

**Vaccines and Related Biological Products  
Advisory Committee March 5, 2021  
Meeting Presentation**

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# Influenza Vaccine Manufacturing

## Industry Perspective for 2020-21 Northern Hemisphere Influenza Vaccine Supply

Vaccines and Related Biological Products Advisory Committee

05 March 2021

Lauren Parker

(AstraZeneca on behalf of Influenza Vaccine Manufacturers)

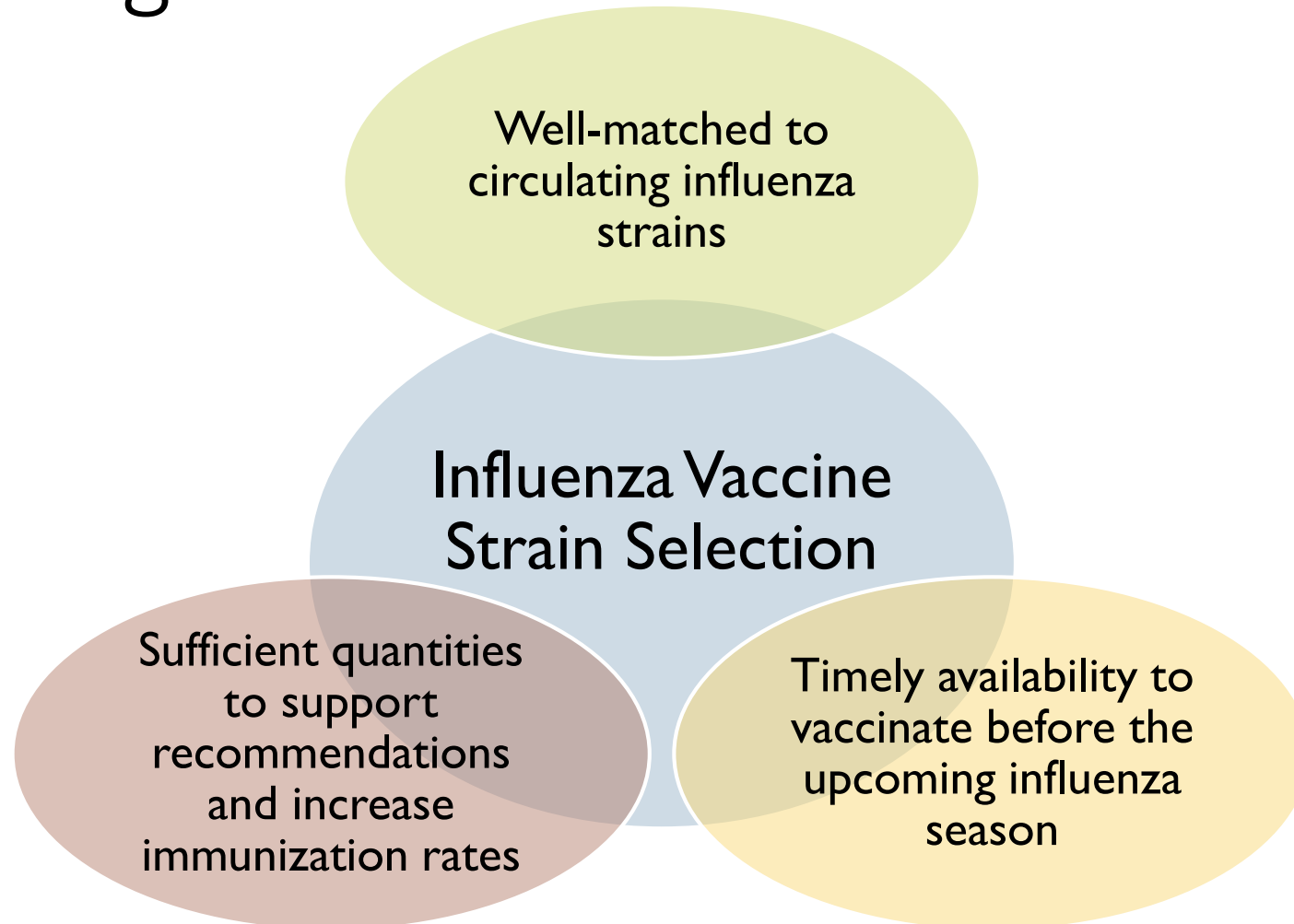
*The FDA CBER requested this annual summary of information from influenza vaccine manufacturers supplying the U.S., for purposes of a general presentation to the VRBPAC. This summary has been prepared from a variety of public sources, and was reviewed by Seqirus, GSK, Protein Sciences, Sanofi Pasteur,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

