PPC for next-generation influenza vaccines

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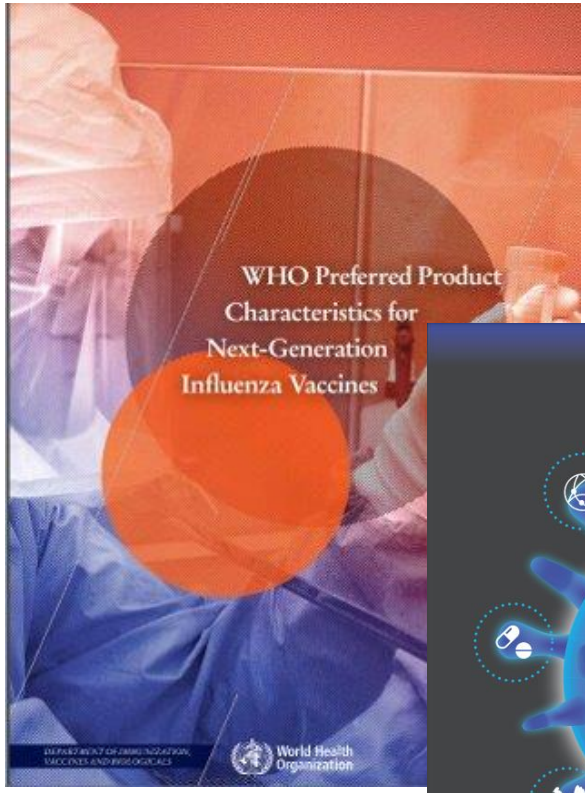
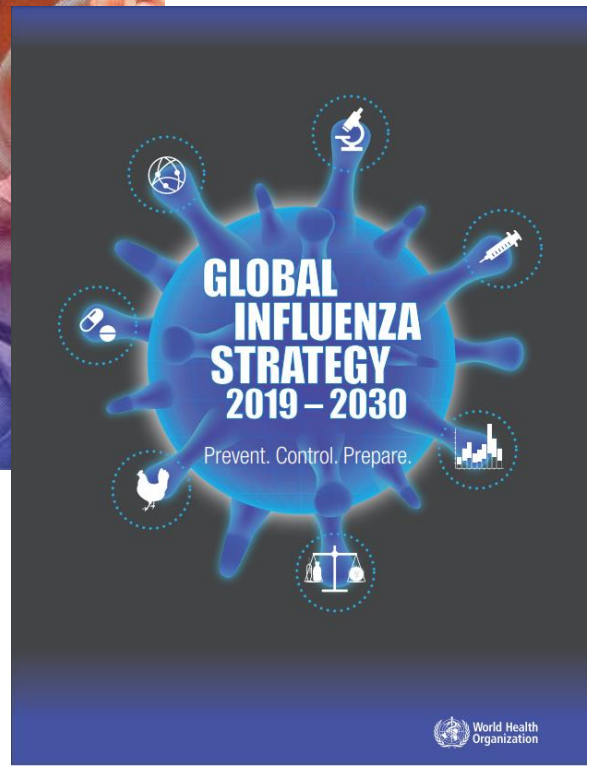
WHO/IVB and WHO/WPE

