New vaccines – cell based vs egg based

Gary Grohmann

IMMUNISATION
COALITION

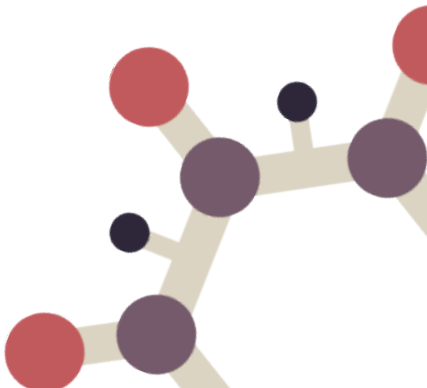
New vaccines – Cell based vs egg based

Presentation outline:

- The problems
- Egg v cell
- Current vaccines
- Flucelvax
- Conclusions

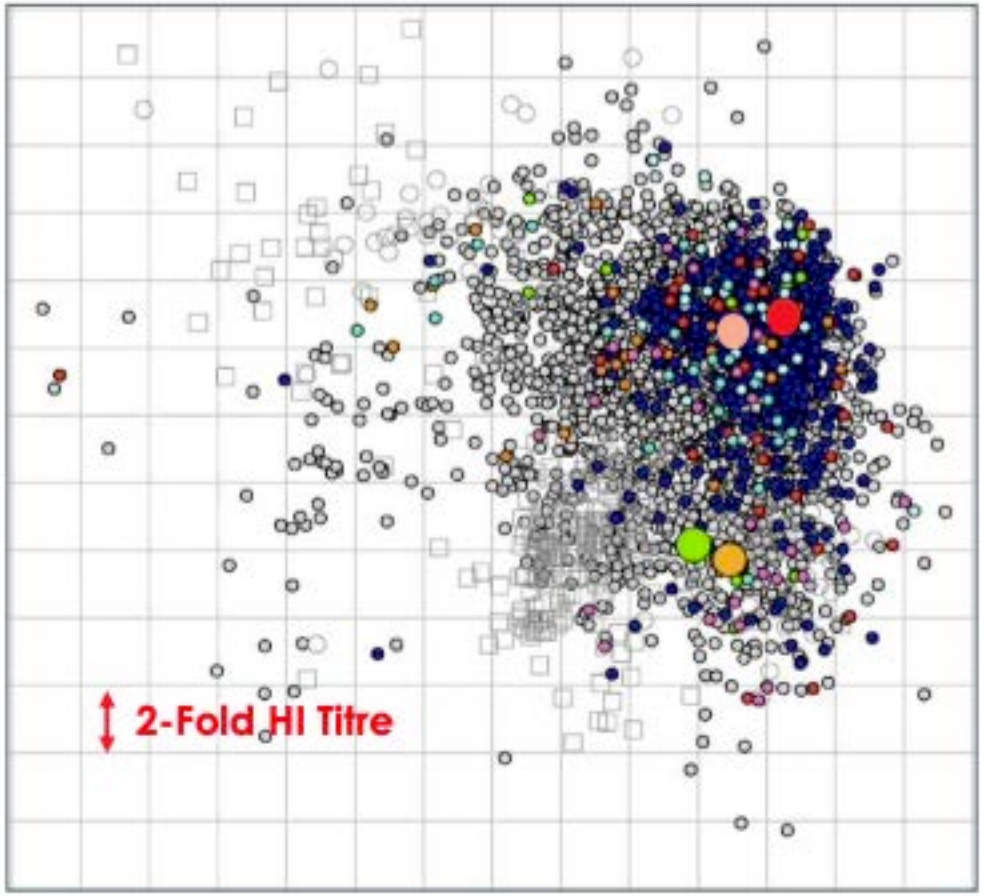
The Problem - Vaccine effectiveness (VE)

- Antigenic drift and egg-adaptation changes likely affect VE
- Cell culture seeds and cell vaccines will likely offer greater VE
  - No definitive studies
  - The difference in VE between egg and cell vaccines can vary between seasons
    - And also between age groups
- Other issues
  - Egg allergy is an issues for some persons
  - Egg supply
  - Vaccine strain selection
  - Vaccine production



