Microarray patch case study: Measles-rubella vaccine

Global Vaccine Immunization Research Forum - Johannesburg, South Africa

Workshop 3: Total Systems Effectiveness

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Current challenges to vaccine delivery

- Limited availability of trained health care workers.
- Increased number of vaccines and target populations.
- Supply chain complexities (e.g., difficulties ensuring that diluents and immunization supplies match vaccine supplies).
- Different standards used for drug delivery (e.g., autodisable syringes used only for vaccines).
- Need for safe injection technology.
- Needlestick injuries to health care workers.
- Risk to communities from improper disposal of sharps and biohazardous waste.

Photo: WHO

Photo: WHO

Technology prioritization: Objectives, approach, and benefits

Objectives

- **Improvement of child health** through increased vaccine availability, safety, efficacy, effectiveness, and/or reduced cost.
- **Development of a framework** that can be used by the global health community to identify, prioritize, and deprioritize opportunities to apply new vaccine technologies to vaccines.
- Initial recommendations for advancement of **paired vaccines and technologies**.

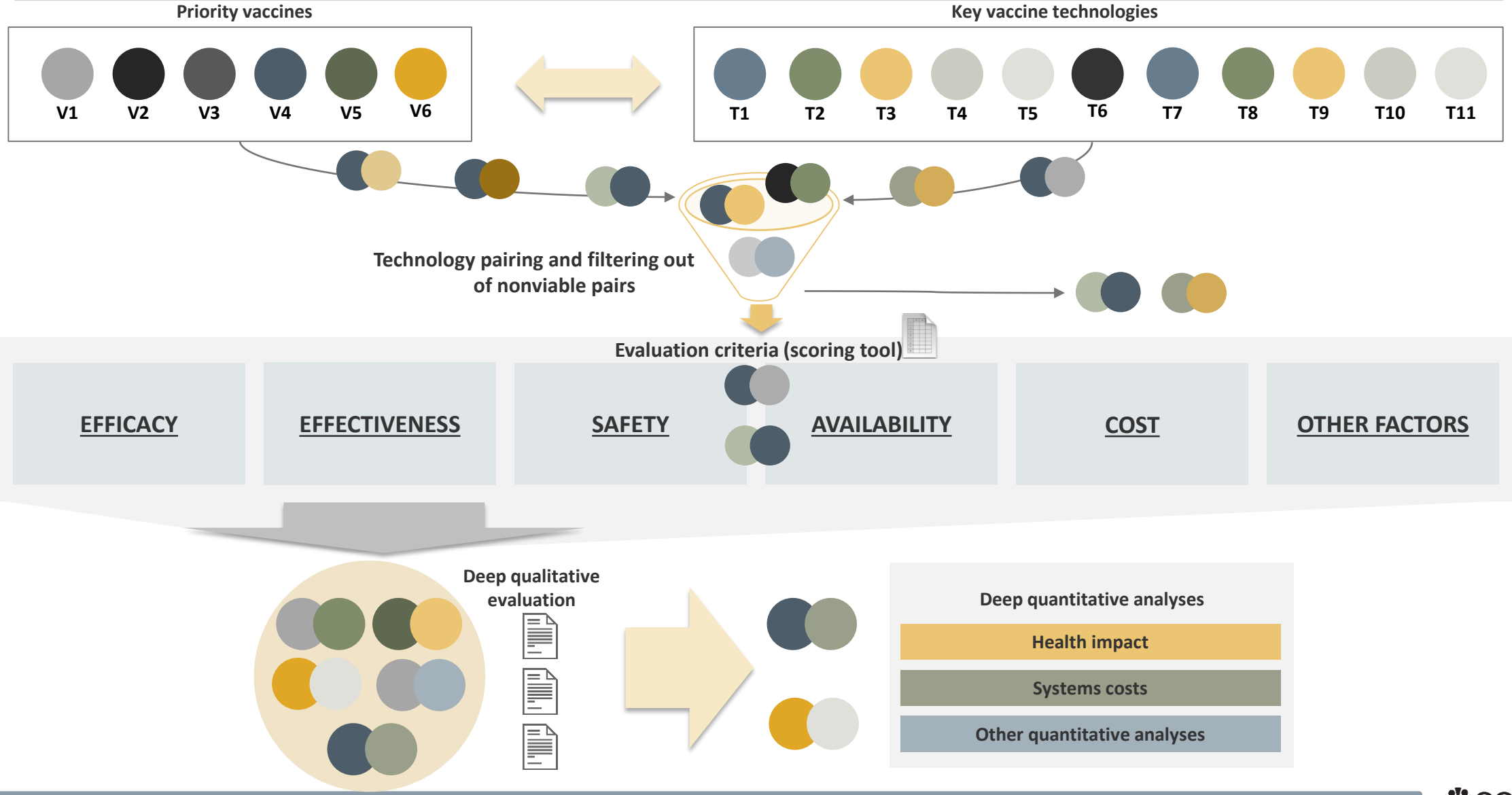
Approach

- Leverage extensive prioritization and landscaping efforts previously undertaken by leading global health organizations to **create an initial set of vaccines and technologies for evaluation**.
- Evaluate **priority vaccines against vaccine technologies** using evaluation criteria that reflect the key ways in which the technologies can improve the vaccine.
- Select **priority pairings** of vaccines and vaccine technologies for further evaluation and advancement.

Benefits

- Inform **investment decision-making**.
- Provide guidance to vaccine technology developers and industry to **inform development priorities**.
- **Deprioritize** technologies.

