

VIPS update and discussion DCVMN webinar

16 July 2020

Objective of this session



- To inform DCVMN vaccine manufacturers about:
 - The VIPS Alliance process and prioritisation outcomes;
 - The VIPS next steps for the 3 prioritised innovations.
- To answer questions.

Agenda



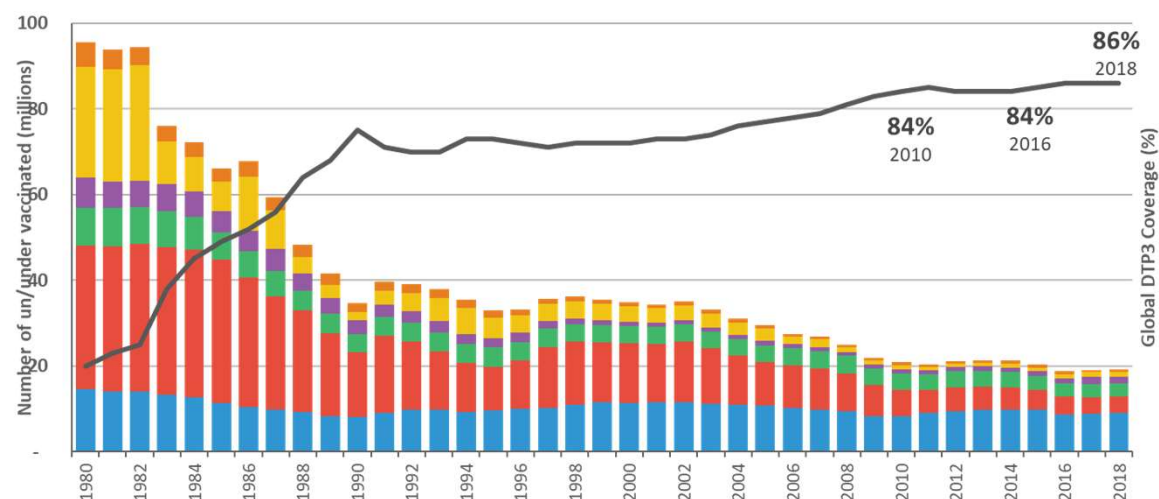
- The rationale for VIPS
- VIPS prioritization process, outcomes & next steps
- Overview of VIPS action plans
- Discussion

Agenda

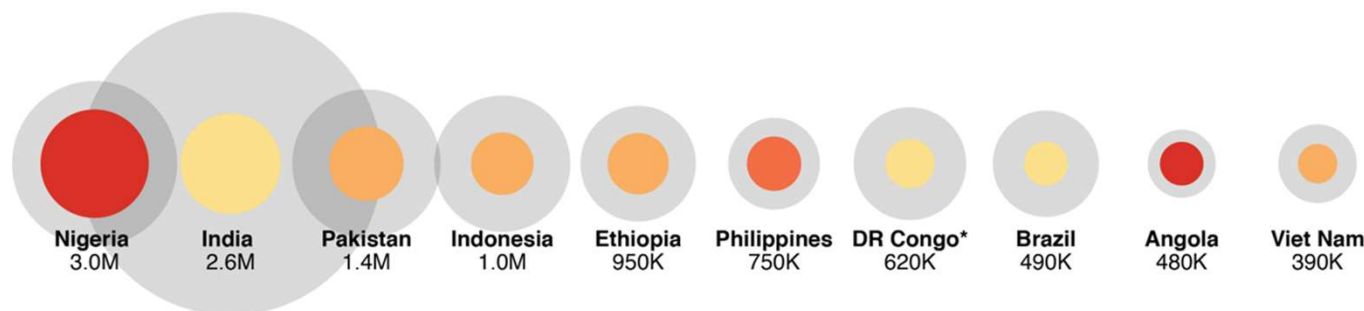


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How are we doing with achieving equitable vaccine coverage?



Coverage has increased by only 5% in the past decade



10 countries account for 60% of unprotected children

Why have some innovations not had impact, or been slow to advance?



Disposable syringe jet-injectors



Controlled temperature chain (CTC)



Compact pre-filled syringes (Uniject)



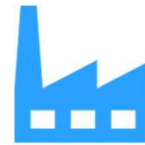
Microarray patches (MAPs)

Why have some innovations not had impact, or been slow to advance?