Antigenic analysis of circulating influenza viruses: Oct 2012 – Jan 2013

CELL-DERIVED VIRUSES MAY MORE CLOSELY MATCH CIRCULATING STRAINS



Adapted from Barr, et al. Vaccine. 2014

Egg-derived vaccine viruses

- H3N2 A/Victoria/361/2011
- H3N2 A/Texas/50/2012

Cell-derived counterparts

- H3N2 A/Victoria/361/2011
- H3N2 A/Texas/50/2012

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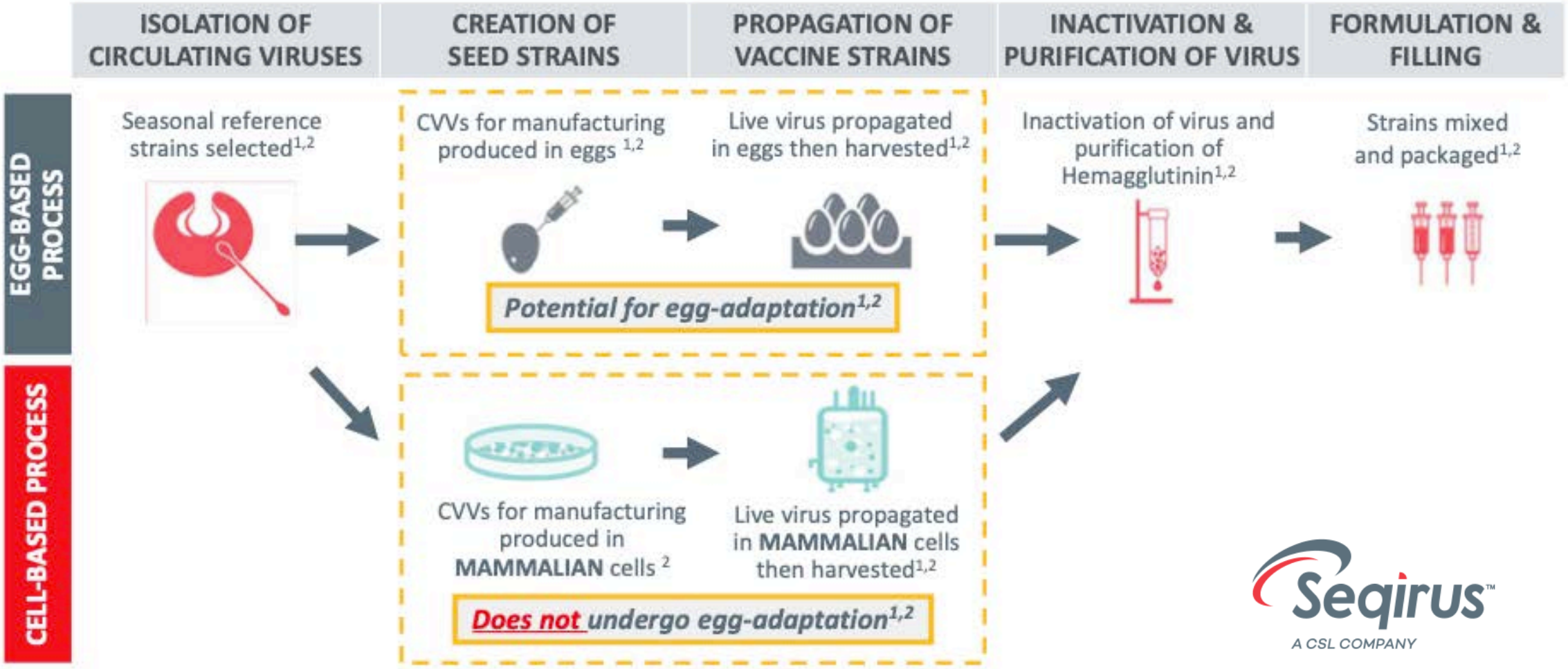
EGG- VS CELL-BASED INFLUENZA VACCINE MANUFACTURING



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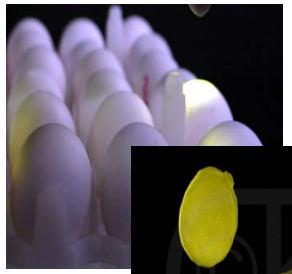
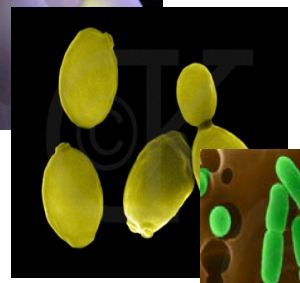
1. Milián E et al. Biomed Res Int. 2015;2015:504831. 2. Rajaram S et al. Ther Adv Vaccines Immunother. 2020;8:1-10.

Better production technologies

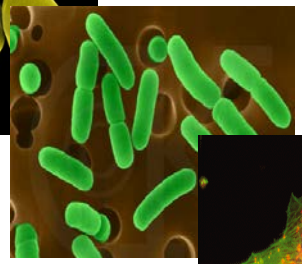
Goal:
Development of technology that will address unmet needs