Technology prioritization: Overview



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Technology prioritization: Priority vaccines

	BMGF*	Gavi**	WHO†	PDVAC††
Existing schedule				
Bivalent oral poliovirus (bOPV 1&3)			✓	
Measles (second dose)		✓		
Pentavalent**	✓	✓	✓	
Trivalent oral poliovirus (tOPV)			✓	
Yellow fever		✓	✓	
Diphtheria, tetanus, whole-cell pertussis (DTwP)			✓	
New introductions				
Human papillomavirus (HPV)**	✓	✓		
Inactivated poliovirus vaccine (IPV)**	✓	✓	✓	
Japanese encephalitis	✓	✓		
Measles-rubella	✓	✓	✓	
Meningitis A	✓	✓		
Pneumococcal conjugate vaccine (PCV)	✓	✓	✓	
Rotavirus (live attenuated oral vaccine)	✓	✓	✓	
Candidate vaccines				
Cholera	✓	✓		
Dengue	✓			
Enterotoxigenic *Escherichia coli*, *Shigella*, norovirus				✓
Group A and B streptococcus				✓
Malaria	✓			
Maternal influenza	✓			
Respiratory syncytial vaccine				✓
Typhoid fever	✓			

Notes: *BMGF priorities based on discussions with Foundation personnel, published materials, and public funding priorities. **Gavi has indicated that these vaccines are part of its vaccine road maps; see also http://www.gavi.org/about/strategy/vaccine-investment-strategy/. †WHO indicates the list of vaccines it prioritizes for prequalification filings. ††http://www.who.int/immunization/research/committees/pdvac/en/.

Abbreviations: BMGF, Bill & Melinda Gates Foundation; PDVAC, Product Development for Vaccines Advisory Committee; WHO, World Health Organization.

Technology prioritization: Key technologies

Technology category	Technology examples
Packaging and presentation	Blow-fill-seal ampoule
	Dual-chamber prefilled syringe
	Dual-chamber vial
	Vial clip
Delivery	Disposable-syringe jet injectors (SC/IM)
	Cartridge-based injection devices
	Compact prefilled autodisable delivery devices
	Implants
	Disposable-syringe jet injectors (ID)
	ID needle-based (e.g., minineedle, hollow microneedles)
	Microarray (microneedle) patches
	Dry powder respiratory delivery
	Liquid respiratory delivery
	Sublingual (fast-dissolving thin film, thermoresponsive gel, fast-dissolving tablet)
Thermostability	Increase heat stability
	Increase freeze stability
	Qualify vaccine for controlled temperature chain use

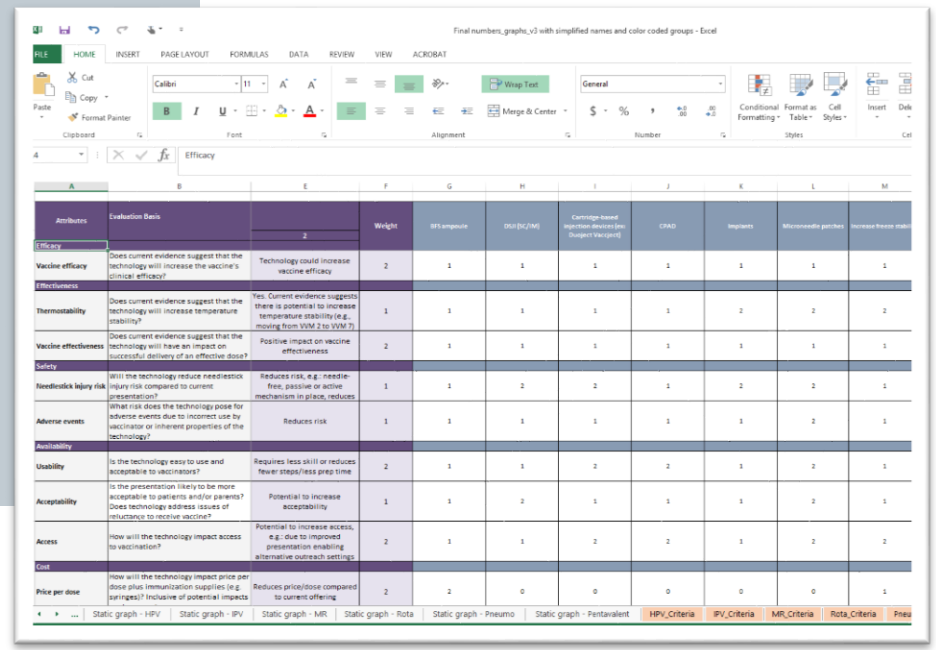
Abbreviations: ID, intradermal; IM, intramuscular; SC, subcutaneous.

Technology prioritization: Evaluation criteria

Efficacy	Reduction of disease in a vaccinated group of people compared to an unvaccinated group, assuming most favorable conditions.
Effectiveness	Ability of vaccine to reduce disease in real-world conditions.
Safety	Ability to reduce risks to patients, health care workers, and communities through use of the technology.
Availability	The ability to increase vaccine coverage by improving immunization program efficiency or facilitating campaigns or outreach.
Cost	Ability of the technology to potentially decrease systems cost.
Other Factors	Other factors that merit consideration.