At the country level:

- Novel Vx products do not reflect country preferences or programmatic fit
- There is insufficient data to demonstrate incremental impact, and clear use case
- Costs are likely to be higher than for existing vaccines
- Lack of a procurement mechanism

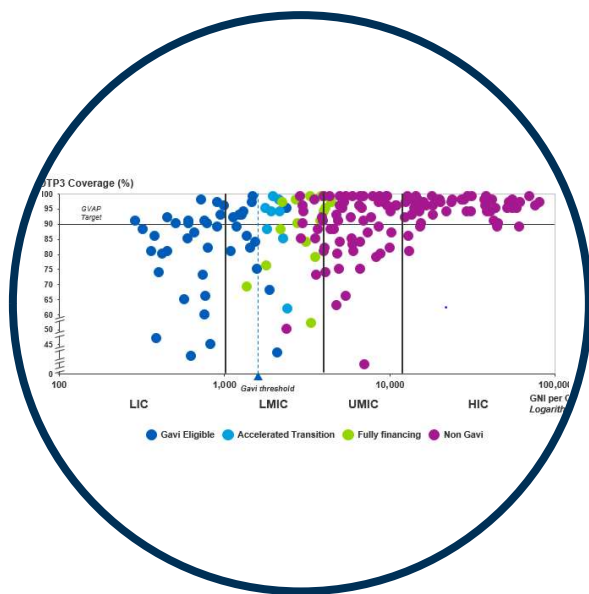


For vaccine manufacturers and product developers:

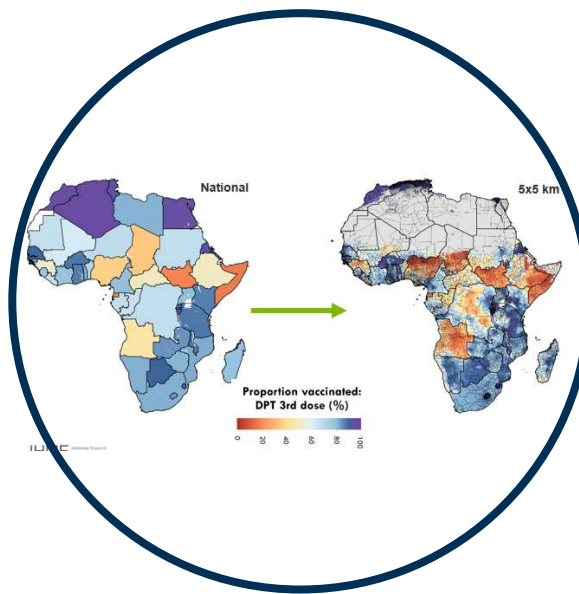
- Effective vaccines often already exist; it requires investment to develop a new product = higher cost
- The demand and development pathway for new vaccines is often not clear = risk
- Lack of a procurement mechanism

➤ Foundation of the VIPS approach is to ensure we will address a relevant problem, through product innovation

Why is VIPS needed?



Innovative delivery approaches will be needed to help achieve the Alliance coverage and equity targets



The next decade will likely need to shift to sub-national use of **differentiated products**



Many innovation initiatives across the Alliance, but strategy and effort **not coordinated or aligned**

VIPS background and goal



**2016 – 2020:
Innovation as one
of the Alliance
priorities for
shaping markets**

The Alliance aims to pursue a **common agenda of driving vaccine product innovation to better meet country needs and support Alliance goals**

Prioritise innovations in vaccine delivery attributes to provide greater clarity to manufacturers and immunisation partners to make investment decisions

VIPS

Members of the VIPS Alliance working group



Marion Menozzi-Arnaud, Tiziana Scarna



Birgitte Giersing, Anna-Lea Kahn



Vivian Hsu, David Sarley



Debbie Kristensen, Courtney Jarrahian, Collrane Frivold,
Mercy Mvundura



Kristoffer Gandrup-Marino (Jean-Pierre Amorij)



Consultants: Julian Hickling, Rebecca Jones



Members of the VIPS Steering Committee



Members	Organisation	Role
Alejandro Cravioto	Facultad de Medicina Universidad Nacional Autónoma de México	Professor; SAGE Chair
David Robinson	Bill and Melinda Gates Foundation	Deputy Director, CMC
Chris Morgan	Burnet Institute	Principal, Vaccines Immunization and Immunity
David Kaslow	PATH	Vice president, Essential Medicines
Jean-Pierre Armorij	UNICEF Supply Division	Vaccine Technology Specialist
Jerome Kim	International Vaccine Institute	Director General
Jon Abramson (SC Chair)	Wake Forest School of Medicine	Professor of Pediatric Infectious Diseases
Kelly Moore	Vanderbilt University School of Medicine	Clinical Assistant Professor of Health Policy
Mark Jit	London School of Hygiene and Tropical Medicine	Professor, Vaccine Epidemiology
Mark Papania	Global Immunization Division, Centers for Disease Control	Medical Epidemiologist
Michael Free	Independent	Independent Consultant; Senior Advisor Emeritus, PATH
Nora Dellepiane	QRB Consultants Sàrl	Independent consultant
Ramanan Laxminarayan	Center for Disease Dynamics, Economics and Policy	Director
Ruth Karron	John Hopkins University	Professor
Samir Sodha	WHO	Routine Immunization Officer
Shelley Deeks	Public Health Ontario	Chief, Communicable Diseases, Emergency Preparedness and Response