# Presenter Disclosure Statement

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



# Successful influenza vaccination campaigns: A balancing act



# It takes a team to beat Influenza



## 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

## Additional challenges for influenza vaccines

Multiple batons

CVVs, Reagents, Vaccine types

Multiple providers

CCs, ERLs, HYR labs

Potential hurdles

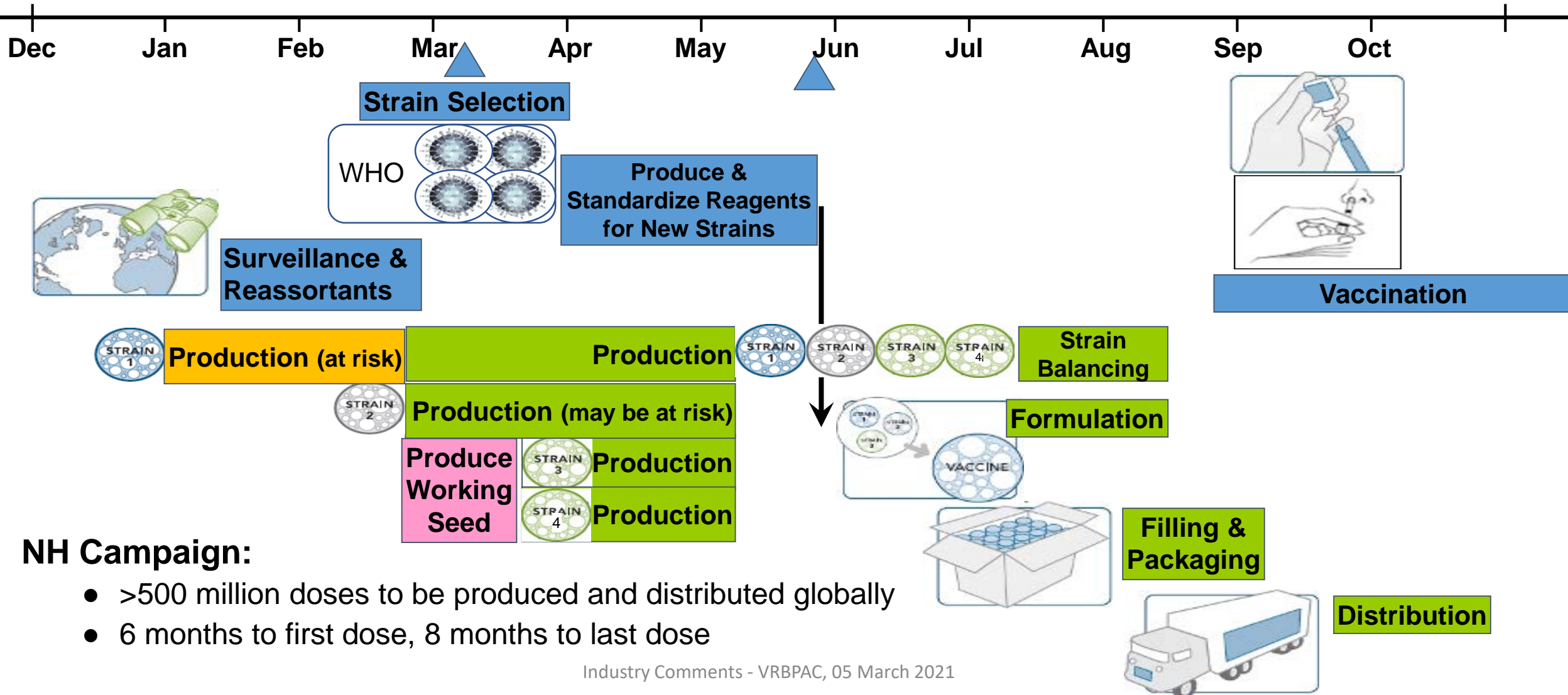
**Unexpected/delayed changes**  
**Nagoya Protocol**