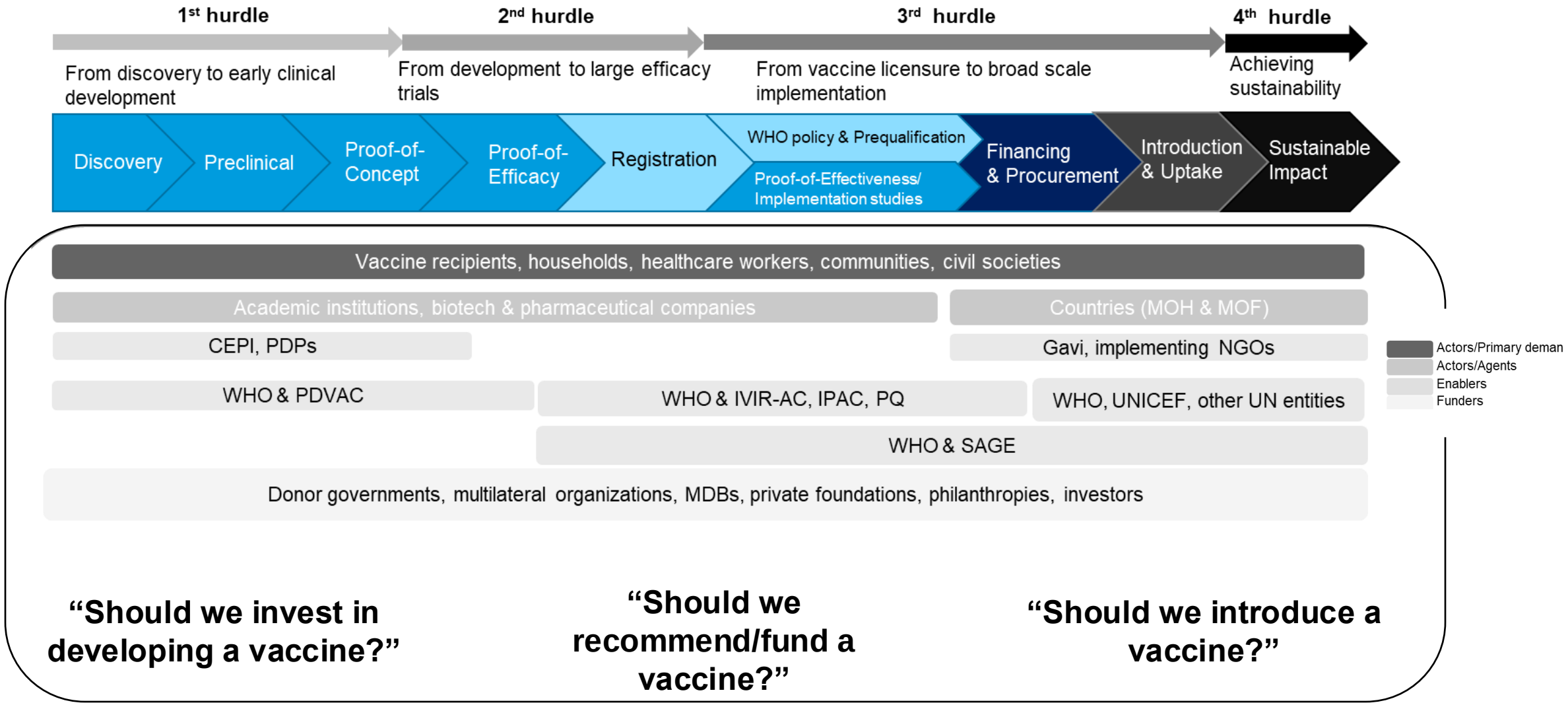
Recent global policies/guidance supports next generation vaccine development

- **2017:** WHO Preferred Product Characteristics for Next – Generation Influenza Vaccines define preferences for parameters of vaccines shaped by “global unmet public health need in a WHO priority disease area”
- **2019:** WHO’s Global Influenza Strategy (GIS) 2019-30 stresses the need to develop new influenza vaccine technologies which improve the suitability of influenza vaccines for all countries
- **Funded by CDC,TFGH, and BMGF, WHO and LSHTM joined forces to complement the guidance available, with a *Full Value of Improved Influenza Vaccine Assessment***
  - To inform global efforts to expand seasonal influenza programs as part of a larger pandemic readiness effort
  - To drive innovative research for next generation influenza vaccines for LMICs





FVVA project to estimate value of improved influenza informs PDVAC-update of PPCs



Hutubessy et al. The Full Value of Vaccine Assessments (FVVA): a framework for assessing and communicating the value of vaccines for investment and introduction decision-making. *BMC Medicine* (2023) 21:229

FVIVA Project structure

Workstream 1: Product development

To collect, synthesize, and document current seasonal and improved influenza vaccine development activities, including vaccine approaches and candidates in clinical and pre-clinical stages of development.

Workstream 2: Market demand

To estimate the potential market for improved seasonal influenza vaccines by assessing country decision-maker preferences for improved influenza vaccines and estimating the potential demand for current seasonal and improved influenza vaccines.