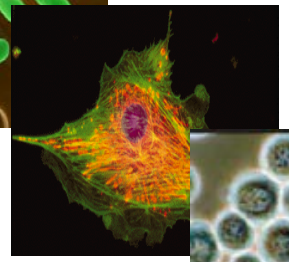
Safety



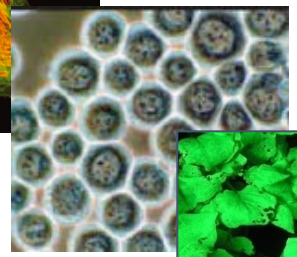
Capacity



Low Cost

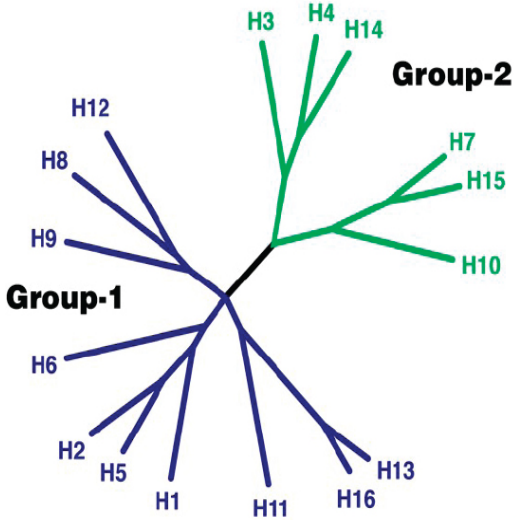


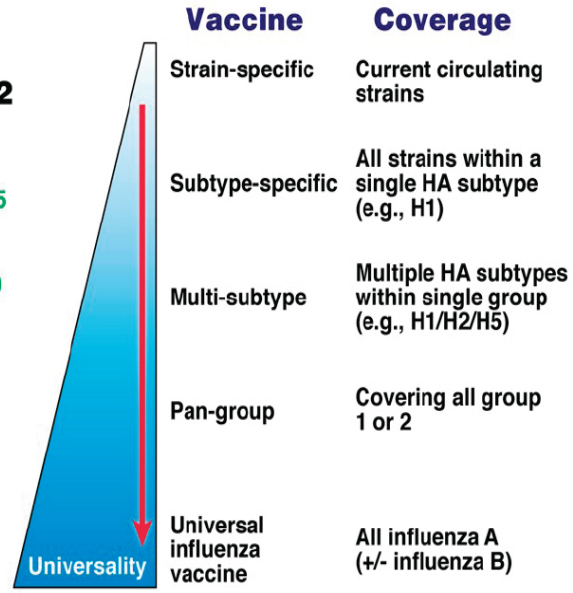
Rapid Response

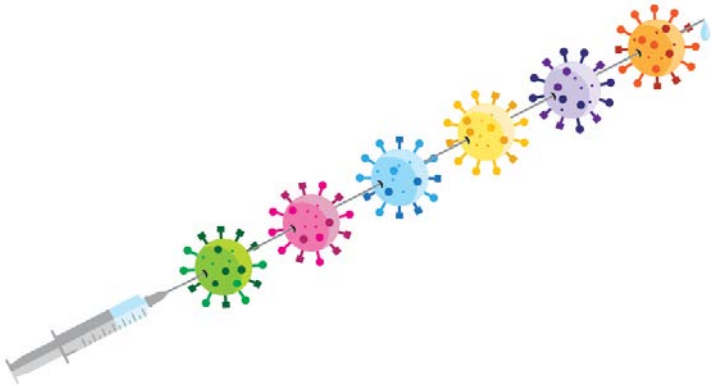


Simple Manufacture

Better Vaccines







Vaccine manufacturing: a long and complex process

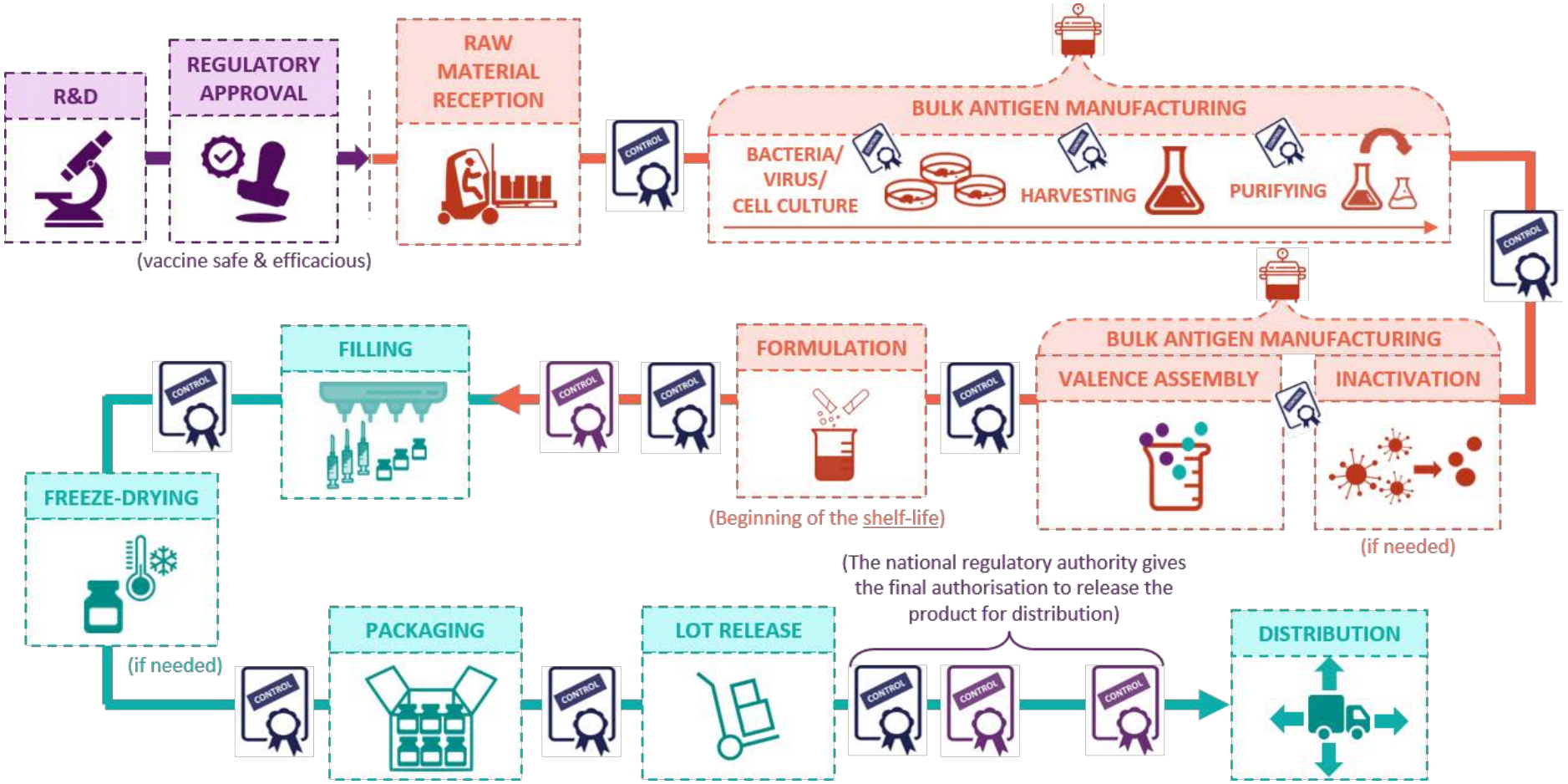


Diagram: Manufacture and testing of final product for marketing authorisation; Modified from: IFPMA: The complex journey of a vaccine (2014) and Presentation by Philippe Juvin – Sanofi Pasteur (ADVAC course, Les Pensieres May 15th 2019) reproduced with permission