WHO IPAC member WHO PDVAC member

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24 vaccine product innovations were assessed through the VIPS process



Primary vaccine containers (without delivery device)

- Blow-fill-seal (BFS) primary containers
- Dual chamber vials

Delivery technologies (not pre-filled)

- AD sharps-injury protection (SIP) syringes
- Disposable syringe jet injectors (DSJI)
- ID syringes

Integrated primary containers and delivery technologies

- Compact prefilled auto-disable devices (CPADs)
- Single-chamber cartridge injectors
- Dual-chamber delivery devices
- Microarray patches (MAPs)
- Prefilled polymer BFS dropper/dispensers
- Prefilled dry-powder intranasal devices
- Solid-dose implants (with applicator)
- Sub-lingual dosage forms
- Oral fast-dissolving tablets

Packaging and safety

- Bundling devices
- Reconstitution vial adapters
- Plastic needles (for reconstitution)

Labelling

- Freeze indicators on primary vaccine container
- Combined Vaccine vial Monitor (VVM) and Threshold Indicator (TI)
- Barcodes
- Radio Frequency Identification (RFID)

Formulation

- Heat stable/controlled temperature chain (CTC) qualified liquid formulations
- Heat stable/ CTC qualified dry formulations
- Freeze damage resistant liquid formulations

VIPS has been delivered through two prioritisation phases

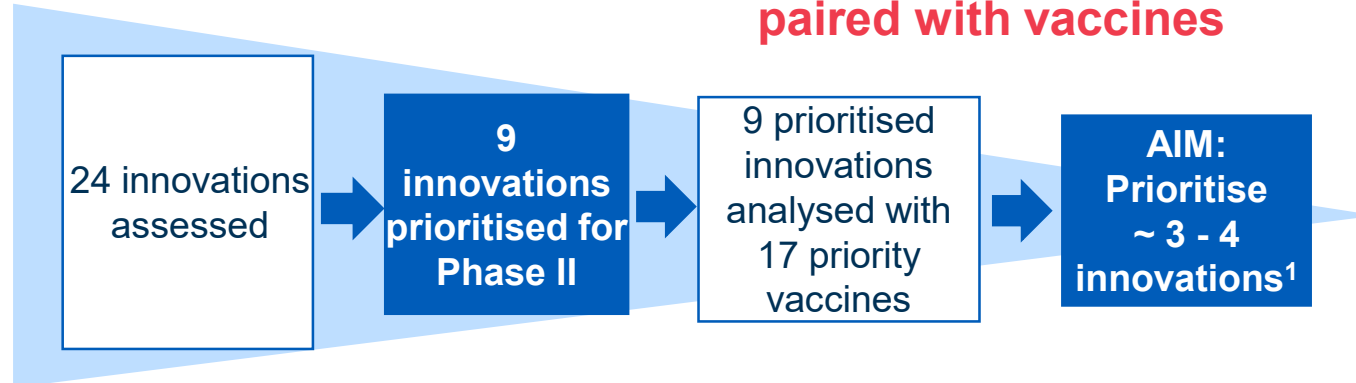


December 2018 – June 2019

July 2019 – MAY 2020

Phase I: Initial prioritisation of innovations

Phase II: Final prioritisation of innovations paired with vaccines



- Innovations' **characteristics** and **potential public health value**;
- **Potential 'breadth of use'** (applicability to several vaccines)

- Short-listed innovations **further analysed with priority vaccines**

We presented to DCVMN last year at the end of Phase I



¹ Purpose is to prioritise innovations "themselves", "as platforms", however it will be signaled for which individual vaccines or types of vaccines the innovation is seen to be most valuable.

9 innovations short-listed for further analysis under Phase II



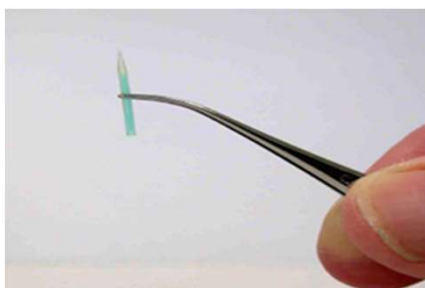
Microarray patches (MAPs)



Compact prefilled auto-disable devices (CPADs)