Full vaue of improved influenza vaccine assessment (FVIVA)

Workstream 3: Impact

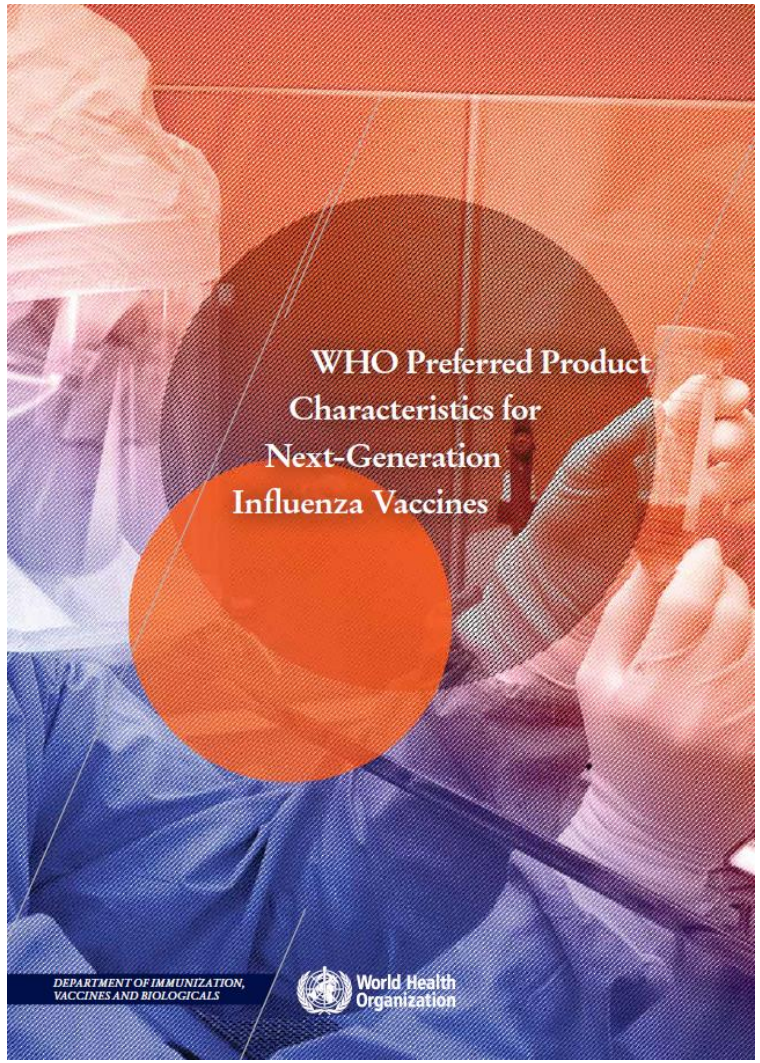
To analyse the health and economic impact of improved seasonal influenza vaccine, including country-specific estimates by measuring and quantifying the incremental health and economic impact of improved seasonal influenza vaccines, based on their characteristics, compared to current seasonal influenza vaccines