Technology prioritization: Methodology

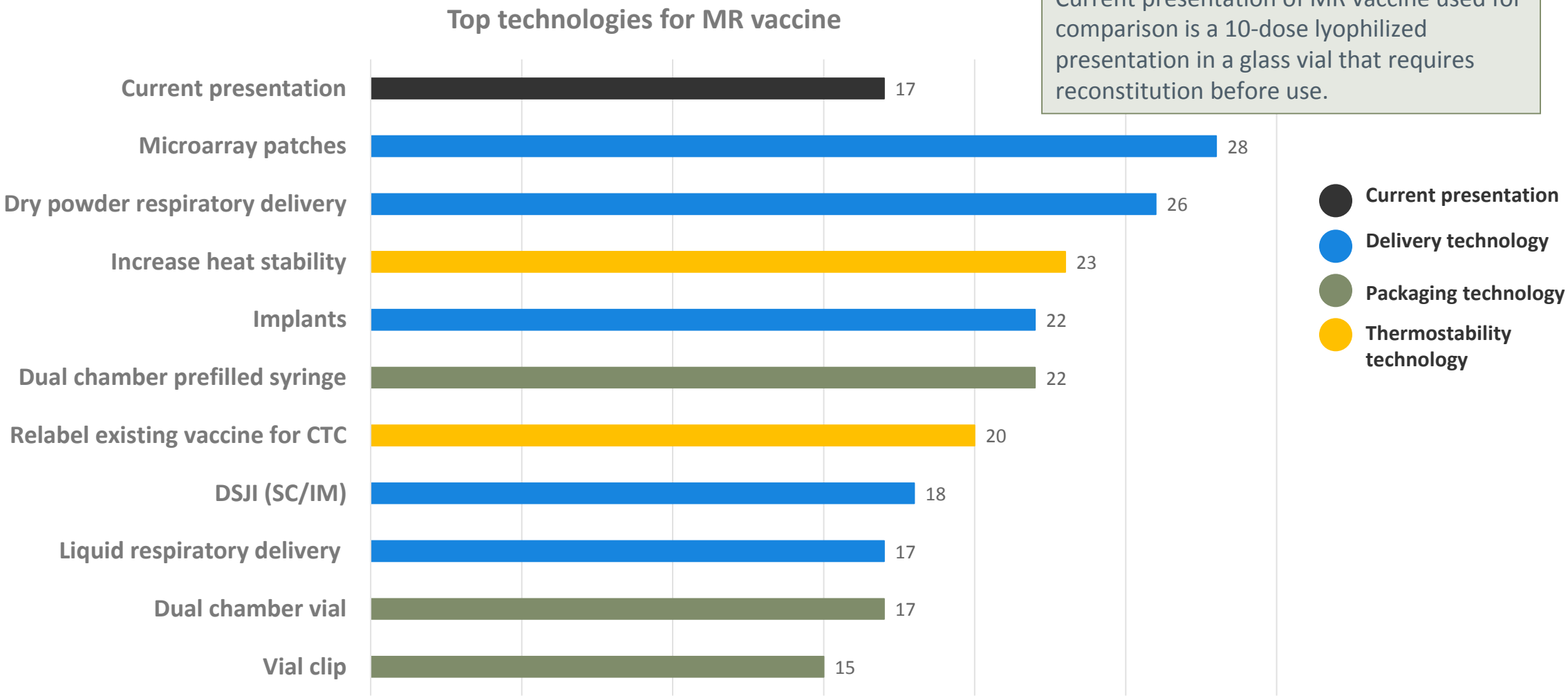
- Each vaccine technology receives weighted scores (0, 1, or 2) across each of the criteria; each criterion includes guidance to evaluate and determine a score.
- The scoring system is broken down as follows:
  - 0: suboptimal; significant issues, challenges, or drawbacks exist relative to current state.
  - 1: neutral; relative to current state.
  - 2: improves upon current state in significant ways.



Screenshot showing an example of a tab in the vaccine prioritization tool.

Technology prioritization: Measles-rubella (MR) vaccine results

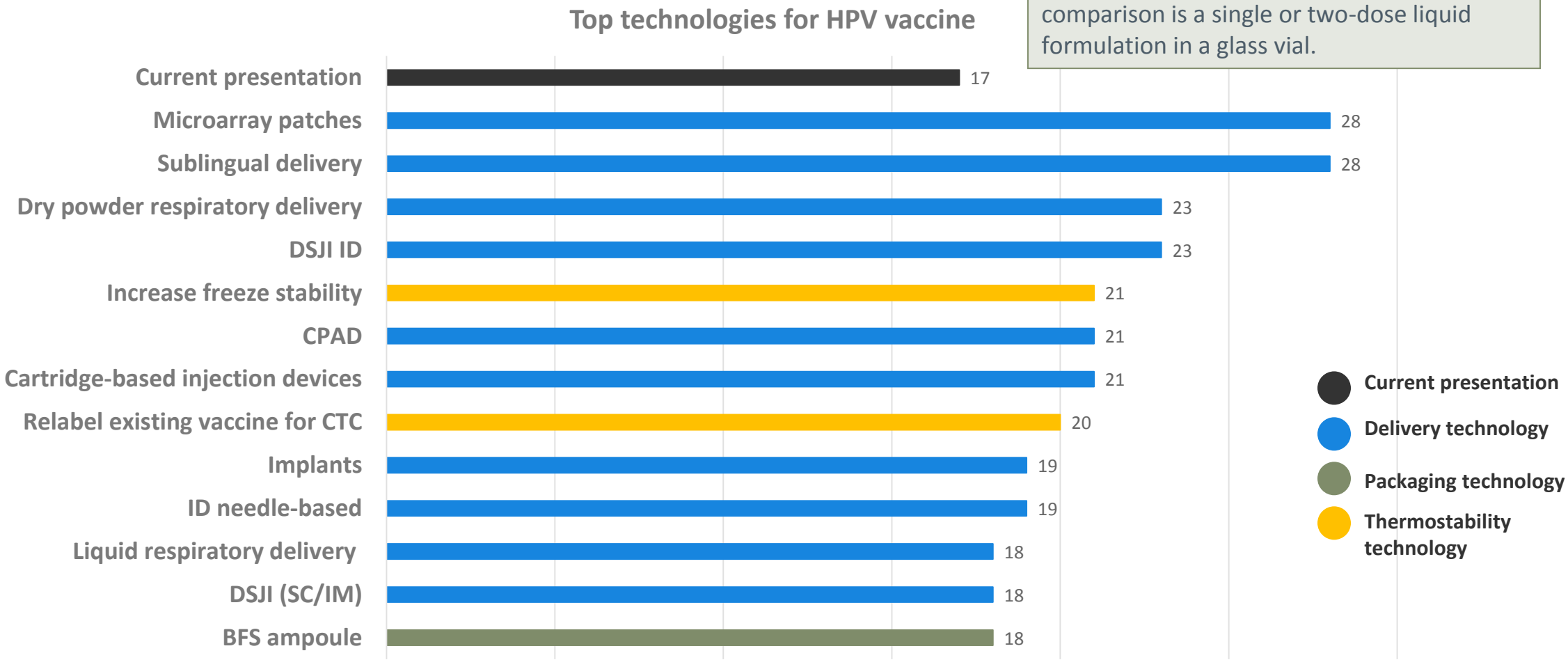
Current presentation of MR vaccine used for comparison is a 10-dose lyophilized presentation in a glass vial that requires reconstitution before use.