AD sharps-injury protection (SIP) syringes



Solid-dose implants



Dual-chamber delivery devices



Freeze damage resistant liquid formulations



Heat stable/controlled temperature chain (CTC) qualified liquid formulations



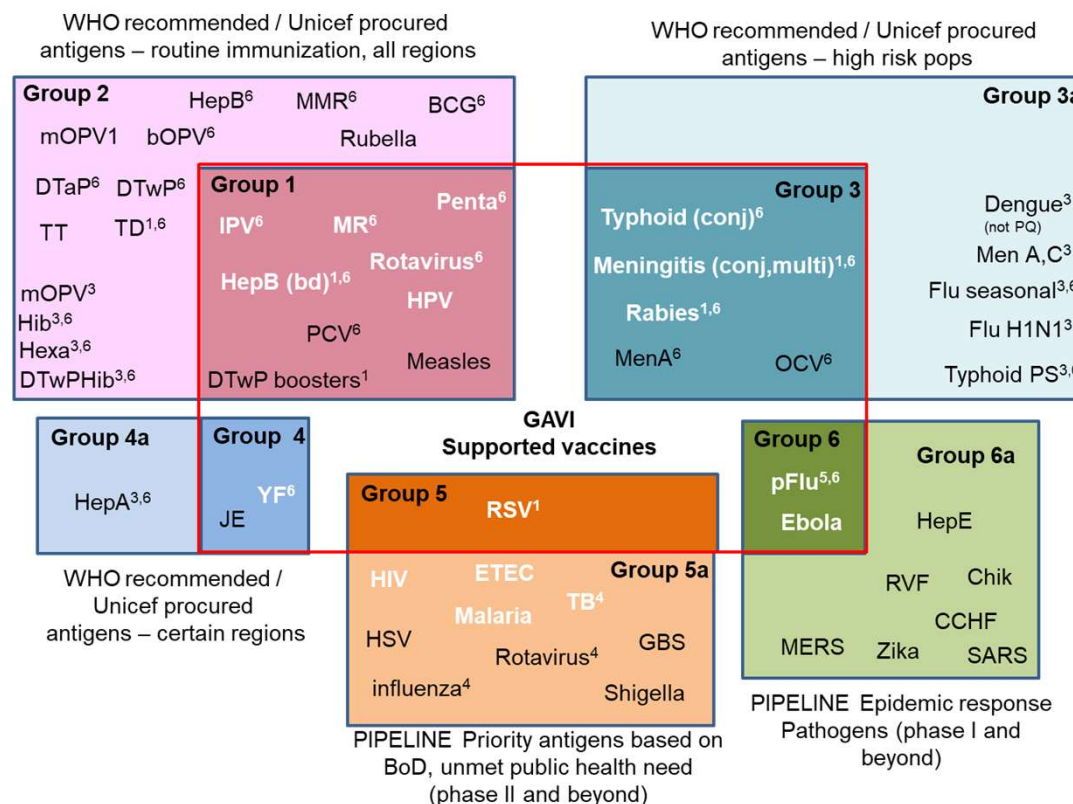
Combined Vaccine vial Monitor (VVM) and Threshold Indicator (TI)



Barcodes on primary packaging

Note: Innovation pictures are just examples of innovations

Phase II 'paired' the 9 short-listed innovations with 17 vaccines (10 licensed and 7 pipeline)



KEY:

- 1 Included in Gavi VIS 5.0
- 2 Phase II or beyond
- 3 Not procured by UNICEF
- 4 Next generation
- 5 Gavi learning agenda
- 6 PAHO Revolving Fund

Evaluation framework for Phase II (1/2)



	Criteria	Indicators
Primary criteria ¹	Health impact	• Vaccine efficacy • Vaccine effectiveness • Ability of the innovation to withstand heat exposure² • Ability of the innovation to withstand freeze exposure²
	Coverage and equity impact	• Number of fully or partially immunised individuals (relative to target pop) • Ease of use from clinical perspective based on product attributes³ • Ease of use based on ability of a lesser trainer person to administer the vaccine or self-administration³ • Ability to facilitate dose sparing • Availability of the innovation in a single-dose presentation or multi-dose with preservative to avoid missed opportunities and reduce vaccine wastage • Acceptability of the innovation to patients/caregivers² • Potential to reduce stock outs based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities²
	Safety impact	• Number of vaccine product-related adverse events • Likelihood of contamination and reconstitution errors² • Likelihood of needle stick injury²

¹ These criteria are evaluated against a comparator.

² Same indicators as for Phase I but further assessed under Phase II due to the antigen/vaccine pairing

³ This indicator was re-assessed in Phase II only when the comparator for a specific vaccine is a MDV, requiring a new evaluation – The comparator SDV was assessed in Phase I.