Workstream 4: Sustainability

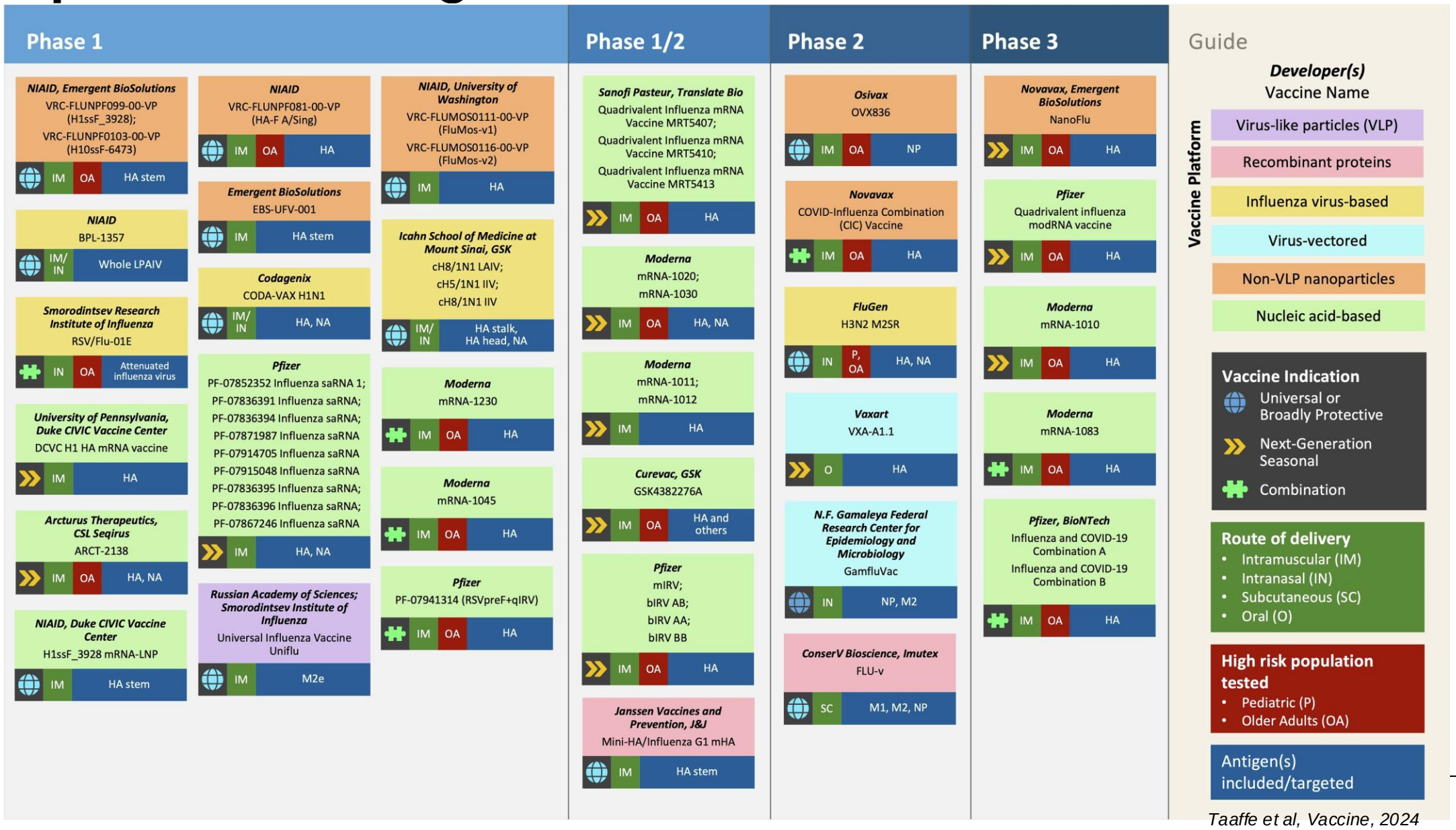
To assess the return on investment and financial sustainability for vaccine developers to develop and commercialise improved influenza vaccines and to identify the barriers and enablers to current seasonal influenza vaccine access that will impact sustainable and equitable delivery of improved influenza vaccines.

WHO 2017 Flu PPC - Update

- **IVB reviews the need to update its PPC and TPP guidance documents every 5 years, or sooner in the event of product or technology innovations or any other change in R&D landscape.**
- 2017 Next-Generation Influenza Vaccines PPCs is deemed obsolete. The document has been updated to reflect:
  - Latest evidence on influenza epidemiology, vaccine R&D
  - Latest SAGE position paper,
  - Lessons learned from COVID-19 pandemic
- **Key challenge** – balance short-term, long-term objectives with the reality of the science and pipeline
- In 2024, WHO established a PPC Working Group + Public Consultation
  → **PPC submitted to PDVAC for review and endorsement**

