May 2019

VIPS Vaccine Product Innovations and Comparators' list

VIPS scope of innovations

VIPS uses the following definition of product innovation to define its scope: "*completely new products or adaptations to existing products that provide measurable financial or programmatic benefits to lower and middle income countries (LMICs), such as increased coverage and equity (e.g., by overcoming a 'last mile' barrier) or vaccine effectiveness*".

The scope of innovations that were assessed was informed by partner and expert consultations, with an agreement to define a broad scope to avoid focusing mainly on 'low-hanging fruit' - innovations that are expected to come to market without requiring incentives - and to include some of the broader vaccine innovative features that have the potential to make an impact in terms of better meeting country programmatic needs or improving coverage and equity.

In scope:

- **Primary vaccine containers (without delivery device):** The immediate receptacle in direct contact with the vaccine as distributed for sale.
- **Integrated primary container and delivery technology:** A stand-alone technology used as the primary vaccine container, and to administer a vaccine by a specific vaccine administration route.
- **Delivery technology (not prefilled):** A stand-alone technology used to administer a vaccine by a specific vaccine administration route
- **Formulation:** The combination of chemical and biological substances used to produce a final vaccine product. For VIPS, formulation innovations will be limited to those with the objective of improving thermostability and enabling use in controlled temperature chain (CTC).
- **Packaging and safety**: Secondary or tertiary packaging for vaccine primary containers and safety devices for vaccine preparation (not delivery).
- **Labelling:** Text, symbols, data or other visual cues provided on the primary packaging of a vaccine or on documents included within the packaging

Out of scope:

- **Cold Chain Equipment (CCE) innovations**: other mechanisms prioritise and incentivise CCE innovations (e.g. the Gavi CCE Optimisation Platform), and the 'end-customers' are different than for vaccines (CCE technology developers vs. vaccine manufacturers and technology developers)
- **Formulation outside of the objective of thermostability and CTC** (e.g. adjuvants to improve efficacy, combination vaccines, new schedules, etc.): covered to some extent by the WHO Immunization and Vaccines related Implementation Research Advisory Committee (IVIR-AC). Additionally, these innovations would be vaccine-specific only, where VIPS starts by prioritising antigen-agnostic innovations.
- **Antigen innovations**: covered by the WHO Product Development for Vaccines Advisory Committee (PDVAC) and Gavi Vaccine Investment Strategy (VIS)
- **Non-vaccines**: Anything that is not directly associated with a vaccine, its packaging and how it is administered is out of scope. This includes all tracking and reminder systems, stock management systems, supply chain improvements or systems. Anything that is not in the control of a vaccine manufacturer or vaccine technology developer is out of scope.

In addition, four selection criteria have been defined and applied to focus the scope of innovations during this round of VIPS. It is possible that innovations excluded by these criteria might be included in future rounds of VIPS:

1. **Innovations that don't meet WHO PSPQ criteria were excluded where specific guidance exists for the innovation:**
    - Prefilled syringes (unless compact and autodisable, in which case they would be considered in scope)
2. **Innovations that could come to a low and middle income country (LMIC) market without any Alliance interventions were also excluded:**
    - Intranasal spray nozzles - currently used for live attenuated influenza vaccines (LAIV). They are off-the-shelf and can be used by a manufacturer who develops a vaccine for intranasal administration.
    - Prefilled intranasal spray dispenser – currently used for LAIV. They are off-the-shelf and can be used by a manufacturer who develops a vaccine for intranasal administration.
    - Prefilled, preformed polymer containers for oral/intranasal vaccines – already in use for oral polio, rotavirus, and cholera vaccines.

- Enteric capsules – already licensed for cholera and adenovirus vaccines and likely to be picked up by manufacturers of enteric vaccines for older children and adults.

3. **Innovations for which development has been discontinued were also excluded:**
   - Dry-powder jet injectors
   - Nebulisers[1]
4. **Innovations used at the time of vaccine application to enhance the immune response to the vaccine and that are separate to the delivery device were excluded:**
   - Electroporation
   - Topical adjuvant creams
   - Laser microporation

24 innovations are proposed in total and are presented in Table 1.

VIPS selection of comparators

VIPS will assess a diversity of innovations, but relatively few of them belong to the same type of innovation, making direct comparisons across innovations very difficult (e.g. compact prefilled auto-disable injection device vs. barcode).

To overcome this issue, it is proposed to assess each innovation against a comparator that most closely matches the innovation and will allow a direct comparison for each indicator and is currently (or could be) used in low- and middle-income countries (LMICs).

14 comparators are proposed in total for the 24 innovations in scope and are presented with the innovations in Table 1.

Assumptions

When creating the comparator list, the following assumptions were made:

1. All comparators and devices are **autodisable (AD),** except for the reconstitution **needle and syringes (N&S)**, which are **reuse prevention (RUP)**.