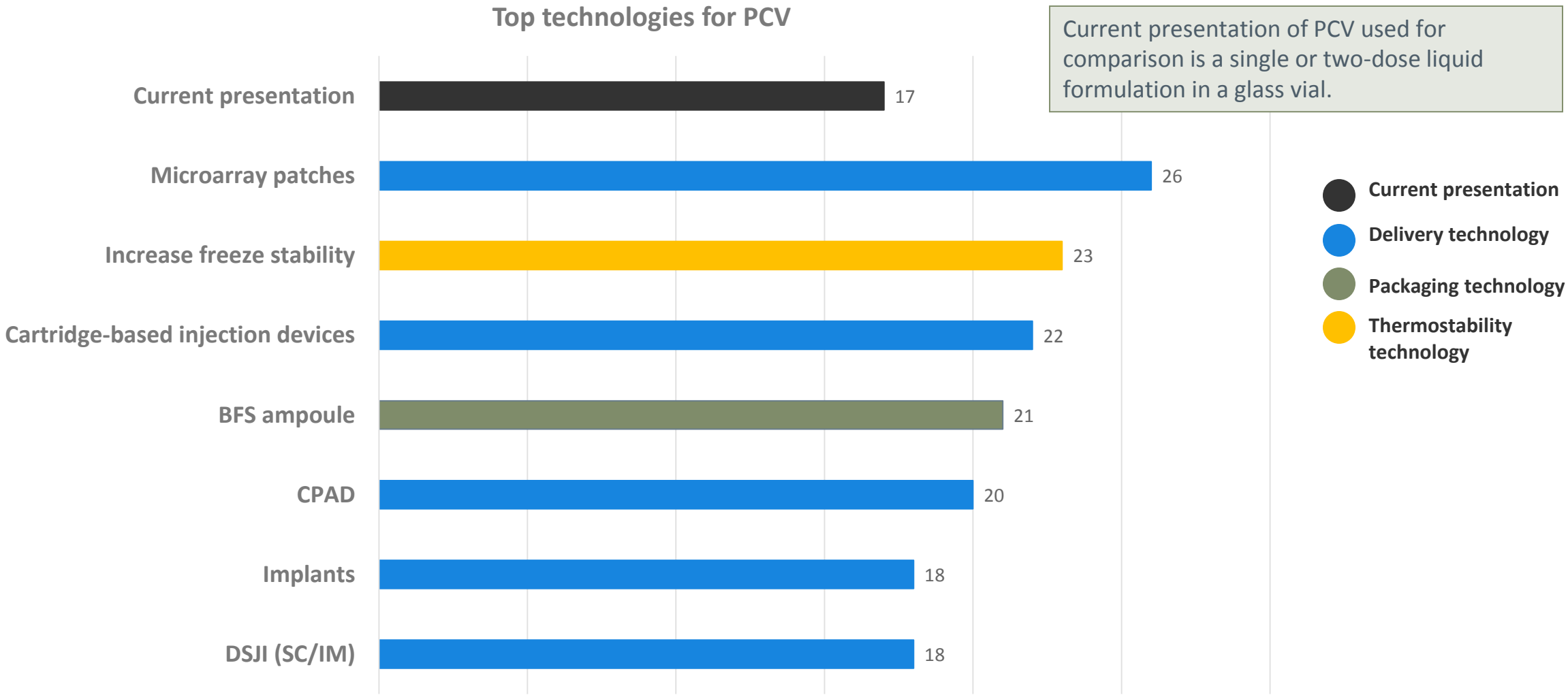
Abbreviations: CTC, controlled temperature chain; DSJI, disposable-syringe jet injectors; IM, intramuscular; MR, measles-rubella; SC, subcutaneous.

Technology prioritization: human papillomavirus (HPV) vaccine results

Current presentation of HPV vaccine used for comparison is a single or two-dose liquid formulation in a glass vial.

