Vaccines and Related Biological Products Advisory Committee March 5, 2021 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 2020-21 Northern Hemisphere Influenza Vaccine Supply

Vaccines and Related Biological Products Advisory Committee

05 March 2021

Lauren Parker

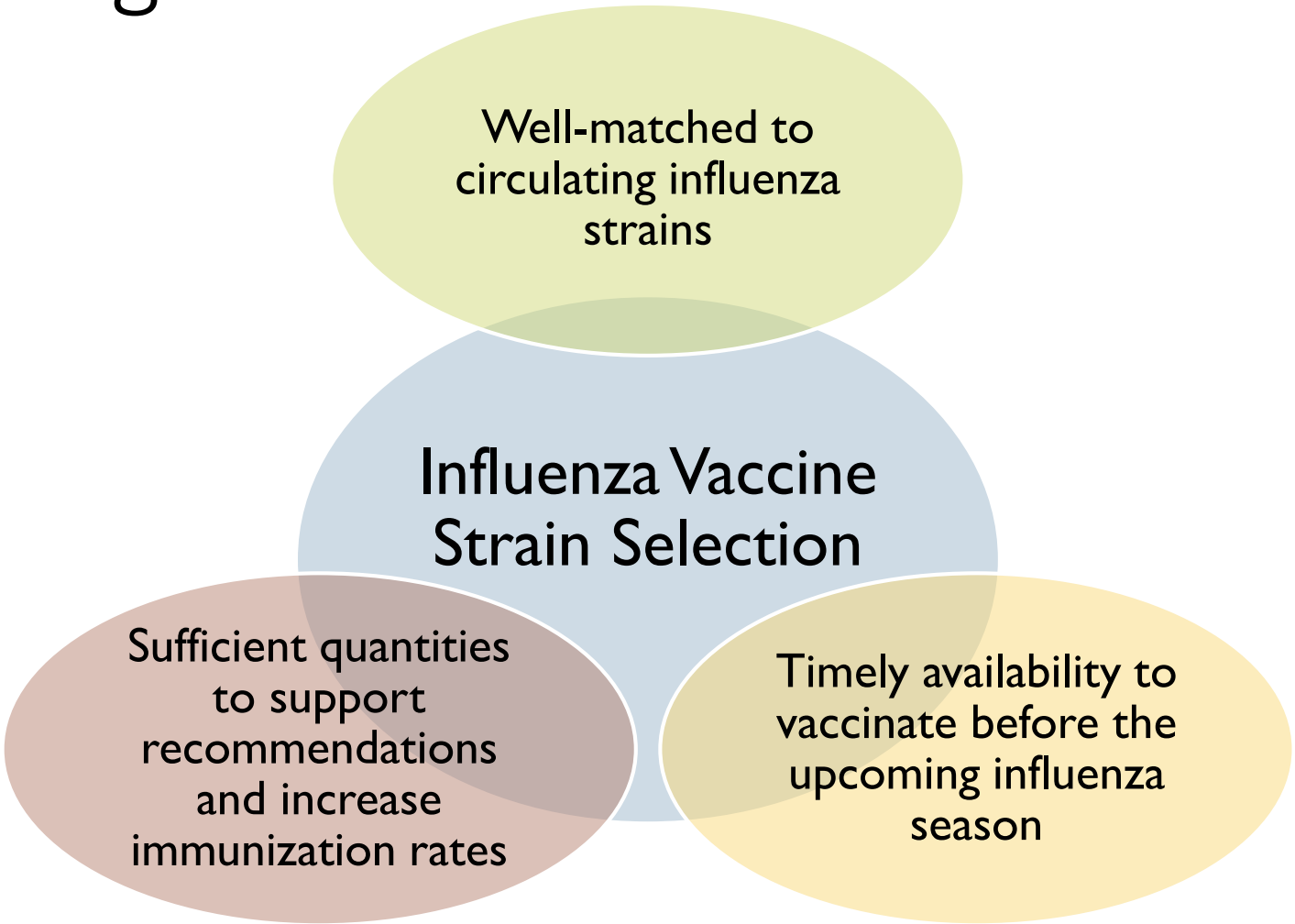
(AstraZeneca on behalf of Influenza Vaccine Manufacturers)