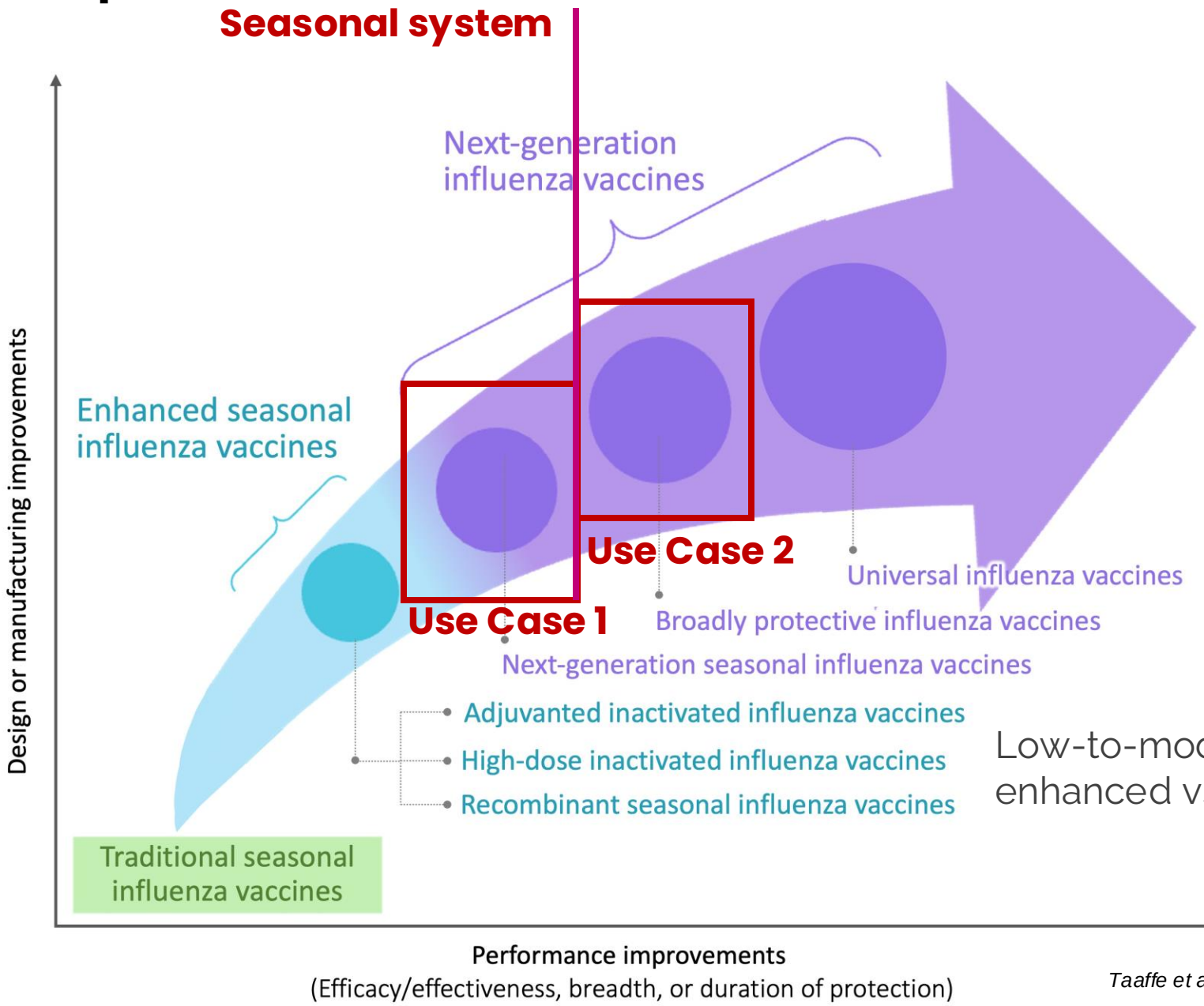


Pipeline of next-generation seasonal influenza vaccines



Taaffe et al, Vaccine, 2024

Improved Influenza Vaccines for Seasonal Influenza (FVIVA)



IMPROVED INFLUENZA VACCINE:
Any influenza vaccine designed to provide ***improvement over traditional, standard dose influenza vaccines*** *in terms of durability, efficacy, breadth of protection, or programmatic suitability.*

Low-to-moderate relative vaccine effectiveness of enhanced vs traditional (e.g. ECDC meta-analysis)