Evaluation framework for Phase II (2/2)



Criteria

Indicators

Primary criteria ¹	Economic costs	• Commodity costs of a vaccine regimen (per person vaccinated) • Delivery costs of the vaccine regimen (per person vaccinated) • Introduction and recurrent costs of the vaccine regimen (per person vaccinated)
	Environmental impact	• Waste disposal of the vaccine regimen (per person vaccinated) and delivery system
Secondary criteria ²	Technology readiness	• Clinical development pathway complexity • Technology development challenges • Regulatory pathway complexity • Complexity of manufacturing the innovation • Robustness of the innovation pipeline
	Commercial feasibility	• Potential breadth of market size • Existence of partnerships to support development and commercialisation • Known barriers to global access to the innovation • Stakeholders' interest

¹ These criteria are evaluated against a comparator.

² These criteria are evaluated in an absolute manner, not relative to a comparator.

In Phase II, VIPS has conducted two country consultations



Countries

Identifying vaccine-specific barriers and needs
(that can be addressed by VIPs innovations)

- **'Targeted' online survey**
- Q4 2019 - Q1 2020
- **209 responses** across **54 Gavi and non Gavi countries**

Feedback on 9 short-listed innovations

- **In-person in-depth interviews**
- Q4 2019 - Q1 2020
- **84 people in 6 countries** at national & subnational levels

Country consultation - summary of top 5 problem statements¹ identified for licenced vaccines



	Penta	MR	Men A	Hep B birth dose	HPV	IPV	Rabies	Rota	TCV	YF
Vaccine ineffectiveness/wastage due to heat exposure	2	1	3	2	4	2	2	1	1	
Vaccine ineffectiveness/wastage due to freeze exposure	1			1	1	1		2	5	3
Cold chain requirements during outreach	4	4	2	3	3	3		3		
Vaccine wastage or missed opportunities due to multi-dose vial		2	1				4	5	2	1
Reconstitution related safety issues		3	4							2
Reduced acceptability due to painful administration	3			5	2	4	3			
Difficult preparation requiring trained personnel				4	5		1		4	
Negative impact on the environment due to waste disposal practices						5		4		5
Needle-stick injuries		5	5				5			4
Contamination risk due to multi-dose vial	5									
Difficult to deliver vaccine to correct injection depth									3	

¹ Numbers represent the ranking order of the top 5 problem statements.

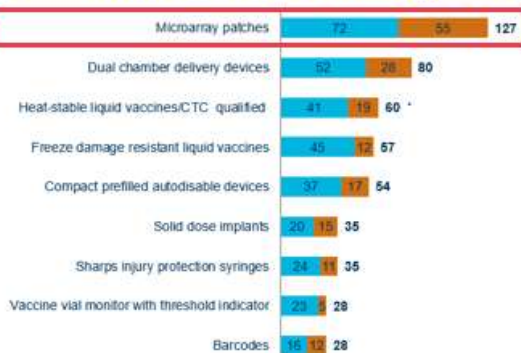
Country consultation - Example of country feedback: MAPs



Based on VIPS country feedback¹, there is strong interest in MAPs

Feedback from in-person country interviews

Innovations' ranking



- MAPs are rated by both immunisation staff and decision makers as the **#1 innovation amongst the 9 tested**, i.e. with the greatest potential impact in helping address their immunisation programme's current challenges.

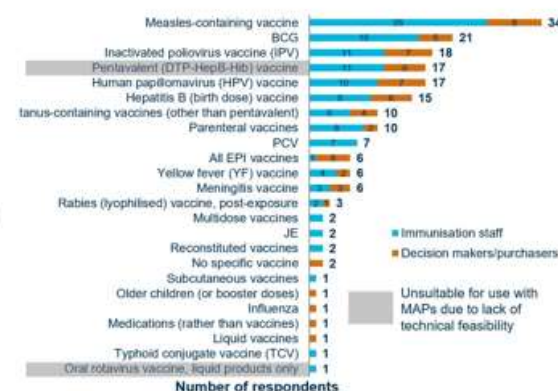
Perceived benefits

- Make **preparation and administration** of vaccines **easier and faster**, **save health care workers time**;
- Increase acceptability**;
- Improve safety**, i.e. reducing needle-stick injuries, contamination or use of wrong diluents;
- Improve coverage & **decrease vaccine wastage**;
- Make delivery **outside health facility easier & enable lesser trained personnel to deliver** vaccines.

Perceived challenges

- Need for community sensitisation** to manage acceptability among patients/caregivers;
- Cold chain volume**;
- HCWs : **time required to use MAPs**; **complexity of the technology**; **possibility of skin reaction** or different absorption by skin type; **no indication that the vaccine has been delivered**;
- Decision makers: **overall cost and training needs**.