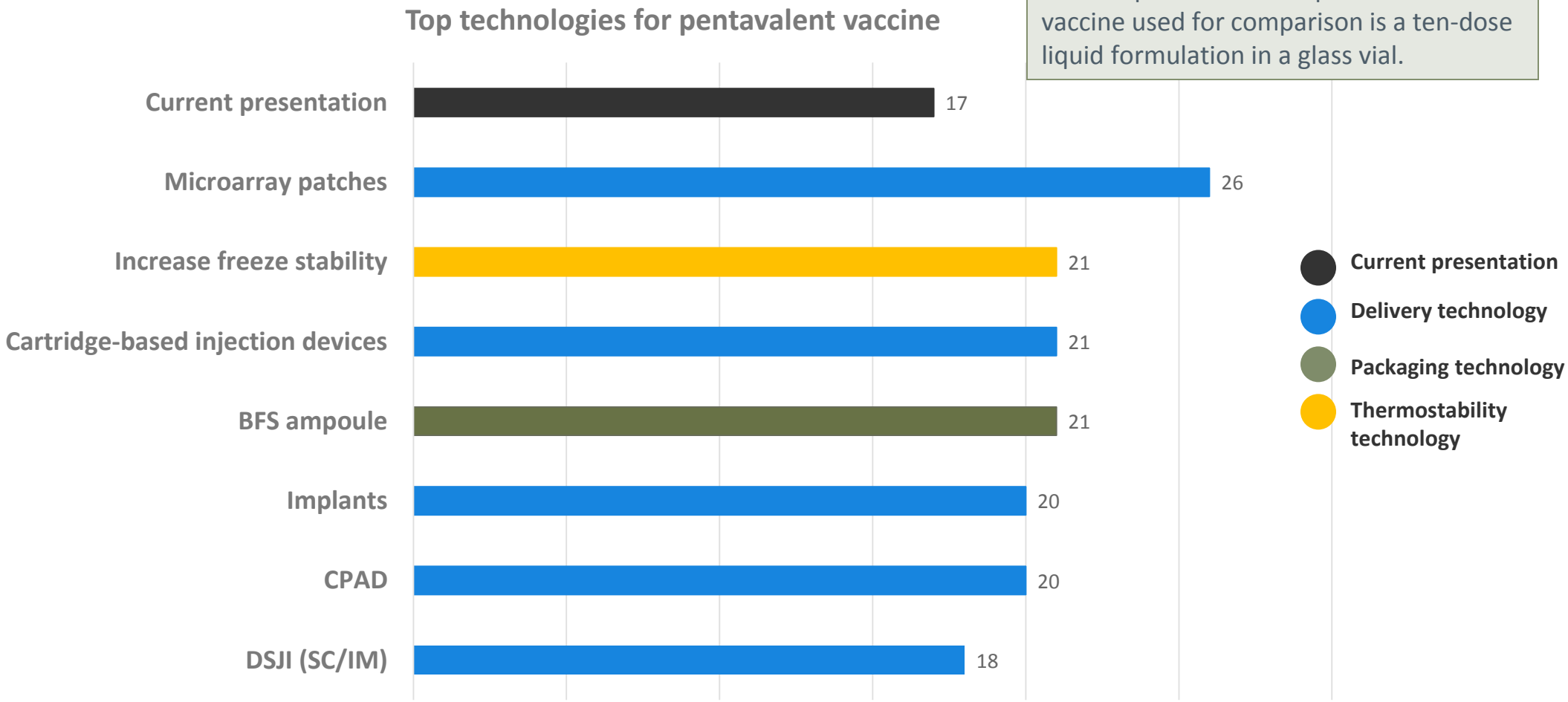


Technology prioritization: pneumococcal conjugate vaccine (PCV) results



Technology prioritization: pentavalent vaccine results

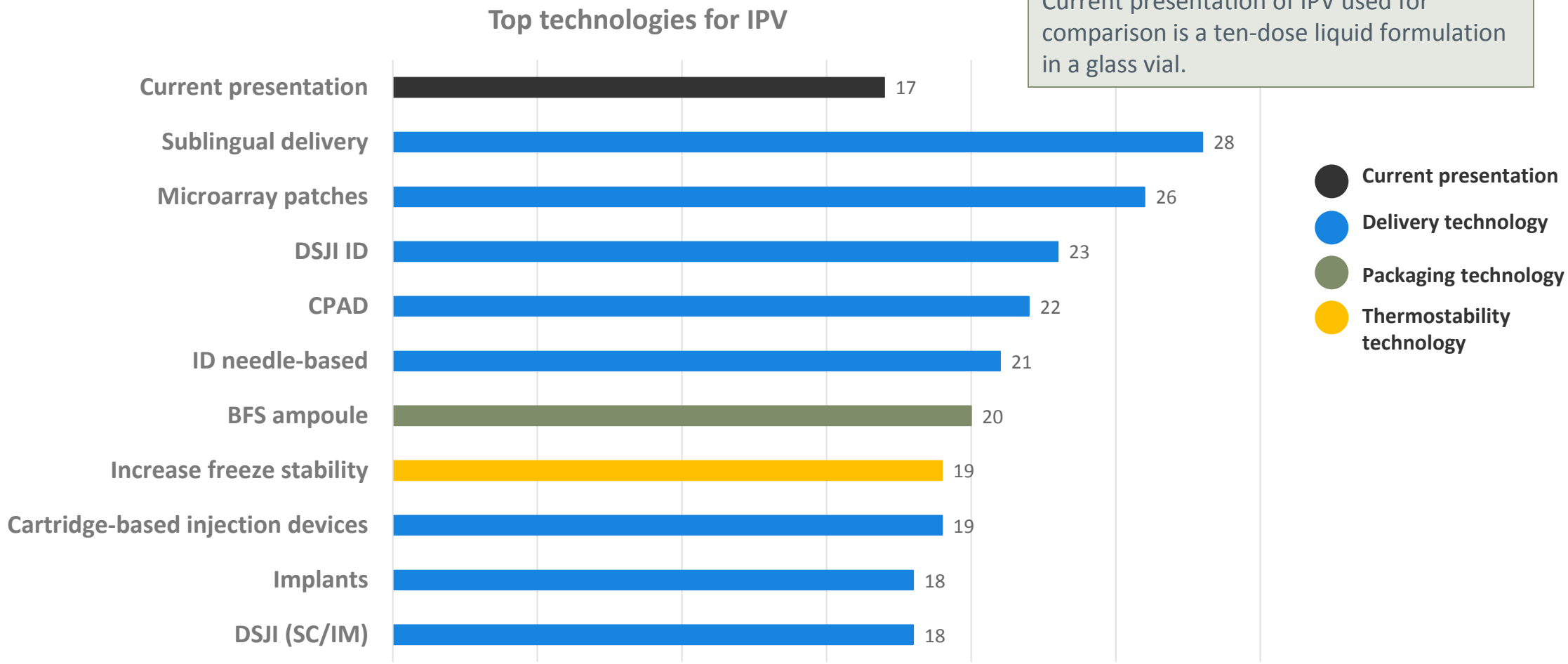
Current presentation of pentavalent vaccine used for comparison is a ten-dose liquid formulation in a glass vial.