Taaffe et al, Vaccine, 2024

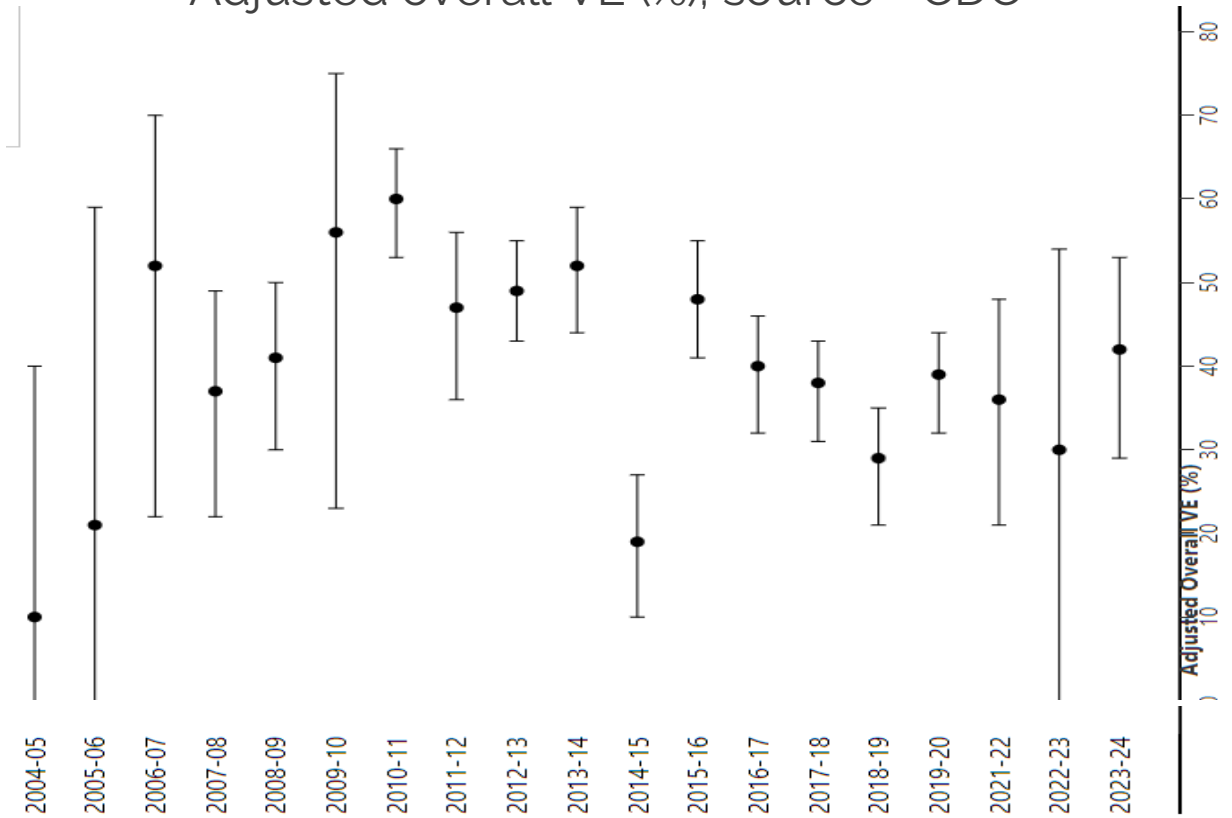
Use case 1 - next-gen seasonal vaccines

Problem 1 – Significant global burden despite broad use of influenza vaccines

Question 1 – How do we further reduce the global burden of influenza and improve flu vaccination programmes in tropical countries ?

- **Burden**
  - 3–5 million severe cases
  - between 290 000 and 650 000 deaths
  - 10% of respiratory hospitalizations in <18
  - Mortality rates are higher in LMICs
- **Vaccine demand (global)**
  - 850M doses (from 122 products)
- **VE issues**
  - Limited and variable protection
  - Programmatic issues in countries with year-round transmission

Adjusted overall VE (%), source - CDC



Use case 2 – broadly protective vaccines

Problem 2 – Many LMICs do not have seasonal influenza programs or limited uptake

Question 2 – How do we make influenza vaccines more attractive (e.g. cost-effective) ?