Vaccines' ranking for MAPs

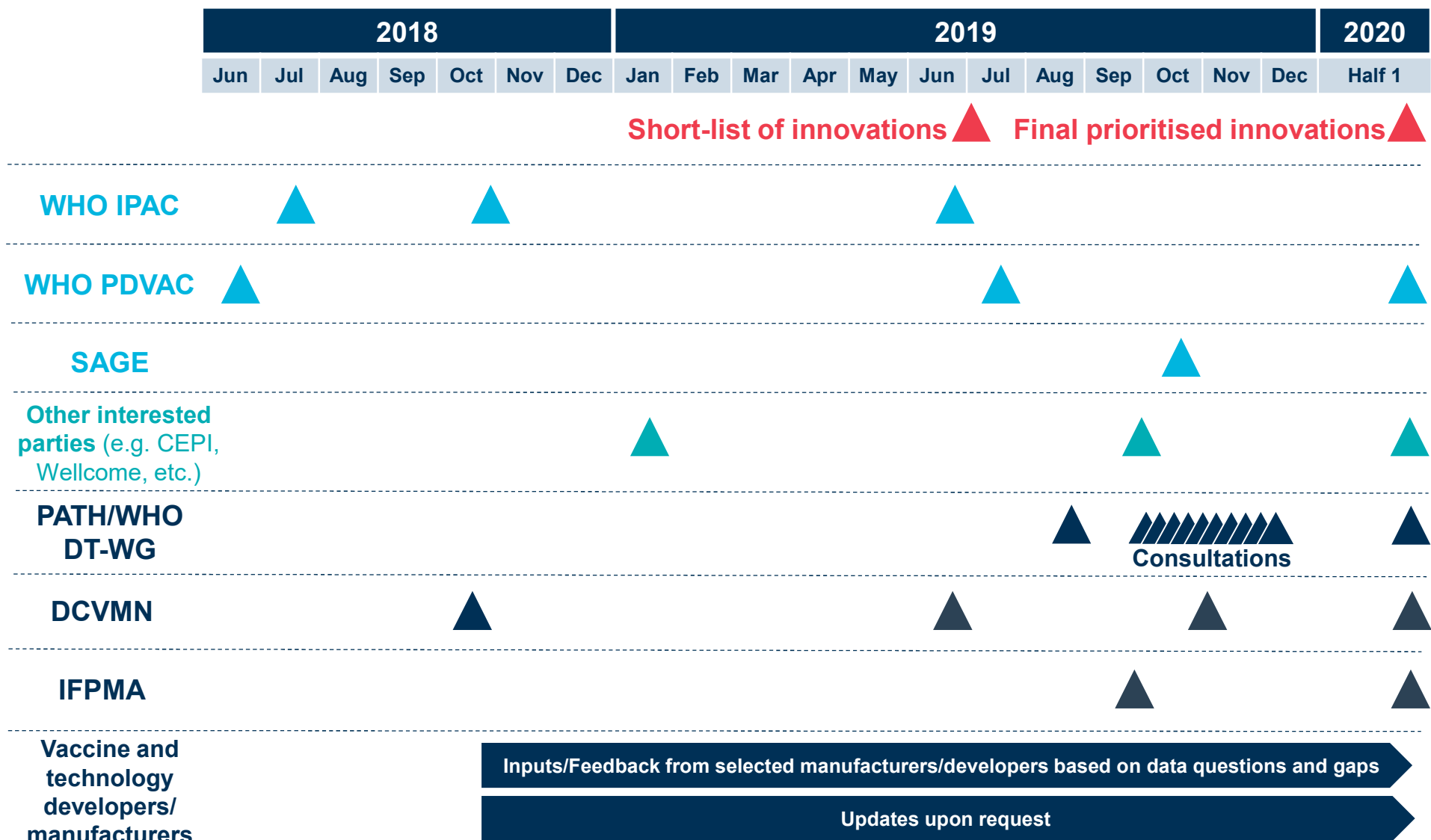


In Phase II, VIPS has also engaged with industry and regulators



Countries		WHO/PATH DT-WG	Regulators
Identifying vaccine-specific barriers and needs (that can be addressed by VIPS innovations)	Feedback on 9 short-listed innovations	Update & feedback on 8 of the 9 short-listed innovations from the perspective of technical feasibility, manufacturability, regulatory hurdles	Feedback/ validation on endpoints/surrogate markers and input on challenges with respect to the clinical development pathway
• 'Targeted' online survey • Q4 2019 - Q1 2020 • 209 responses across 54 Gavi and non Gavi countries	• In-person in-depth interviews • Q4 2019 - Q1 2020 • 84 people in 6 countries at national & subnational levels	• Broader set of immunisation stakeholders, including industry	• FDA, EMA, AVAREF, PEI on endpoints /surrogate markers • Ex-FDA and EMA officials on clinical development pathway challenges

Beyond countries, VIPS also ensures alignment and engagement with existing committees and industry



VIPS innovations and COVID-19



- The primary goal of VIPS was to prioritise innovations that would ensure **access and increase coverage for existing vaccines**.
- This becomes even more important in light of the **impact of COVID-19 on RI services and the likely future increase of supplemental and outreach immunisation activities** to catch-up millions of children who will miss out on essential services during this pandemic.
- Additionally, the COVID-19 pandemic creates **potential funding opportunities** for innovations that are relevant for both COVID and other priority vaccines, that could accelerate their product development and/or implementation.
- **‘Win-win’ scenarios** were thus sought to prioritise innovations that have the potential to both increase equitable coverage for existing vaccines, particularly post-COVID-19, and be valuable for COVID-19 vaccine delivery.