**COVID-19 Pandemic**

# “Hurdles” of the 2020-2021 season

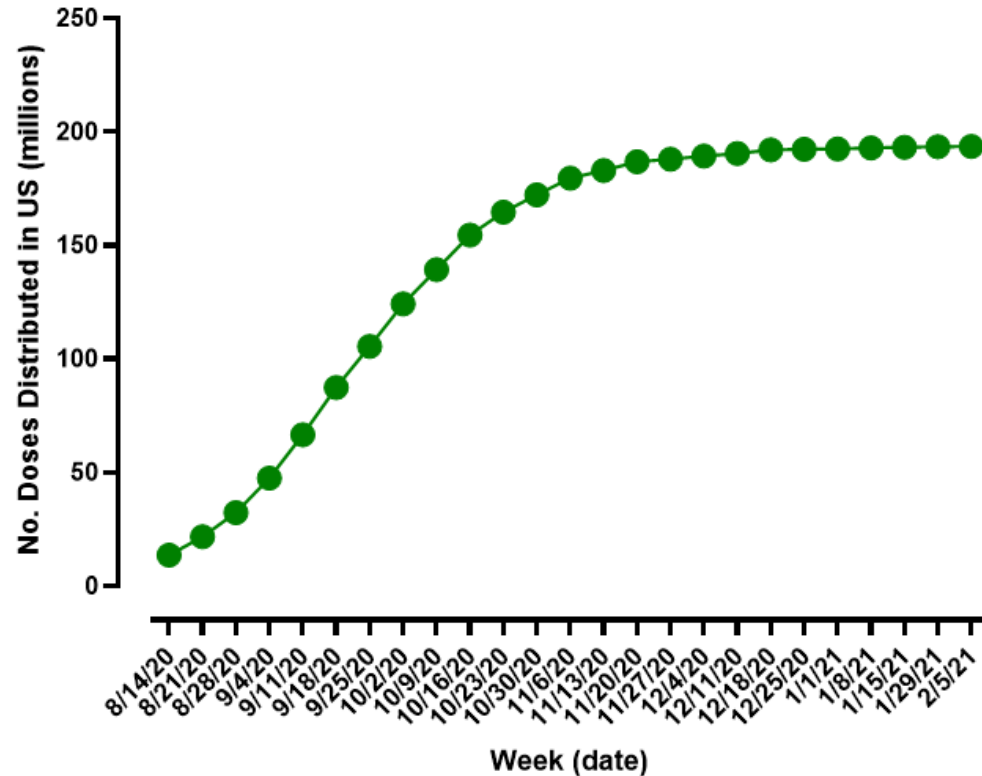


# Annual Influenza Vaccine Manufacturing Timeline for US Supply



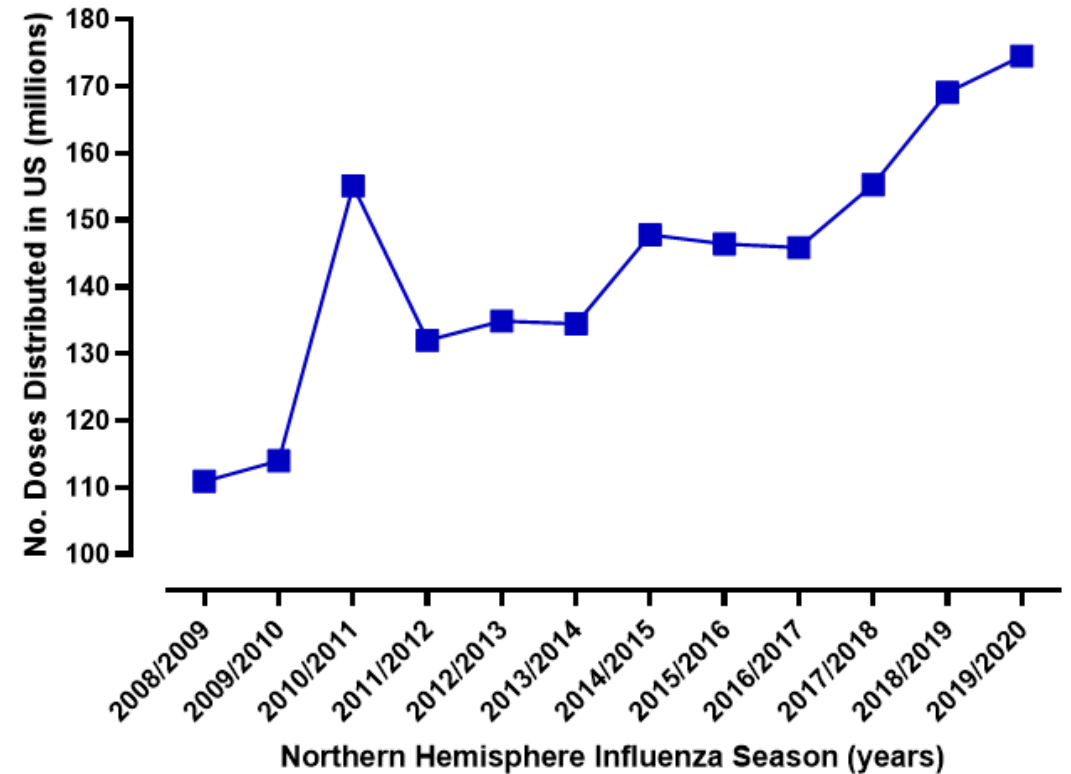
# US Influenza Vaccine Distribution

Total Doses of Influenza Vaccines Distributed (2020-2021 season)



<https://www.cdc.gov/flu/prevent/vaccine-supply-distribution.htm>

No. of Influenza Vaccine Doses Distributed in US by Season



<https://www.cdc.gov/flu/prevent/vaccine-supply-historical.htm>



# Northern Hemisphere Strain Recommendations

Subtype	2019-2020	2020-2021	2021-2022 (WHO)
A/H1N1pdm09	A/Brisbane/02/2018-like	<b>Egg-based: A/Guangdong Maonan/SWL1356/2019-like</b>  <b>Cell &amp; recombinant: A/Hawaii/70/2019-like</b>	<b>Egg-based: A/Victoria/2570/2019-like</b>  <b>Cell &amp; recombinant: A/Wisconsin/588/2019-like</b>
A/H3N2	A/Kansas/14/2017 –like	<b>Egg-based: A/Hong Kong/2671/2019</b>  <b>Cell &amp; recombinant: A/Hong Kong/45/2019-like</b>	<b>A/Cambodia/e0826360/2020 -like</b>
B strain for TIV	B/Colorado/06/2017-like (B-Victoria lineage, Δ2)	<b>B/Washington/02/2019-like (B-Victoria lineage, Δ3)</b>	B/Washington/02/2019-like (B-Victoria lineage, Δ3)
Additional B-Strain for QIV	B/Phuket/3073/2013-like (B-Yamagata lineage)	B/Phuket/3073/2013-like (B-Yamagata lineage)	B/Phuket/3073/2013 -like (B-Yamagata lineage)

# Overview of 2020-21 NH Campaign

3 strain changes from NH 2019-2020:

A/H1N1pdm09

A/H3N2

B-Victoria

Bi-weekly WHO-Industry teleconferences  
September to February

CFWG Influenza Hub fully implemented

COVID-19 pandemic affected international  
transport & freight, but overall, issues resolved