WHO Policy and market study

- 34% LMIC (excl. UMIC) reported having a policy for seasonal influenza
- 95% of seasonal vaccines consumed in HIC and UMIC

Use case 3 – considerations for pandemic vaccines

Question 3 – Are we ready to respond ? Speed, Impact and Access considerations

Ideally, broadly protective vaccines would provide some level of protection against pandemic subtypes

WHO PPC – attributes and specifications

	Next-Generation Seasonal influenza vaccines	Broadly Protective or Universal influenza vaccines
Indication	Prevention of severe influenza illness	
Target population	**All groups at particular risk** of severe influenza or complications (as per SAGE) *Previous: Children aged 6 weeks to 59 months*	**All groups at particular risk** of severe influenza or complications and **those at increased risk of exposure to or transmission** of influenza virus *Previous: Persons aged 6 weeks and older belonging to a group at high risk of severe illness*
Safety	Mild reactogenicity acceptable; Severe reactogenicity and adverse events at a rate comparable to currently approved seasonal influenza vaccines *Previous: Mild reactogenicity acceptable; Severe reactogenicity at a rate ≤ current PQ'd seasonal vaccines*	
Co-administration	Demonstration of favorable safety and immunologic non-interference upon co-administration or co-formulation with other vaccines recommended for use	
Efficacy	**Better than that of currently approved seasonal influenza vaccines for currently circulating strains** *Previous: Better than that of current PQ'd seasonal vaccines for vaccine-matched strains OR for circulating antigenically drifted strains*	**Better than that of currently approved seasonal influenza vaccines for currently circulating subtypes (+ ideally pandemic subtypes)** *Previous: Better than that of current PQ'd seasonal vaccines for vaccine-matched strains AND for circulating antigenically drifted strains*
Duration of protection	**Minimum of 1 year for currently circulating strains** *Previous: Minimum of 1 year*	**Minimum of 3 years for currently circulating subtypes** *Previous: Minimum of 5 years*

2024 WHO Preferred Product Characteristics for Next-Generation Influenza Vaccines

	Next-Generation Seasonal influenza vaccines	Broadly Protective or Universal influenza vaccines
Formulation/ Presentation	Vaccines seeking WHO prequalification should meet WHO-defined criteria for programmatic suitability regarding formulation, presentation, packaging, thermostability and disposal	
Route of administration	Injectable, inhaled, or oral administration are acceptable	
Manufacturing time	Less than 5 months from vaccine strain selection to finished product *Not included previously*	(no preference indicated)
Product stability and storage	Vaccines stable under refrigerated conditions (2–8°C) for at least 12 months	
Access and affordability	Favourable cost-effectiveness and safety profile should be established and price should not be a barrier to access and within-country distribution, including in LMICs.	

WHO PPC – Considerations for pandemic vaccines

- **Most critical characteristics of a pandemic vaccine** for a rapid R&D response and timely deployment
  - Efficacy
  - Time to production
  - Scalability
- **Vaccines easily administered**, especially for mass vaccination scenarios, and **reduced reliance on cold-storage** more important in pandemic scenario
- **Technology or platforms used by Next-Generation Seasonal Vaccines** may allow for rapid production of strain-specific vaccines
- **Broadly Protective Vaccines could offer some level of protection** to a novel virus before a strain-specific vaccine is made; Universal Influenza Vaccines could be a solution to both seasonal and pandemic influenza
- **Manufacturing capacity must be sustained** during interpandemic periods
- Vaccination target groups may change; **critical that safety and efficacy data is available before a pandemic** for all high-risk groups

PDVAC comments #1

1. Could the rationale behind the differences from the 2017 PPCs be explained? (especially when the characteristics have been made less specific)

2. What is the target for production time esp during a pandemic?

3. Why is reduction of transmission not even a secondary aim, when many countries do have this as an aim of their flu programme - and it may become more feasible if improved vaccines are developed?

Efficacy use case 2 - “Effectiveness against disease transmission should be explored.”

4. The difference between breadth, duration of protective immunity and efficacy is not clear since these are very overlapping characteristics. The difference between next-generation and "universal" is also not that clear.

5. Are Healthcare workers not a priority population for the Next-Generation Seasonal influenza vaccines

6. When it is mentioned- vaccine efficacy should be better , is there any way to provide more guidance on this e.g. in terms of a target, range with/ or without confidence limits etc?