Outcomes of VIPS process: prioritised innovations



VIPS plans to **engage in advancing development, policy and access** of the following:

- Upstream novel delivery device – **Microarray patches**
- A combined formulation, regulatory, and novel programmatic approach to vaccine management – **Heat stable and Controlled Temperature Chain qualified vaccines**
- An implementation/system innovation – **Barcodes on primary containers**

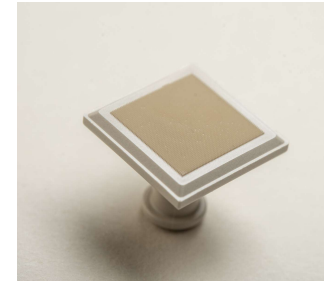


Note: Innovation images are examples

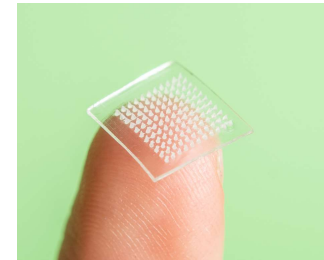
Microarray patches



- Patches consist of **hundreds or thousands of tiny projections** that deliver dry vaccines or drugs into the skin.
- MAP projections are typically **shorter than 1 mm** (typically 50–900 μm in height; projections longer than 1 mm are referred to as mini-needles).
- Applied to the skin, and **projections penetrate into the top layer of skin**.
- Some platforms require an **applicator** for delivery (integrated or separate).
- Typically perceived as **less painful than an injection**.
- Wear times range from a **few seconds to hours** to release their API payload, depending on their design.



Coated microarray patch (early-stage development).



Dissolving microarray patch (early-stage development).

MAPs: high consensus, ranked #1



- **Potential to address most vaccine problems identified by countries**, due to:
 - Improved thermostability; better ease of use; avoidance of reconstitution and associated errors and risks; improved safety (sharps-free); SDV presentations, thereby avoiding missed opportunities due to reluctance to open a MDV.
- Applicable to a **number of use cases** including routine, supplemental, house-to-house and outbreak immunisation.
- Should be developed for use with several vaccines, including those with elimination agendas (e.g., **MR, HPV, IPV**) and **other priority vaccines**.
- May have a positive impact on **‘life-course’ immunization for broader populations** beyond children, including adults and older adults.
- Could be co-developed with vaccines to be positioned for **future emergency response or for use with COVID-19 vaccines in the longer term**.
- **Significant technical, biological and commercial barriers to overcome** before MAPs can be implemented, which will require substantial funding.
- A significant unknown: will the **prices for vaccines in MAPs be acceptable to end-users** - likely to cost more to procure but expected to reduce delivery costs and help overcome immunisation barriers?

Heat stable formulations and controlled temperature chain



- This innovation refers to liquid vaccine formulations that are **sufficiently heat stable to be kept in a controlled temperature chain (CTC)**.
 - Dry vaccine formulations are included if used in synergy with other innovations
- CTC use of vaccines allows for a single planned excursion of the vaccine into ambient temperatures not exceeding **+40°C for a minimum of 3 days**, just prior to administration.
- Heat-stable vaccines differ in the length of time they can be stored in a CTC and the maximum temperature they can endure while remaining stable and potent.
- CTC qualification involves regulatory approval and prequalification by WHO.

Heat stable and Controlled Temperature Chain (CTC) qualified vaccines: high consensus, ranked #2



- Thermostability identified as the **top priority by countries. Directly addresses the equity issue.**
- Prioritisation of **heat stable and CTC-qualified vaccines, including both liquid and dry formulations.**
 - Enhanced thermostability is a desirable feature for all vaccines to enable higher temperature storage and transport in a CTC.
- Vaccine candidates for **CTC use**, whether liquid or dry, should have the following attributes: **adequate heat stability to achieve regulatory and WHO prequalification for CTC with the longest CTC duration possible, contexts of use that benefit from CTC, and formats that do not increase vaccine wastage or safety risks when used in a CTC.**
 - A WHO CTC working group has been active since 2014, and VIPS will synergise with this effort.
- **Synergistic with Vaccine Vial Monitors integrated with Threshold Indicators (VVM-TIs)** to facilitate temperature monitoring.
- May be a relatively 'easy win' for existing thermostable vaccines and many pipeline vaccines; higher barrier for existing vaccines that require reformulation, so should be pursued if vaccines undergo reformulation for another reason.