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

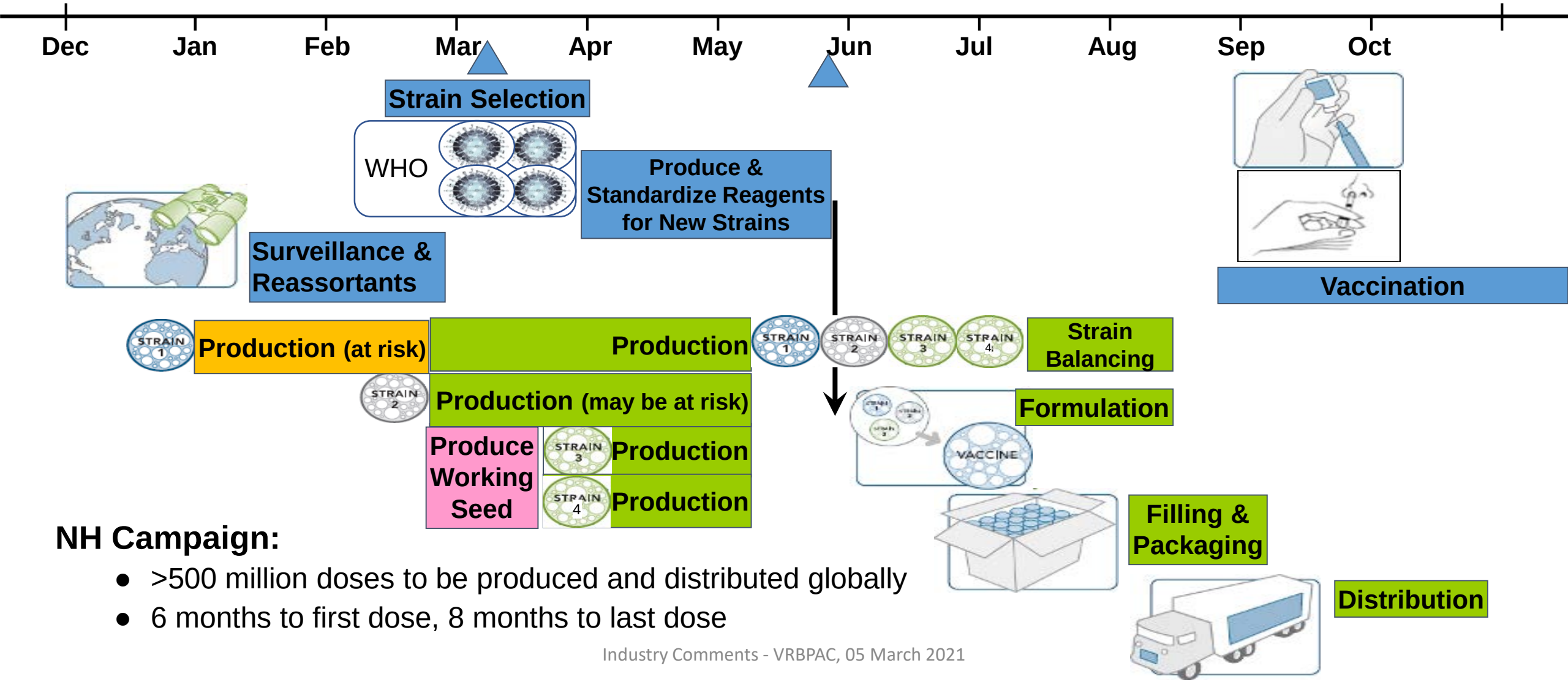


It takes a team to beat Influenza

