VIPS VACCINE INNOVATION PRIORITISATION STRATEGY

VIPS Phase I executive summary: Heat-stable/Controlled Temperature Chain (CTC) qualified liquid formulations

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Gavi The Vaccine Alliance

World Health Organization

BILL & MELINDA GATES foundation

PATH

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

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About Heat-stable/CTC qualified liquid formulations

- This innovation refers to liquid vaccine formulations that are **sufficiently heat stable to be kept in a CTC.**
- CTC use of vaccines allows for single 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.

Stage of development

- There are currently **two liquid vaccines that are thermostable and qualified for CTC use**.
  - Merck's **Gardasil® 4 (quadrivalent human papillomavirus vaccine)** that could be used at temperatures up to 42°C for 3 days
  - **Shantha Biotechnics Shanchol™ (oral cholera vaccine)** that could be used at temperatures up to 40°C for 14 days.
- A number of vaccine manufacturers are in the **process of qualifying their existing and pipeline liquid vaccines for CTC use.**
- Several developers have created approaches to stabilising formulations, some of which are proprietary, that may be applicable to a variety of vaccines to improve their heat stability in liquid formulations.

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

Comparators: Current liquid and lyophilised formulations

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Quality of evidence: Moderate to high

VIPS Criteria		Indicators	Comparators: Liquid formulations	Comparators: Lyophilised formulations	Priority indicators - Country consultation: RI* Facility	RI* Community	Campaigns
Primary criteria	Health impact	Ability of the vaccine presentation to withstand heat exposure	Better	Better	+	++	++
		Ability of the vaccine presentation to withstand freeze exposure	Better	Neutral			
	Coverage & Equity impact	Ease of use [a]	Neutral	Better	+	+	++
		Potential to reduce stock outs [b]	Neutral	Better			
		Acceptability of the vaccine presentation to patients/caregivers	Better	Better		+	+
	Safety impact	Likelihood of contamination	Neutral	Better			+
		Likelihood of needle stick injury	Neutral	Better			
	Economic costs	Total economic cost of storage and transportation of commodities per dose	Better	Considerably Better	+		
		Total economic cost of the time spent by staff per dose	Better	Better	++	++	+
		Total introduction and recurrent costs [c]	Neutral	Neutral			
Secon-dary criteria	Potential breadth of innovation use	Applicability of innovation to one or several types of vaccines	All vaccines that are currently liquid and thermostable.				
		Ability of the technology to facilitate novel vaccine combination	No				

* RI : Routine immunisation

++	Given significantly more importance
+	Given more importance
	Kept neutral

[a] Ease of use can prevent missed opportunities and impact ability for lesser trained personnel to administer the vaccine, including self-administration

[b] Based on the number of separate components necessary to deliver the vaccine or improved ability to track vaccine commodities

[c] Total economic cost of one-time / upfront purchases or investments required to introduce the innovation and of recurrent costs associated with the innovation (not otherwise accounted for)

Heat-stable/controlled temperature chain (CTC) qualified liquid formulations: Antigen applicability

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- Heat stable/CTC qualified liquid formulations could potentially be **applied to any vaccine, but inactivated/subunit vaccines are more likely to be feasible** to **achieve a CTC-qualified liquid formulation.**
- The **benefits of CTC-qualification** are greatest for vaccines that are used in **campaigns or special strategies** (e.g. **meningococcal group A conjugate vaccine**).
- **HPV and hepatitis B birth dose** are two VIPS priority antigens that **WHO has prioritised for CTC use.**

Heat-stable/controlled temperature chain (CTC) qualified liquid formulations: Assessment outcomes

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KEY BENEFITS

✚✚ **Heat stable liquid formulations improve vaccine effectiveness** as they are **less susceptible to heat damage**.

- May also **reduce the likelihood of freeze exposure**, in comparison to freeze sensitive liquid vaccines that are not CTC qualified, since the vaccines can be kept out of the cold chain for a specified period of time.

- Depending on the vaccine format, heat stability/CTC qualification can **potentially increase coverage and equity by enabling alternative delivery scenarios** where the vaccine is transported and stored outside of the cold chain – easing cold chain logistics for health care workers.

✚✚ May **increase acceptability** among caregivers/vaccinees due to increased access to the vaccines.

- **Additional potential positive impact on coverage and equity** against standard lyophilised formulations comparator**:**
  - ✚✚ **Easier to use** as it removes the need for reconstitution.
    - **Potential to reduce stock-outs** since reconstitution related components are not needed.

✚ May **increase safety** compared to standard lyophilised formulations, by reducing the **risk of contamination and needle stick injuries** since reconstitution is not needed.

- May **reduce delivery costs:**
  - ✚ May **reduce storage and transportation volume and associated costs** as volume reduced just before vaccine delivery and since reconstitution components are not needed.
  - ✚✚ May **save health care worker time:**
    - Compared to standard lyophilised formulations as it **removes the need for reconstitution.**
    - For both comparators, as vaccinators may be able to **reduce travel time**, avoiding returning unused vaccines to health facilities at the end of outreach sessions and in some cases storing vaccines in their communities during the specified CTC duration. Using vaccines in CTC also **removes the time needed to prepare icepacks**.

- **Broad applicability** to all vaccines that are currently liquid and thermostable.

KEY CHALLENGES

- No key challenges related to Phase I assessment have been identified.

✚✚ Important attribute for at least 2 settings or for the 3 settings based on the country consultation (see slide 3)

✚ Important attribute for campaigns or routine facility-based immunisation based on country consultation (see slide 3)

Heat-stable/controlled temperature chain (CTC) qualified liquid formulations: Rationale for prioritisation

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- Heat stable/CTC qualified liquid formulations **are recommended to be prioritised** for further analysis under Phase II given their **high potential positive impacts in the areas of health impact, coverage and equity, safety, and delivery costs**.
- This recommendation also **supports WHO's strategy for CTC use of vaccines** as well as the **Global Vaccine Action Plan (2011-2020) strategic objective to expand CTC use of vaccines.**

Additional important information to be analysed in phase II (if prioritised for Phase II)**:**

- Identification of liquid priority antigens for CTC use and analysis of the technical feasibility for obtaining CTC qualification.
- How best to align with and provide complementary value to WHO's CTC strategy.

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