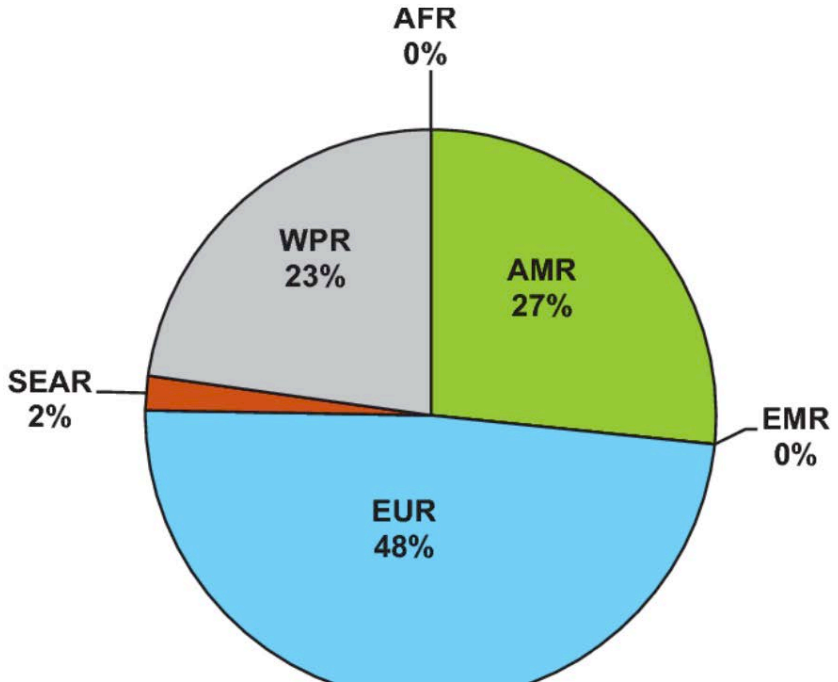
Global production capacity

Sparrow et al 2019: https://www.sciencedirect.com/science/article/pii/S0264410X20315851?dgcid=rss_sd_all
Grohmann et al 2016 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5357709/

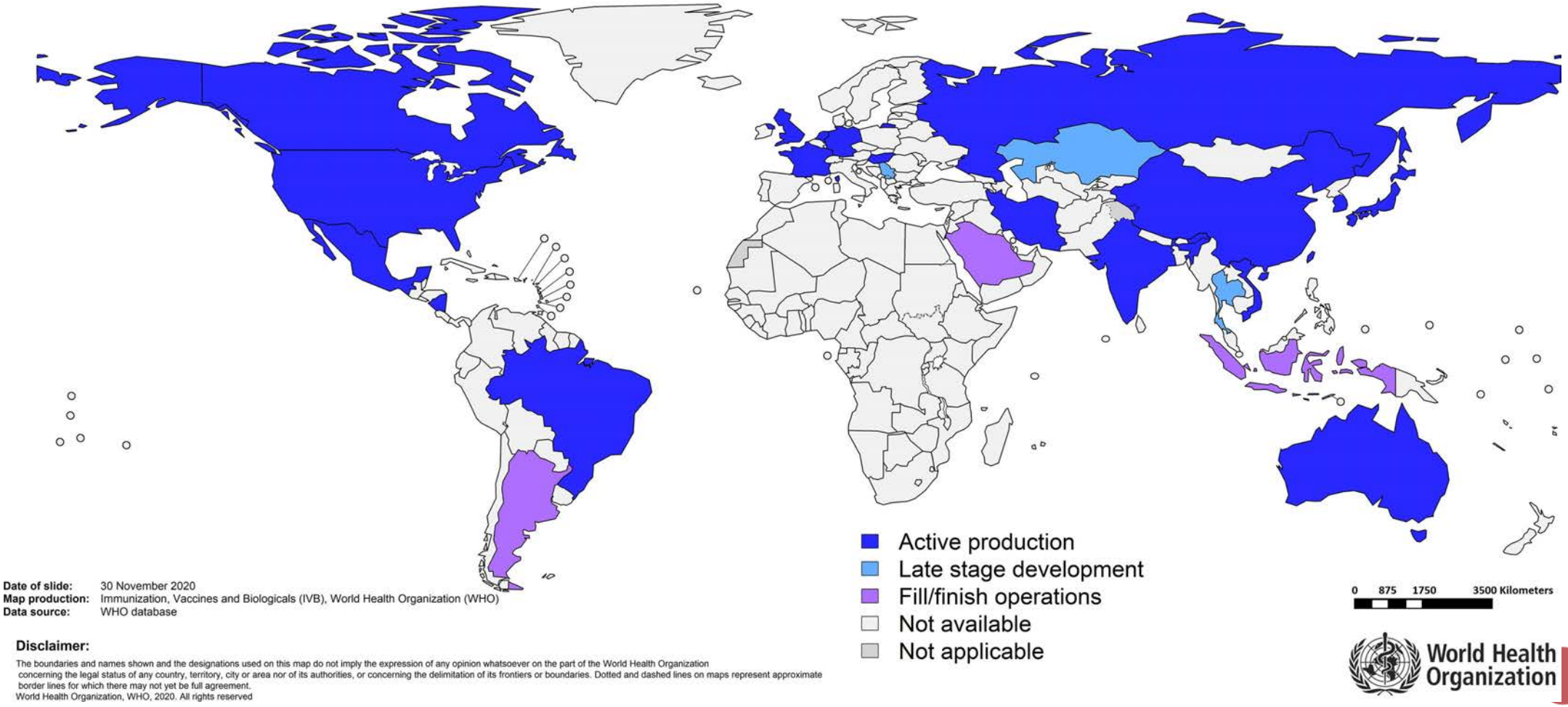
Summary of estimated production capacities in 2019.