Barcodes on primary packaging



- Barcodes can encode vaccine specific information in a small space.
 - ***product numbers, serial numbers, supplier data, batch numbers and expiry dates***
- Barcodes can **enable tracking of vaccine products** in supply chains, providing information to manufacturers, transport providers, health facilities, assuming the supporting infrastructure is in place.
- Barcodes can be integrated with other data operating systems, such as **patient electronic medical records**, enabling healthcare providers to monitor vaccination of individual patients or AEFIs associated with vaccination.



Barcodes on primary containers: good consensus, ranked #3



- Track and trace considered a priority for vaccines and 2D barcodes on primary containers would **support the transition to electronic record keeping, in line with the objectives of advancing digital health in Primary Health Care.**
- Mature technology; a 'push' for implementation at the primary packaging level for LMICs could **build upon the existing efforts of UNICEF and Gavi** to place barcodes on vaccine secondary packaging.
- COVID-19 crisis seen as an opportunity to leverage investment to catalyse implementation for immunisation programmes more generally and **may be the right moment to push barcodes on primary containers and digital health and VIPS may be the right avenue.**
 - Also seen as **highly valuable for COVID-19 vaccine deployment in terms of tracking inventory, immunisation coverage, and AEFIs.**
- Clear recognition that barcodes themselves are not an innovation but part of a broader innovation ecosystem that will need coordination and integration across all levels of delivery.

VIPS communication



- Creation of a VIPS page on the **Gavi website** by end of July, with **all assessment documents uploaded**.
- Three planned publications:
 - A **methodology and outcomes document**, summarising the VIPS process, methodology and final outcomes (July).
 - A **summary of the country consultations**, including the methodology and results of the three country consultations conducted in phase I and II (September).
 - A **perspective** assessing strategically what is needed and the unique remit and role of VIPS to position delivery innovations for success (November).

Next phase of VIPS: Accelerate access in LMICs to VIPS prioritised innovations by providing targeted Alliance support



Define an action plan per prioritised innovation

- Targeted **consultations with developers, manufacturers, existing working groups, other stakeholders**
- Key 'roadblocks' and **potential gaps** to innovation development and uptake
- **End-to-end strategy**, proactively seeking to address the barriers and bottlenecks through an integrated approach

Create an enabling environment needed for vaccine innovations uptake

Policy, procurement, delivery/ system implications & related needs

Create a continuous learning and evaluation mechanism

Learnings from VIPS prioritisation phase, **continuous learning & evaluation process**, i.e. horizon scanning of new data

Agree and implement VIPS operationalisation

Align on **VIPS operationalisation** & how to work together

If needed, **broader resource mobilisation**

- **Implement, monitor and adjust** innovations' **action plans**

- Implement '**enabling environment**'

- Implement '**learning and evaluation mechanism**'

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Alliance Action Plans



The next phase of VIPS will develop Action Plans for the three prioritised innovations: **MAPs, Heat stable and CTC vaccines and barcodes on primary containers.**

Consult with **vaccine manufacturers** and **developers** to get their input

Identify:

- **Challenges and barriers** facing the innovation development for use in LMICs
- Ways to **accelerate development.**



Action Plan Structure:

1. Development status and pipeline overview
2. Development challenges
3. Existing global activities
4. Summary of feedback from consultations
5. Unaddressed gaps
6. Action plan objectives and target outcomes

Slide 35

MM [2]60 Julian/Gitte: I felt this session at PDVAC was slightly confusing as people kind of understood that we were doing this only for MAPs and asked about CTC in the chat. Reflecting about this, somehow I think that the next slide about MAPs activities did not bring much and could be removed (also because we have a lot to cover in one hour) and thought that the remaining 2 slides could be 'genericised' to talk about the 3 innovations instead of focusing on MAPs. This could be presented by you Gitte as I'm not sure if Julian is joining?

Marion Menozzi-Arnaud; 13 Jul 2020

Action Plan consultations with manufacturers and developers focus on 4 areas



Vision

- Five-year view for the innovation
- General and company-specific
- Impact of COVID-19

Challenges

- Technical, manufacturing, regulatory, commercial challenges
- Solutions to challenges/barriers
- Potential roles for Alliance partners

Vaccines

- Priority targets
- Factors influencing choice of vaccine targets
- Opinion on products for global-health/LMIC use

Commercial

- Commercial attractiveness of the innovation; key drivers
- Time to first innovation-vaccine product for LMICs
- Approaches to accelerate time to first product

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► Discussion