Nagoya Protocol/ABS issues continue to be of  
concern

Increased global demand for influenza vaccines

~20% globally

>10% increase in supplied doses to US

# Supply of Critical Potency Reagents for 2020-21 Season (1).

<b>A/H1N1pdm09 Critical Reagents</b>			
<b>ERL</b>	<b>CVV / Recombinant Antigen</b>	<b>Egg/Cell/ Recombinant</b>	<b>Calibration date</b>
TGA	A/Victoria/2454/2019 IVR-207	Egg	19 May 2020
NIBSC	A/Guangdong-Maonan/SWL 1536/2019 CNIC-1909	Egg	29 May 2020
NIBSC	A/Victoria/2454/2019 IVR-207	Egg	10 Jun 2020
CBER	A/Guangdong-Maonan/SWL 1536/2019 CNIC-1909	Egg	09 Jun 2020
CBER	A/Nebraska/14/2019	Cell	01 Jun 2020
CBER	A/Hawaii/70/2019	Recombinant	04 Jun 2020

**Despite concern over reduced staffing levels & reduced focus on Influenza, ERLs prioritised generation & calibration of critical reagents**

# Supply of Critical Potency Reagents for 2020-21 Season (2)

<b>A/H3N2 critical reagents</b>			
<b>ERL</b>	<b>CVV / Recombinant Antigen</b>	<b>Egg/Cell/ Recombinant</b>	<b>Calibration date</b>
TGA	A/Hong Kong/2671/2019 IVR-208	Egg	27 May 2020
NIBSC	A/Hong Kong/2671/2019 NIB-121	Egg	29 May 2020
NIBSC	A/Hong Kong/2671/2019 IVR-208	Egg	04 Jun 2020
CBER	A/Hong Kong/2671/2019 IVR-208	Egg	09 Jun 2020
CBER	A/Delaware/39/2019	Cell	01 Jun 2020
CBER	A/Minnesota/41/2019	Recombinant	01 Jun 2020

**The efforts made by ERLs resulted in calibrated reagent availability in time frame similar to previous seasons**

# Impact of COVID-19 Pandemic

Smaller pool of strains for CVV generation

Increased demand for influenza vaccines

Confirmation that SARS-CoV-2 is not adventitious agent

Greatly reduced numbers of Influenza viruses circulating

Reduced staff numbers

## RAPID COMMUNICATION

**SARS-CoV-2 does not replicate in embryonated hen's eggs or in MDCK cell lines**

Ian G Barr<sup>1,2,3</sup>, Cleve Rynehart<sup>1</sup>, Paul Whitney<sup>1,2</sup>, Julian Druce<sup>4</sup>

1. The WHO Collaborating Centre for Reference and Research on Influenza, The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia
2. Department of Microbiology and Immunology, The University of Melbourne, The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia
3. Faculty of Science and Technology, Federation University, Gippsland, VIC, Australia
4. Victorian Infectious Diseases Reference Laboratory, The Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia

**SARS-CoV-2 susceptibility of cell lines and substrates commonly used in diagnosis and isolation of influenza and other viruses**

Li Wang, Xiaoyu Fan, Gaston Bonenfant, Dan Cui, Jaber Hossain, Nannan Jiang, Gloria Larson, Michael Currier, Jimma Liddell, Malania Wilson, Azaibi Tamin, Jennifer Harcourt, Jessica Ciomperlik-Patton, Hong Pang, Naomi Dybdahl-Sissoko, Ray Campagnoli, Pei-Yong Shi, John Barnes, Natalie J. Thornburg, David E. Wentworth, Bin Zhou



62% drop in influenza virus shipments to WHO CCs



94% drop in genetic sequences uploaded to GISAID

Supply chain & logistical challenges

# Nagoya Protocol Update



NP objectives are to ensure:

- Oversight of access to genetic resources and related traditional knowledge for R&D and potential commercial utilization
- Users and providers of genetic resources and related traditional knowledge agree on fair and equitable sharing of benefits arising from their utilization

- **As of 21 Feb 2021: 129 countries have ratified and entered the NP into legal force**
  - Requires national consent to access (genetic resource/s) and pre-agreed terms for fair, equitable benefit sharing prior to R&D
  - Failure to comply may lead to accusation of biopiracy, litigation, product restrictions, a claim on income or halt in orders
  - A number of countries have also passed national access and benefit sharing (ABS) legislation, which is independent of NP, and in some cases includes genetic sequence data (GSD) or digital sequence information (DSI) as well as biological samples.
- Pathogens, including influenza, fall within the scope of the Nagoya Protocol. It is the sovereign right of each country to determine if pathogens are included in its national ABS/NP legislation. The PIP Framework is recognized by some countries/regions to be a specialized international instrument, which means that influenza strains with pandemic potential are exempt in those countries/regions.
- Time (~ 3 months) required to formalize legal benefit sharing arrangements to use the genetic resources from each source NP participating country
- **Potential risk regarding impact to seasonal influenza vaccine supply for the U.S. market**

# Nagoya Protocol Issues Continue

CVVs with NP authorisation	CVVs with tacit authorisation	CVVs requiring MTA's	Current CVVs without established authorisation**
A/Switzerland/8060/2017	A/Slovenia/2794/2019	A/Bretagne/1565/2017	A/Finland/183/2020
A/Switzerland/2656/2017	A/Netherlands/10260/2018	B/Guyane/005/2018	A/Cambodia/e0826360/2020
A/Switzerland/3330/2017	A/Belgium/G0023/2019	A/Paris/2572/2019	A/Bangladesh/3011/2020
A/Switzerland/0007/2017	A/Norway/2228/2019	A/Paris/2554/2019	A/Bangladesh/2003/2020
A/Hong Kong/2671/2019	A/Norway/2279/2019		A/Bangladesh/4005/2020
A/Hong Kong/4394/2019	B/Norway/2409/2019		A/Bangladesh/911009/2020
A/Guangdong-Maonan/SWL1536/2019			B/Cyprus/F938/2020
			B/Slovenia/1584/2020
			B/Stockholm/10/2020

**\*\*Plus an additional 5 older CVVs with no established authorisation**

# NP / ABS Risks & Concerns

- An increasing number of countries have NP or National ABS Legislation in place, resulting in an increase in number of NP/ABS impacted viruses
- The NP/ABS legislation is different in each country and is not always clear. As the number of different national procedures increases, the interpretation of requirements becomes more challenging
- Increase in time to obtain clarity and receive authorization to use viruses
- Some countries have national ABS legislation restricting use of genetic resources independent of NP
- Several countries have already passed legislation which includes GSD/DSI, with others considering amending existing legislation to include it
- Lack of legal clarity if viruses supplied by NICs through WHO can be used for development & manufacturing

**Risk to supply: delays due to required clarification, negotiation, and/or notification costs by manufacturers to address & resolve**



# Summary

- Influenza is a serious, yet often underestimated disease, for which vaccination is the best means of prevention
- There is a continued increase in demand for vaccines, in same constrained timeframe
- Delayed/unexpected strain selection may impact supply, and therefore vaccine usage/uptake
- Nagoya Protocol & ABS legislations continue to challenge and impact ability to select & manufacture “best” vaccine strains
- **Flu vaccination will continue to be of great importance going into the next NH season as COVID-19 vaccinations increase and restrictions/travel bans are lifted**

- ✓ COVID-19 pandemic did not significantly impact 2020-21 season vaccine supply, and increased demand met successfully in most cases
- ✓ NP / ABS issues resolved ahead of time
- ✓ Due to the efforts of ERL & HYR labs, all seasonal CVVs, reagents, were available in time

**We are all in this 'race' together to ensure adequate supply of the best possible vaccines, and most importantly, public health**

# Thank you for your attention