Breakdown of production capacities	Seasonal Influenza	Pandemic influenza
Total Annual Production Capacity		
Seasonal influenza vaccines	1.48 billion doses	
Pandemic influenza vaccines (moderate case)		4.15 billion doses
Pandemic influenza vaccines (best case)		8.31 billion doses
By vaccine type		
IIV	89.6%	88.9%
LAIV	5.0%	3.4%
Recombinant	5.4%	7.7%
By substrate		
Embryonated eggs	84.5%	79%
Cell culture	15.5%	21%

World Health Organization



Countries with Influenza Vaccine Production in 2019



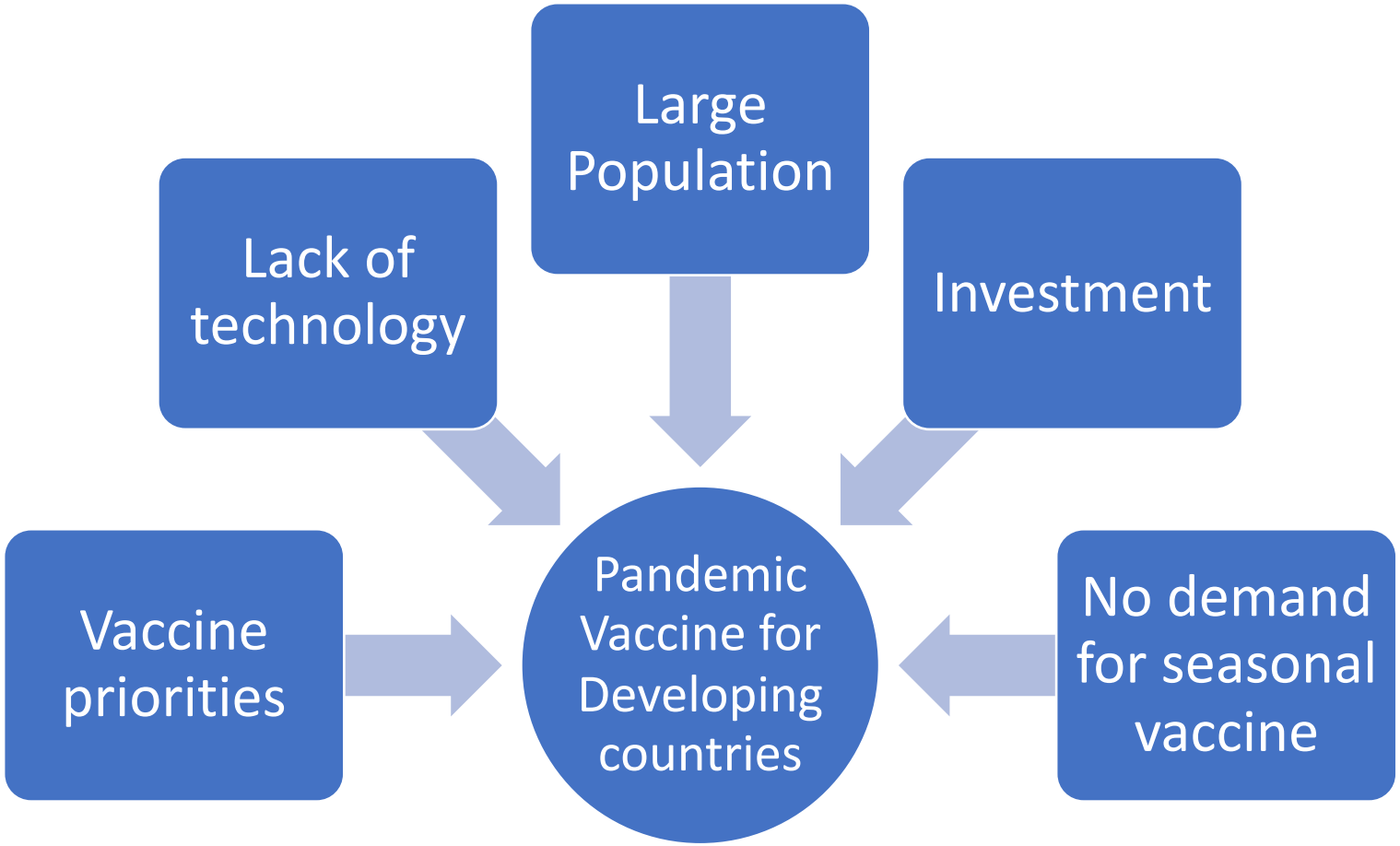
Date of slide: 30 November 2020
Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization (WHO)
Data source: WHO database

Disclaimer:

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area nor of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Sparrow et al 2019:
https://www.sciencedirect.com/science/article/pii/S0264410X20315851?dgcid=rss_sd_all

Dilemma for Developing countries



Available Influenza Vaccines

Trade name (Manufacturer)	Platform	Presentation(s)	Age indication
Afluria Quadrivalent (Seqirus)	Egg	0.25ml PFS 0.5 ml PFS 5.0ml MDV	6-35 mo ≥3 yrs ≥ 6 mo
Fluarix Quadrivalent (GlaxoSmithKline)	Egg	0.5-mL PFS	0.5-mL PFS
FluLaval Quadrivalent (GlaxoSmithKline)	Egg	0.5-mL PFS	≥6 mo
Fluzone Quadrivalent (Sanofi Pasteur)	Egg	0.5-mL PFS 0.5-mL SDV 5.0-mL MDV	≥6 mo ≥6 mo ≥6 mo
Flucelvax Quadrivalent (Seqirus)	**Cell**	0.5-mL PFS 5.0-mL MDV	≥4 yrs ≥4 yrs
Flublok Quadrivalent (Sanofi Pasteur)	Recombinant HA	0.5-mL PFS	≥18 yrs