[1] Excluded under this criterion because the WHO work on nebulizers for measles vaccine was discontinued.

2. The comparators chosen for each type of innovation are the **combination of existing components that most closely match the innovation, and that are also currently (or could be) used in LMICs**.

3. **Single dose vials (SDV), rather than multi-dose vials (MDVs) are** used for the comparators, because in most cases the innovation being considered is a single-dose presentation. Using single-dose vials will allow a more direct comparison with the innovation's characteristics and make the incremental gains/losses easier to compare. However, when MDVs are currently used by countries for specific vaccines, a comparison against an MDV will also be conducted under Phase II for those vaccines if this innovation is prioritized.

4. **Intradermal (ID) injection** using the Mantoux technique was assumed to be significantly different to intramuscular (IM) and subcutaneous (SC) injection; however, it was assumed that IM and SC injection are sufficiently similar not to need different comparators.

Table 1. List of innovations in scope of VIPS, at the category and type levels, with comparators

Innovation category		Innovation type	Comparator(s)
A	**Primary vaccine container (without delivery device)**	1. Blow-fill-seal (BFS) primary container	• SDV (liquid vaccine)
		2. Dual chamber vial	• SDV (lyophilized or "lyo" vaccine), diluent, and RUP (reconstitution or "recon") N&S
B	**Integrated primary container and delivery technology**	3. Compact prefilled auto-disable device (CPAD) • Sub-type: Preformed CPAD • Sub-type: BFS CPAD • Sub-type: Other types	• SDV (liquid) and AD N&S
		4. Single-chamber cartridge injectors	• SDV (liquid) and AD N&S
		5. Dual-chamber delivery device	• SDV (lyo), diluent, RUP recon N&S, and AD N&S
		6. Microarray patch (MAP)	• SDV (liquid) and AD N&S; • SDV (lyo), diluent, RUP recon N&S, and AD N&S

Innovation category		Innovation type	Comparator(s)
		7. Prefilled polymer BFS dropper/dispenser	• SDV (liquid) and dropper/dispenser
		8. Prefilled dry-powder intranasal device	• SDV (lyo), diluent, RUP recon N&S, and AD N&S[2]
		9. Solid-dose implants (with applicator)	• SDV (liquid) and AD N&S; • SDV (lyo), diluent, RUP recon N&S, and AD N&S
		10. Sub-lingual dosage form	• SDV (oral/liquid) and dropper/sprayer; • SDV (oral/lyo), diluent, RUP recon syringe, and dropper sprayer; • SDV (injectable/liquid) and AD N&S; • SDV (injectable/lyo), diluent, RUP recon syringe, and AD N&S
		11. Oral fast-dissolving tablets	• SDV (oral/lyo), diluent, RUP recon syringe, and dropper; • SDV (injectable/liquid) and AD N&S
C	**Delivery technology (not pre-filled)**	12. AD sharps-injury protection (SIP) syringe	• AD N&S without SIP feature
		13. Disposable syringe jet injector (DSJI) a. Subtype: DSJI for intramuscular/subcutaneous delivery b. Subtype: DSJI for intradermal (ID) delivery	a. AD N&S b. Bacille Calmette-Guerin (BCG) AD N&S[3]
		14. ID syringes a. Subtype: needle hubs and ID adapters (with ID needles) b. Subtype: syringe adapters (no needle) c. Subtype: field-filled ID syringes	• BCG AD N&S[3]
D	**Formulation**	15. Heat stable/controlled temperature chain (CTC) qualified liquid formulations	• Use without innovation (i.e. current liquid or lyophilized formulation)
		16. Heat stable/ CTC qualified dry formulations	• Use without innovation (i.e. current liquid or lyophilized formulation

[2] A footnote will be added in the Technical note in Phase I that a comparison against IN sprays will also be required under Phase II if there is a vaccine (antigen) that is currently delivered as liquid spray in the scope of vaccines.
[3] ID injection using an AD BCG needle and syringe and the Mantoux technique

Innovation category		Innovation type	Comparator(s)
		17. Freeze damage resistant liquid formulations	• Use without innovation (i.e. current liquid formulation)
E	**Packaging and safety**	18. Bundling devices	• Use without innovation (i.e. vaccine and diluent in separate packaging)
		19. Reconstitution vial adapters	• Use without innovation (i.e. RUP N&S for reconstitution)
		20. Plastic needle (for reconstitution)	• RUP N&S (with metal needle)
H	**Labelling**	21. Freeze indicator on primary vaccine container	• No freeze indicator on the primary vaccine container and use of standalone freeze indicators and temperature monitoring devices
		22. Combined Vaccine vial Monitor (VVM) and Threshold Indicator (TI)	• VVM on primary containers used with stand-alone TI
		23. Barcodes	• Use without innovation (i.e. no barcode)
		24. Radio Frequency Identification (RFID)	• Use without innovation (i.e. no RFID tag)