Next slide

PDVAC comments #2

Efficacy	Vaccine efficacy should be better than traditional IIV	
Duration of protection	Minimum of 1 year for currently circulating strains	Minimum of 3 years for currently circulating subtypes

- Use Case 1 – better means VE should be **better/IIV** and VE should be **preserved for at least 1 year** against circulating strains (as per the WHO CVV)

- Use Case 2 – better means VE should be better/IIV and **VE should be preserved for at least 3 years against all circulating subtypes** (and ideally against pandemic subtypes)

About setting a VE target…

- More «enhanced vaccines» would have limited PH value – need to avoid that situation
- VE is extremely variable (e.g. populations, setting, subtypes, over time)
- Needs to be defined in the context of efficacy trials
  - We need consensus on efficacy trial design (e.g. NI margin, endpoints)

PPC WG members – thank you

- William Ampofo,
- Joseph Bresee,
- Marco Cavaleri,
- Kari Johansen,
- Jorge Kalil,
- Michael Osterholm,
- Punnee Pitisuttithum,
- Kanta Subbarao

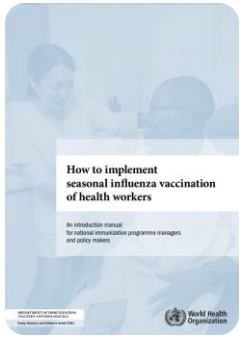
WHO seasonal influenza vaccine documents

Policy

WHO, 2022. Vaccines against influenza: WHO position paper – May 2022

Planning and programmatic implementation

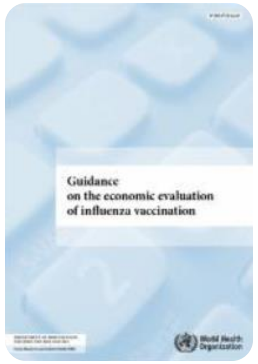
WHO, 2017. How to implement influenza vaccination of pregnant women



WHO, 2019. How to implement seasonal influenza vaccination of health workers

WHO, 2023. Seasonal influenza vaccination: developing and strengthening national programmes – policy brief

Economic evaluation and costing tool



WHO, 2016. Guidance on economic evaluation of influenza vaccination

WHO, 2020. WHO Seasonal Influenza Immunization Costing Tool

Online course: Flutool Plus - using the WHO Seasonal Influenza Immunisation Costing (openwho.org)

Monitoring & reporting

- Policies
- Vaccine use
- Coverage

WHO Immunization Data Portal – Influenza vaccination (eJRF)

WHO/MPP mRNA Influenza R&D

- **Sinergium** appointed to lead the development of a mRNA pandemic influenza vaccine (initial focus on H5)
- H5 HA mRNA candidate vaccine (lead) (plan to go Phase 1 Q1 2026)
- HA/NA mRNA candidate vaccine (research)

New initiative launched to advance mRNA vaccine development against human avian influenza (H5N1)

29 July 2024 | Joint News Release | Geneva, Switzerland |Reading time: 2 min (547 words)

A new project aiming to accelerate the development and accessibility of human avian influenza (H5N1) messenger RNA (mRNA) vaccine candidates for manufacturers in low- and middle-income countries has been launched today. The Argentinian manufacturer Sinergium Biotech will lead this effort leveraging the World Health Organization (WHO) and the Medicines Patent Pool (MPP) mRNA Technology Transfer Programme.

The mRNA Technology Transfer Programme, jointly developed by WHO and MPP, was launched in July 2021 with the aim to build capacity in low- and middle-income countries (LMICs) for the development and production of mRNA-based vaccines. Sinergium Biotech, a partner in the mRNA Technology Transfer Programme, has developed candidate H5N1 vaccines and aims to establish proof-of-concept in preclinical models. Once the preclinical data package is concluded, the technology, materials, and expertise will be shared with other manufacturing partners, aiding the acceleration of the development of H5N1 vaccine candidates, and bolstering pandemic preparedness efforts.

"This initiative exemplifies why WHO established the mRNA Technology Transfer Programme – to foster

Thank you