Available Influenza Vaccines

Trade name (Manufacturer)	Platform	Presentation(s)	Age indication
FluMist Quadrivalent (AstraZeneca)	Egg	0.2-mL prefilled single-use intranasal sprayer	2 through 49 yrs
Fluzone High-Dose Quadrivalent (Sanofi Pasteur	Egg	0.7-mL PFS	≥65 yrs
Fluad Quadrivalent (Seqirus)	Egg	0.5-mL PFS	≥65 yrs
Fluad Trivalent (Seqirus)	Egg	0.5-mL PFS	≥65 yrs

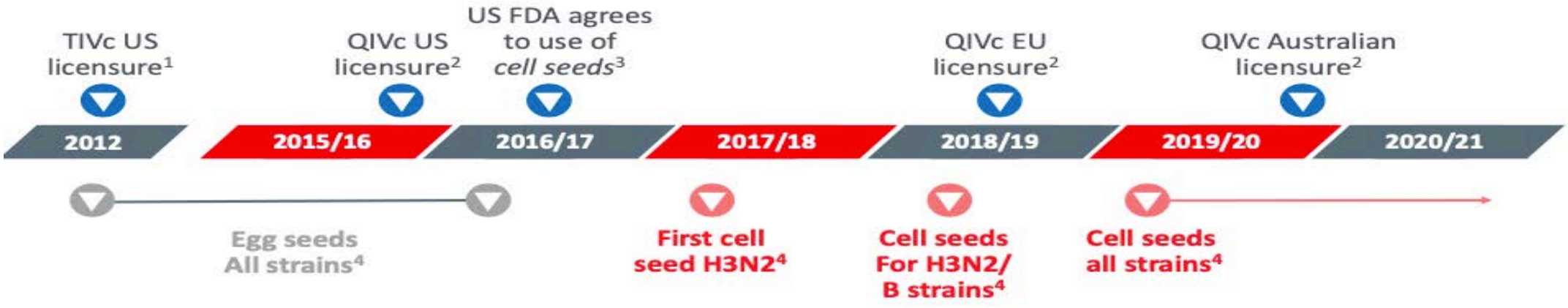
Influenza Vaccines in Australia (2020)

Sponsor	Tradename	Age group
Sanofi-Aventis	FluQuadri	6 months and over*
	Vaxigrip Tetra	6 months and over*
GlaxoSmithKline	Fluarix Tetra	6 months and over*
Mylan Health	Influvac Tetra	3 years and over
Seqirus	Afluria Quad	5 years and over
Seqirus	Fluad Quad	65 years and over

- Seqirus. Flucelvax. Quadrivalent. Adults and Children 9 years of age and older.

Flucelvax

- First licensed in 2016 (USA) and >100 million doses; distributed worldwide
- Available in Australia by private prescription only in 2021
- Sub-unit Vaccine containing Haemagglutinin and Neuraminidase
- Propagated in Madin Darby Canine Kidney (MDCK) cells

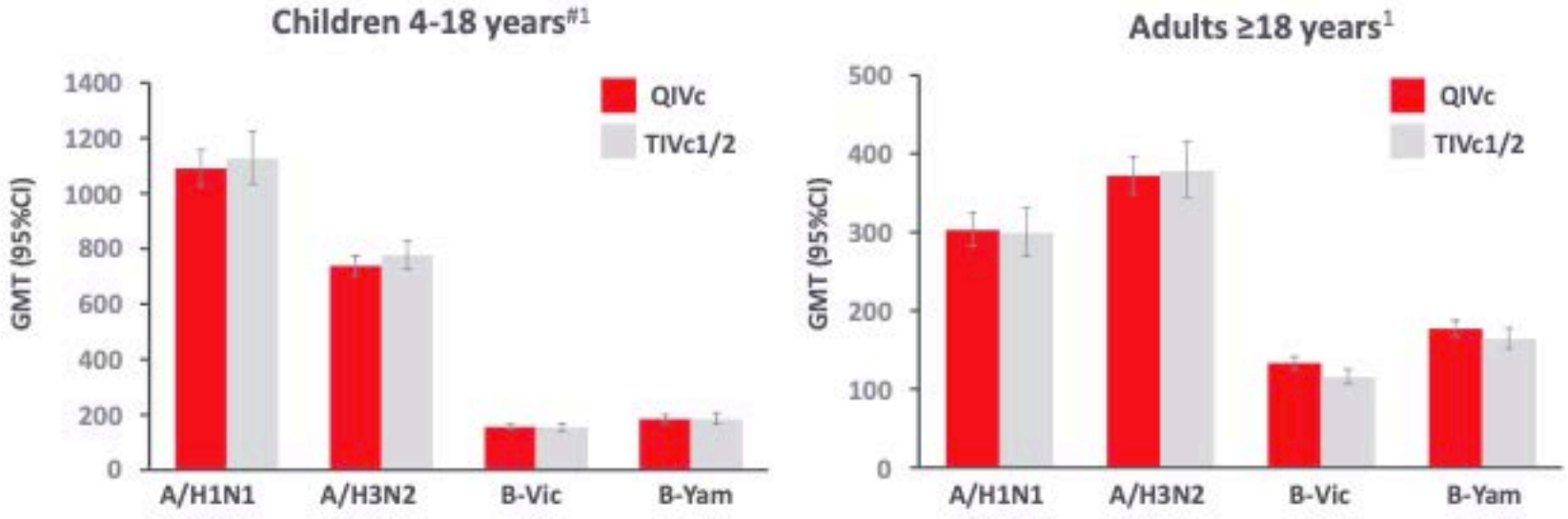


1. http://wayback.archive-it.org/7993/20170723030346/https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm328684.htm
2. https://www.tga.gov.au/sites/default/files/auspar-quad-quadrivalent-influenza-vaccine-201217.pdf
3. https://wayback.archive-it.org/7993/20190425010822/https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM522280.pdf