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

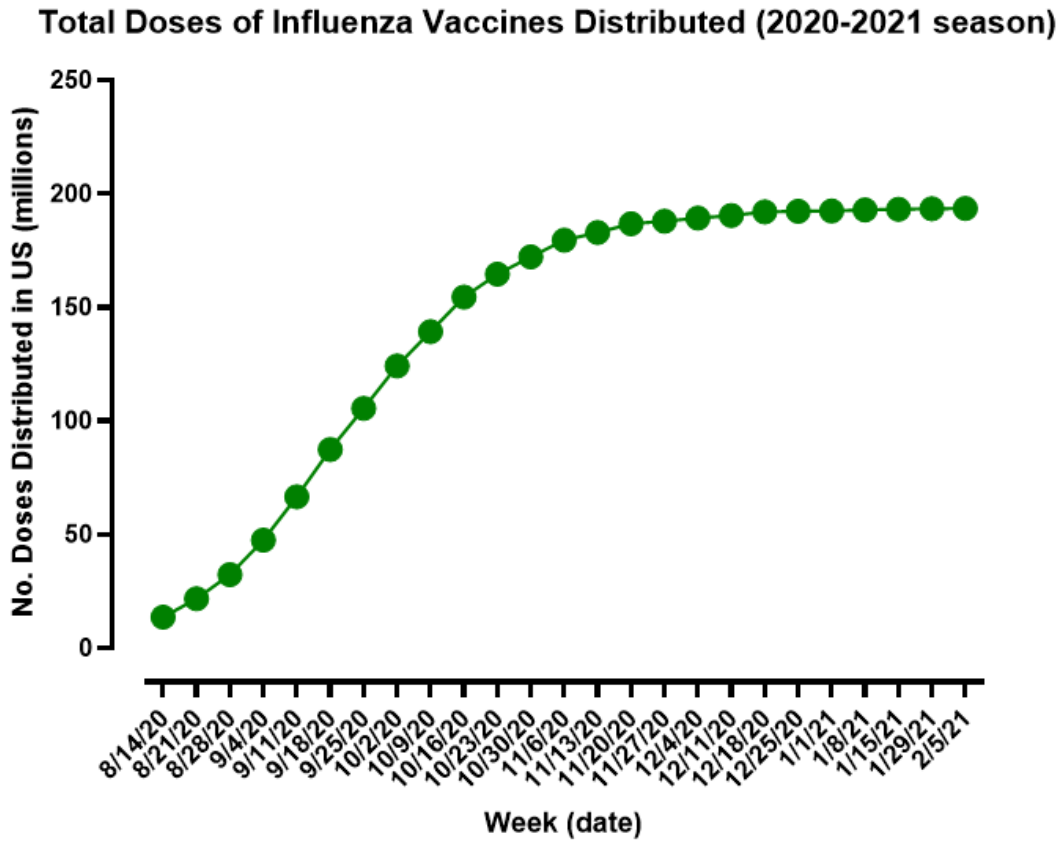
Annual Influenza Vaccine Manufacturing Timeline for US Supply