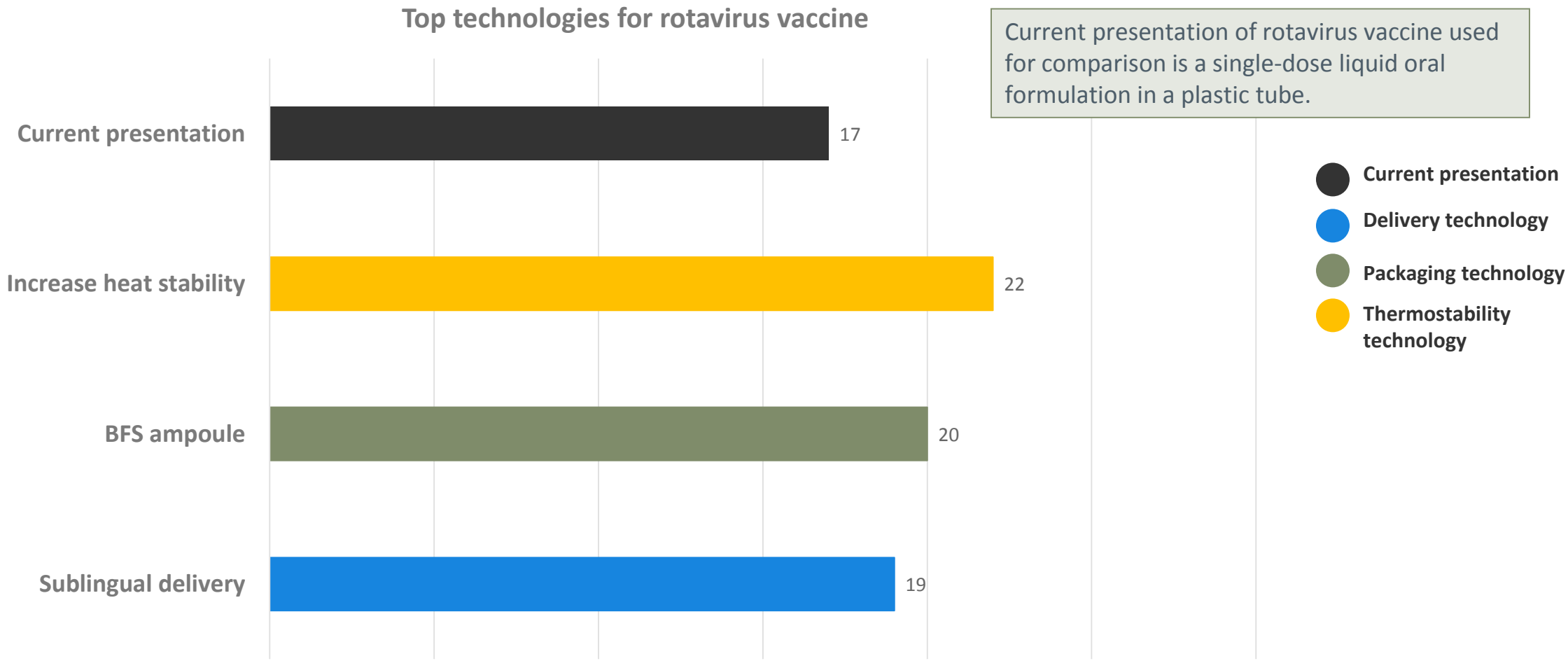
Abbreviations: BFS, blow-fill-seal; CPAD, Compact prefilled autodisable delivery devices; DSJI, disposable syringe jet injector.

Technology prioritization: inactivated poliovirus vaccine (IPV) results

Current presentation of IPV used for comparison is a ten-dose liquid formulation in a glass vial.