QIVc elicited robust immune response in children and adults

HA ANTIBODY RESPONSE IN CHILDREN AND ADULTS

*Flucelvax Quad is indicated for use in children and adults aged 9 years and above



HA Antibody GMT ratios (QIVc/TIVc) and differences in seroconversion rates (QIVc-TIVc) at 22 days post-vaccination met criteria for immunological non-inferiority

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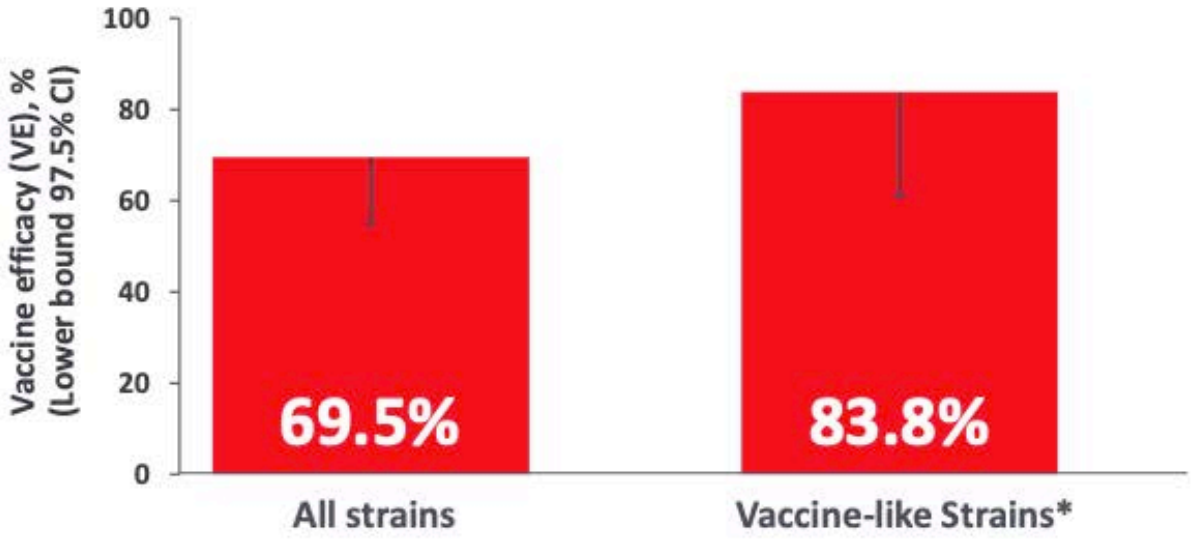
1. Flucelvax Quad Approved Product Information

EFFICACY OF TIVc IN ADULTS AGED 18-49 YEARS

Phase 3, randomized, placebo-controlled, multicenter study (2007-2008) in United States, Finland, and Poland



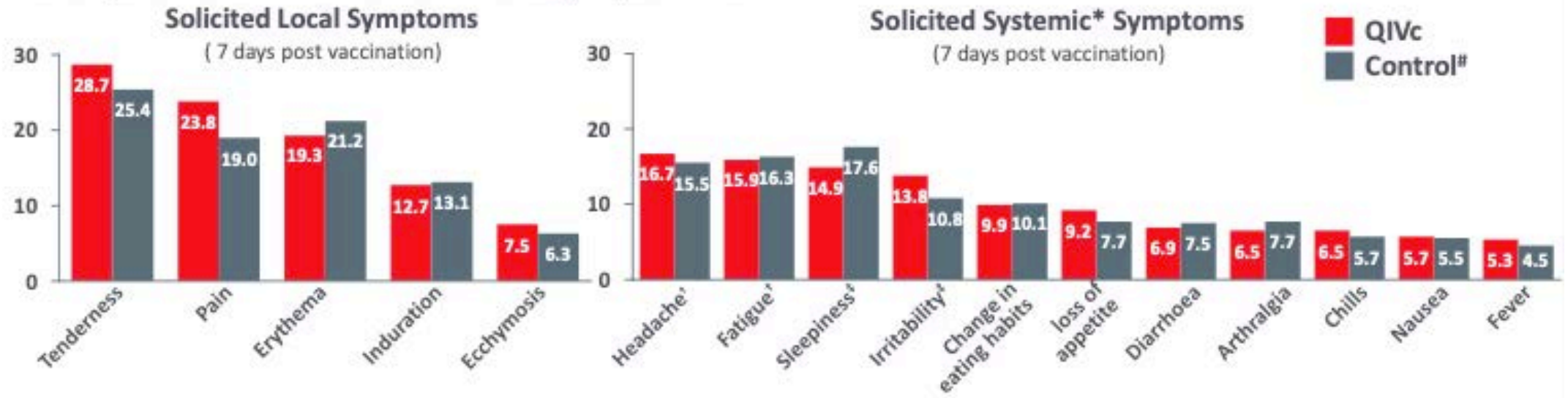
Influenza defined as:
fever ≥37.8C + sore throat/cough, with subsequent laboratory confirmation.

