Adapting the annual influenza vaccine strain selection process to mRNA influenza vaccines

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Outline

- Current vaccine options
- Current vaccine composition decision process and timelines
- Where mRNA vaccines could shorten timelines

Caveat: These are my opinions and do not reflect WHO GISRS policy
Available Influenza Vaccines

**Inactivated**
- Killed virus
  - grown in eggs or cells
  - Trivalent or quadrivalent
  - 15\( \mu \)g of HA/dose injected

**Recombinant**
- Expressed protein
  - grown in insect cells
  - Trivalent or quadrivalent
  - 45\( \mu \)g of HA/dose injected

**Live**
- Live, weakened virus
  - grown in eggs
  - Trivalent or quadrivalent
  - given intranasally
  - for healthy individuals aged 2-49 years in the US and school aged children in the UK
The influenza vaccine development timeline

- **1947**: First influenza vaccine (Pocono Biological Laboratories - U.S.)
- **1968**: Trivalent influenza vaccine
- **1978**: Quadrivalent influenza vaccine
- **2003**: Cell based vaccine
- **2010**: First high-dose influenza vaccine
- **2014**: Adjuvanted vaccine licensed in USA
- **2015**: Developing an mRNA-based influenza vaccine
- **2017**: First recombinant influenza vaccine

Oldest network in WHO: begun in 1952, 140+ NIC’s in >110 countries, 5 WHO CC’s for human influenza + 2 for animal influenza + 4 essential regulatory labs,
Influenza viruses sequenced and available in GISAID in 2019

- A(H1N1)pdm09: 2238
- A(H3N2): 3524
- B-Victoria: 1093
- B-Yamagata: 315
Total viruses antigenically characterized during 3 recent southern hemisphere reporting periods

**Methods**: Haemagglutination inhibition or neutralisation using post-infection ferret antisera and pools of post-vaccination human sera
Antigenic cartography

WHO CC Crick HI data

WHO CC Atlanta FRA data

University of Cambridge
Panels of post-vaccination sera from different age groups are tested against vaccine strain and circulating variants in HAI or neutralisation tests.
Influenza vaccine effectiveness is monitored in several locations by several independent groups (GIVE) – similar study designs. Results are from the real world, BUT are not prospective - they look at past performance.

With increased numbers VE from age groups, vaccine types, for viruses in different types/subtypes/clades....


Slide courtesy Dr John McCauley, WHO Influenza Collaborating Centre at the Francis Crick Institute, UK
### Vaccine composition recommended for 2022/23 seasons

#### 2023 Southern hemisphere
- **H1N1pdm09:** A/Sydney/5/2021-like*
- **H3N2:** A/Darwin/9/2021-like**

**Quadrivalent vaccine:**
- B/Yam: B/Phuket/3073/2013-like
- B/Vic: B/Austria/1359417/2021-like

**Trivalent vaccine:**
- B/Vic: B/Austria/1359417/2021-like

**Cell- or recombinant-based vaccines:**
- *A/Sydney/5/2021 (H1N1pdm09)-like
- **A/Darwin/6/2021 (H3N2)-like

#### 2023/24 Northern hemisphere
- **H1N1pdm09:** A/Victoria/4897/2022-like*
- **H3N2:** A/Darwin/9/2021-like**

**Quadrivalent vaccine:**
- B/Yam: B/Phuket/3073/2013-like
- B/Vic: B/Austria/1359417/2021-like

**Trivalent vaccine:**
- B/Vic: B/Austria/1359417/2021-like

**Cell- or recombinant-based vaccines:**
- *A/Wisconsin/67/2022 (H1N1pdm09)-like
- **A/Darwin/6/2021 (H3N2)-like
The time line for influenza vaccine manufacture

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<td>Mass-production of viruses</td>
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Chen J Biomed Sci 2020; 27:33
mRNA might allow later decisions for vaccine virus selection

Flunet Northern Hemisphere lab confirmed influenza

Too late to grow virus, analyse by HI/VNT

VCM 4 weeks later would allow more viruses to be analyses in most years

Slide courtesy of Ian Barr
Challenges and changes to GISRS as new influenza vaccine platforms are introduced

• NIC’s
  – Increased demands and expectations for sequencing capacity especially NGS
  – Loss or deprioritisation of basic virology skills eg virus isolation

• CC’s
  – How to best support both new and existing vaccine platforms

• Reassorting labs
  – Determine when there will be a reduction in the need for egg/cell reassortant viruses or number of labs performing reassorting to match demand

• ERL’s
  – New methods required to replace existing assays/reagents and harmonize new assays for mRNA

Slide courtesy of Ian Barr
Acknowledgements

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