Technology prioritization: rotavirus vaccine results (live attenuated oral vaccine)



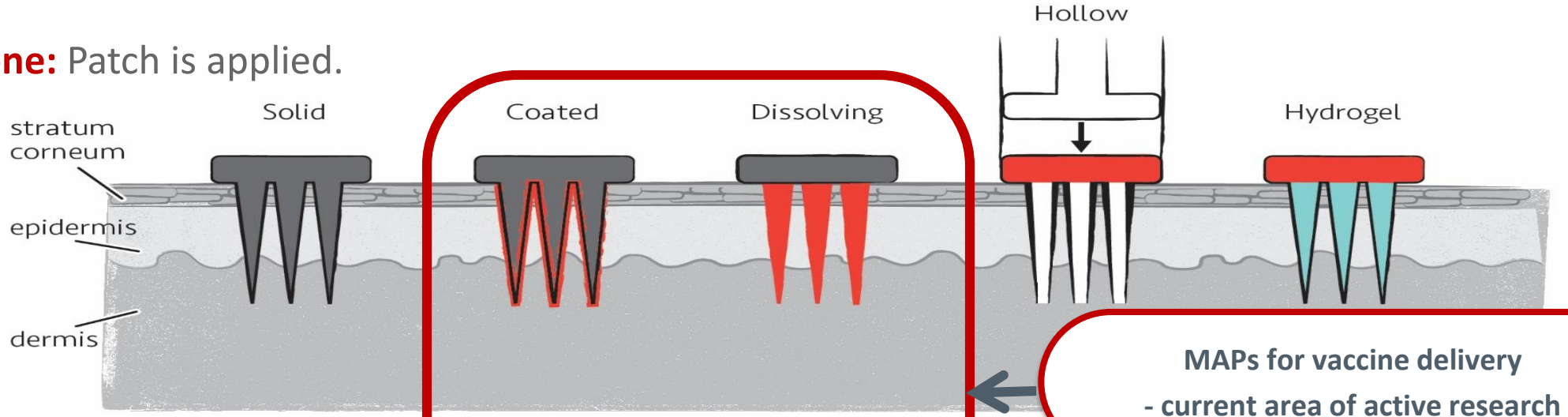
Technology prioritization: Next steps

- Technologies scoring above baseline could be considered for further investigation, starting with the top-scoring technologies.
- Conduct deep-dive qualitative evaluation of selected top-scoring pairings.
- Conduct quantitative analyses (health impact, systems costs, etc.) of selected top-scoring pairings.
- Provide recommendations and map out future strategies to advance development of most promising vaccine technology pairings.
- Identify areas where further technical feasibility analysis is needed.
- Review by the VPPAG Delivery Technology Working Group and IPAC.

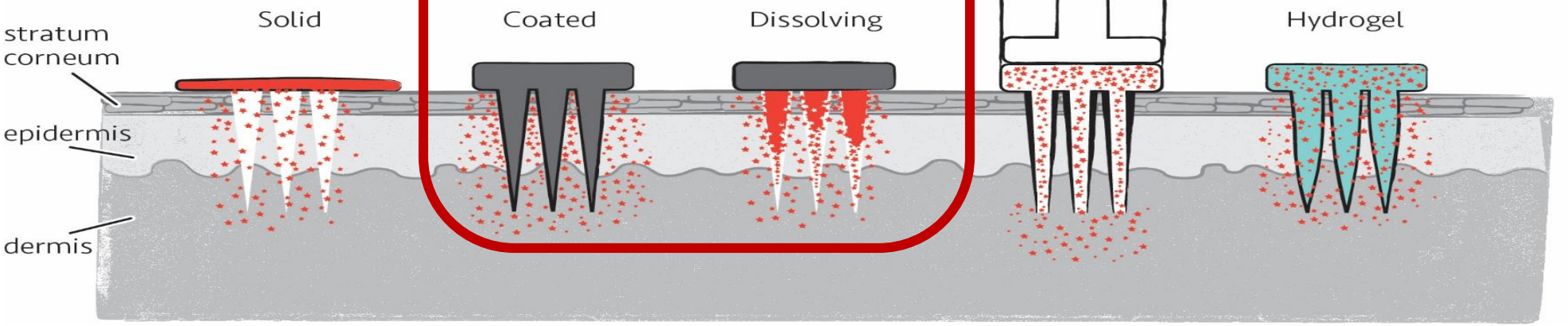
Abbreviations: VPPAG, Vaccine Presentation and Packaging Advisory Group; IPAC, Immunization Practices Advisory Committee.

Microarray patch (MAP) technologies

Step one: Patch is applied.



Step two: Vaccine is released.



MAPs for vaccine delivery
- current area of active research

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Microarray patch (MAP) technologies

Patches consist of hundreds of tiny projections that deliver solid vaccine into the skin. Some platforms require an applicator for delivery (integrated or separate).

Georgia Tech

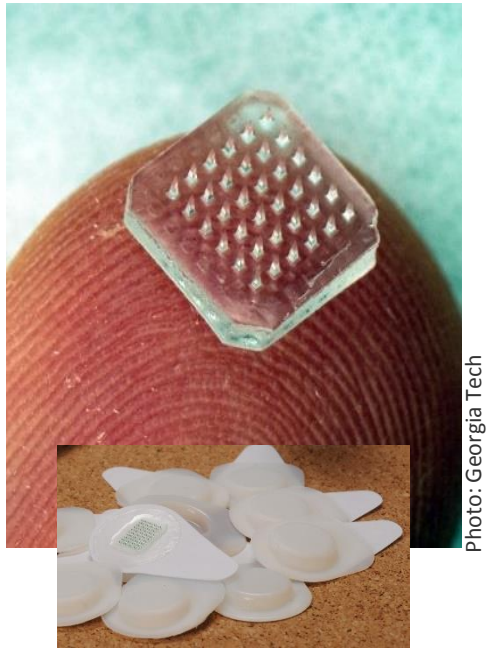

Photo: Georgia Tech

Corium (applicator)