TIVc was immunogenic/ efficacious against vaccine strain influenza and well tolerated

Frey S et al. Clin Infect Dis. 2010;51:997-1004. Flucelvax Quad Approved Product Information

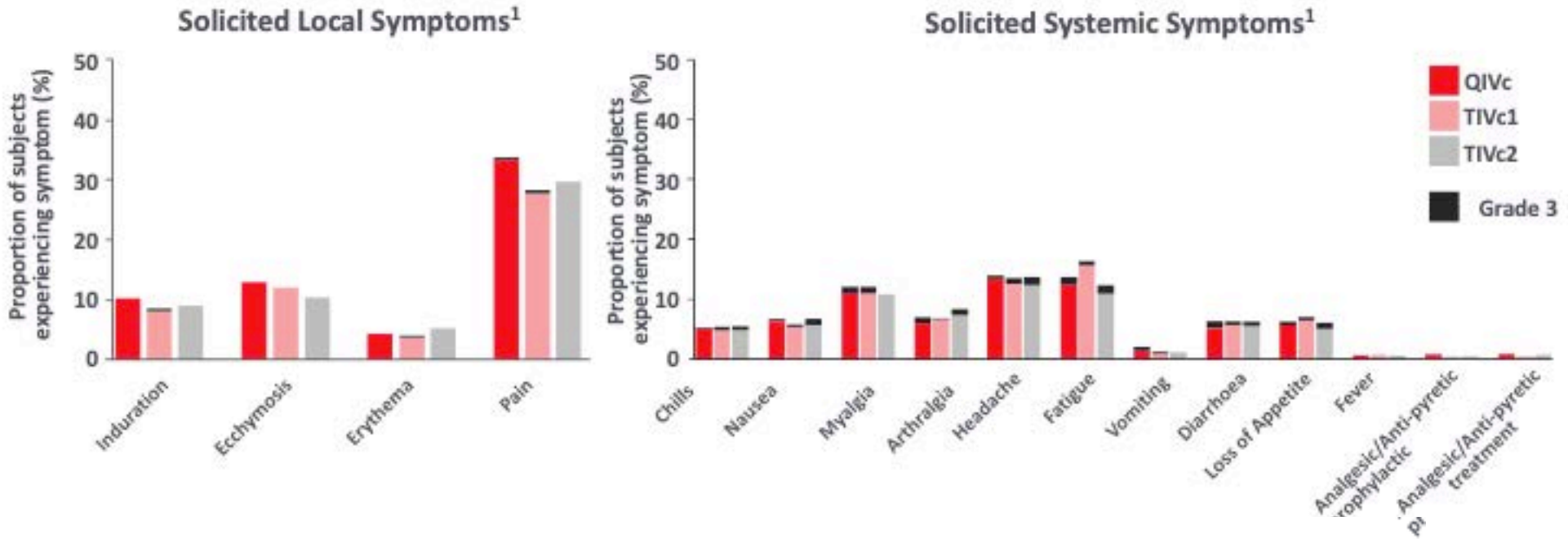
ADVERSE EVENT PROFILE: CHILDREN 2-18 YEARS^

^Flucelvax Quad is indicated for use in children and adults aged 9 years and above



- Reported incidence of unsolicited AEs was similar across groups
- No vaccine-related serious AE's were reported

ADVERSE EVENT PROFILE: ADULTS AGED ≥18 YEARS



- Similar percentages of unsolicited AEs and medically attended AEs between vaccine groups
- No vaccine-related serious AE's were reported

Bart et al. HUMAN VACCINES & IMMUNOTHERAPEUTICS 2016, VOL. 12, NO. 9, 2278–2288

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AUSTRALIA'S NEW WORLD-CLASS BIOTECH FACILITY

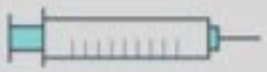
AUD $800 MILLION
investment

MID-2026
Site to be operational

ONLY CELL-BASED
influenza vaccine manufacturing facility in the Southern Hemisphere

Supporting a $300 million supply chain annually

HIGH SPEED
vaccine filling and packaging line



Will produce **PANDEMIC AND SEASONAL** influenza vaccines and **MF59® ADJUVANT**

Will produce **ANTIVENOMS** and the **WORLD'S ONLY HUMAN VACCINE** for **Q FEVER**

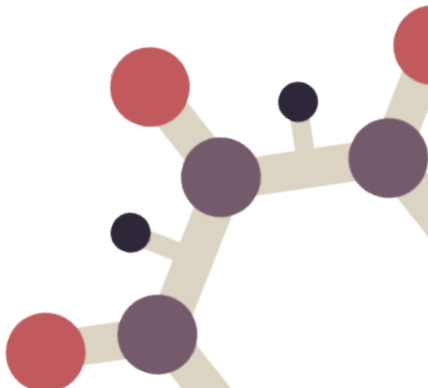
https://www.seqirus.com.au/news/seqirus-will-build-world-class-vaccine-manufacturing-facility

Potential advantages of Cell based vaccines

- Shorter Production time than egg based
  - Lead to better matched viruses for vaccines
- Improved process control
- Lack of dependence on egg supply
  - Eliminates egg allergy
- Potential for increased output
- Closed production system lowers the risk of contamination
  - antibiotics and preservatives are not needed

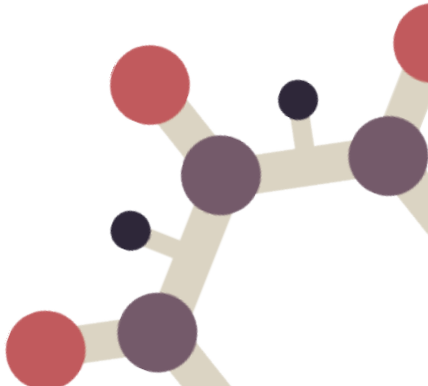
Potential drawbacks of Cell based vaccines

1. Expense
2. Variety of platforms needed for both seasonal and pandemic vaccines
3. Tech transfer



Conclusions

- Cell culture vaccine solves the egg adaption issue
- Cell vaccines will likely offer greater VE
  - Further studies needed
  - A step in the right direction to make better vaccines
- Cell vaccines will lead to better strain selection for vaccines
  - Eliminates egg allergy and dependance on egg supply
- Could be transferred to developing countries in time given proper training and experience
  - Investment; expense to the consumer; egg tech more likely



Acknowledgements

- Dr Jonathan Anderson
- Dr Erin Sparrow
- Dr Ian Barr
- Jenny Herz

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World Health Organization

WHO Collaborating Centre for Reference and Research on Influenza VIDRL

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Biointelect