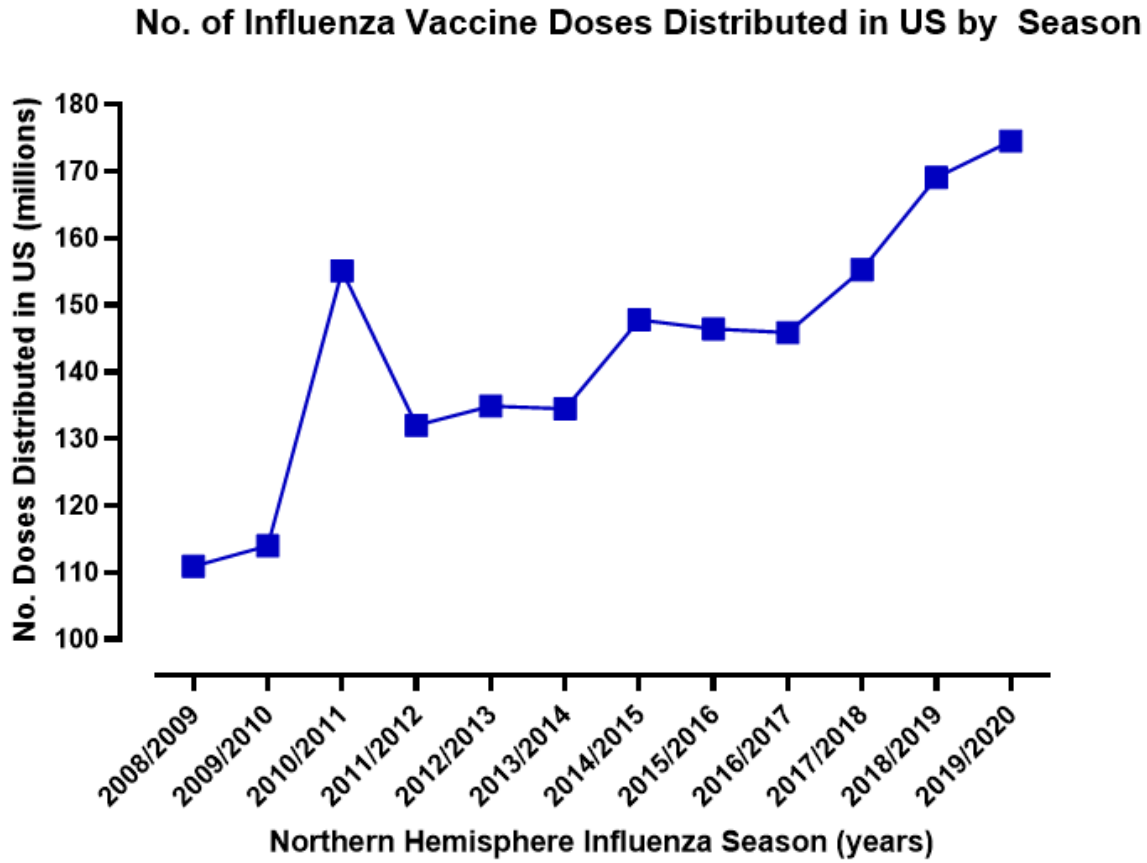


NH Campaign:

- >500 million doses to be produced and distributed globally
- 6 months to first dose, 8 months to last dose

US Influenza Vaccine Distribution





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

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	**Egg-based: A/Guangdong Maonan/SWL1356/2019-like** **Cell & recombinant: A/Hawaii/70/2019-like**	**Egg-based: A/Victoria/2570/2019-like** **Cell & recombinant: A/Wisconsin/588/2019-like**
A/H3N2	A/Kansas/14/2017 –like	**Egg-based: A/Hong Kong/2671/2019** **Cell & recombinant: A/Hong Kong/45/2019-like**	**A/Cambodia/e0826360/2020 -like**
B strain for TIV	B/Colorado/06/2017-like (B-Victoria lineage, Δ2)	**B/Washington/02/2019-like (B-Victoria lineage, Δ3)**	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).

A/H1N1pdm09 Critical Reagents			
ERL	**CVV / Recombinant Antigen**	**Egg/Cell/ Recombinant**	**Calibration date**
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)

A/H3N2 critical reagents			
ERL	**CVV / Recombinant Antigen**	**Egg/Cell/ Recombinant**	**Calibration date**
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

Greatly reduced numbers of Influenza viruses circulating

62% drop in influenza virus shipments to WHO CCs

94% drop in genetic sequences uploaded to GISAID

Increased demand for influenza vaccines

Reduced staff numbers

Supply chain & logistical challenges

Confirmation that SARS-CoV-2 is not adventitious agent

RAPID COMMUNICATION

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

Ian G Barr[1,2,3], Cleve Rynehart[1], Paul Whitney[1,2], Julian Druce[4]
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

Nagoya Protocol Update

Convention on Biological Diversity

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

- **<u>As of 21 Feb 2021: 129 countries have ratified and entered the NP into legal force</u>**
  - 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