update on US seasonal uptake Jan 20 - | National Adult and Influenza Immunization Summit (izsummitpartners.org)

Teamwork is needed to get the influenza vaccine over the finish line, which includes getting people vaccinated.
In the interests of public health, focus on COVID-19 vaccinations must not negatively impact other vaccinations including for influenza.

Thank you for your attention