Photo: Corium

Vaxxas Nanopatch™ (applicator)

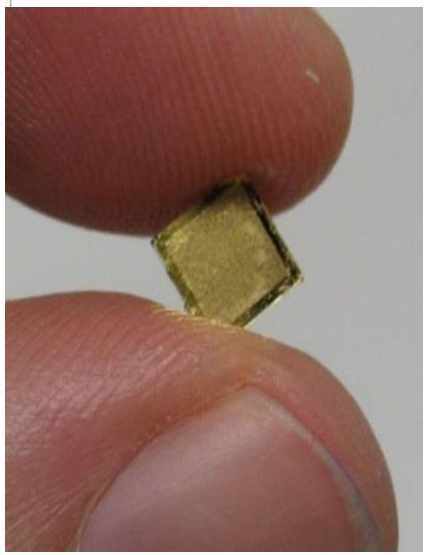

Photo: Vaxxas

THE ROLEX AWARDS FOR ENTERPRISE, MARK KENDALL, AUSTRALIA, 2012 LAUREATE
Professor Mark Kendall applies a Nanopatch to a child's hand, using his specially designed applicator.
Brisbane, Australia, 2012
RAE12MK_02-001 | ©Rolex Awards/ Julian Kingma

Dissolving microarray

Coated microarray

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MAPs: Opportunity for measles containing vaccines

Disease	Global health need	Reasons	Opportunity
Measles	• Very high vaccination coverage—95 percent—is required to interrupt and eliminate measles. • Global coverage with the measles vaccine has been stagnant at 85 percent.	• Injectable vaccines currently given in campaigns, such as measles vaccine, are generally limited to fixed-post rather than very mobile, house-to-house delivery. • Achieving high coverage has been constrained by the logistical challenges. • Vaccine wastage—hesitancy to open a multidose vial.	• Having a simple patch administered by minimally trained vaccinators could help increase vaccination coverage and achieve the goal of measles elimination.

MAPs: Potential value to global public health

	Near-term benefits	Long-term benefits
Ease of administration	Potential to be delivered by trained volunteers to expand the use in supplemental immunization (campaigns).	Depending on thermostability and regulatory acceptance, potential for at-home use for vaccines, drugs, and diagnostics.
Thermostability	Increased thermostability could allow MAPs to be removed from the cold chain for the last few days during final stages of vaccine delivery in remote areas.	Potential to be licensed for CTC use (≥ 3 days up to 40°C), with significant shelf life outside of the cold chain.
Waste disposal	Obviates need for sharps disposal. Even if sharps disposal is required, significantly reduces waste disposal quantities, logistics and risks.	No sharps disposal required.
Campaigns	House-to-house campaigns; reduces logistics and cold chain burden for all campaigns.	Enables house-to-house campaigns for most/all vaccines and reduces logistics and cold chain needs for all campaigns.
Dose-sparing	Possibility for dose-sparing, but unknown whether initial vaccines will benefit; potential for reduced costs if dose-sparing is feasible.	Potential for reduced costs through dose-sparing for most/all vaccines.

Abbreviations: CTC, controlled temperature chain.

MR MAP: Preferred product characteristics

Indication: prophylactic vaccination against measles and rubella infection of at-risk infants, children, adolescents, and young adults.

Use case: routine and SIAs including outbreak response.

Dose regimen: two vaccinations: first at 9–15 months, second at 15–18 months or up to school age.

Characteristic	Minimally acceptable target	Optimal target
Target population	9 months–young adults	Addition of ages 6–9 months
Target countries	All countries in EPI	All countries
Safety	AEs comparable to SC route of administration	AEs lower than with SC route of administration
Immunogenicity	Noninferiority with SC	Superiority with SC
Stability	Comparable to current MR (VVM 14)	Enhanced thermostability, CTC
Dosage	Similar quantity of antigen required	Reduced quantity of antigen required

Abbreviations: AE, adverse event; CTC, controlled temperature chain; EPI, Expanded Programme on Immunization (WHO); SIA, supplemental immunization activity; SC, subcutaneous; MR, measles-rubella; VVM, vaccine vial monitor.

MR MAP: Preferred product characteristics

Characteristic	Minimally acceptable target	Optimal target
Applicator	Single use, autodisable	No applicator or reusable
Packaging	Secondary packaging no more than single-dose vial of SC MR (26 cm^3)	Secondary packaging volume no more than a 10-dose vial of SC MR (3 cm^3)
Skill level	Minimal training required	No device training needed
Wear time	5 minutes for delivery	2 minutes for delivery
Delivery time	Comparable with SC administration	Reduced time compared to SC administration
Delivery indication	Design cue to confirm vaccine delivery	Same as minimum
Cost per dose delivered	Comparable to SC administration	Lower than SC administration
Disposal	Less sharps waste volume compared to SC	No sharps waste; biohazard or ordinary waste disposal

MR MAP: Current status

- Preclinical research phase — Georgia Institute of Technology*
  - Immunogenicity:
    - Measles and rubella comparable to SC.
  - Thermostability:
    - no loss of potency after 6 months at 25°C.
    - < 10-fold decrease in potency after nearly 4 months at 40°C.
- WHO MAP Product Development Workshop 2015
  - Developers, vaccine manufacturers, global public health stakeholders, regulators.
  - Challenges, resources required, strategy.

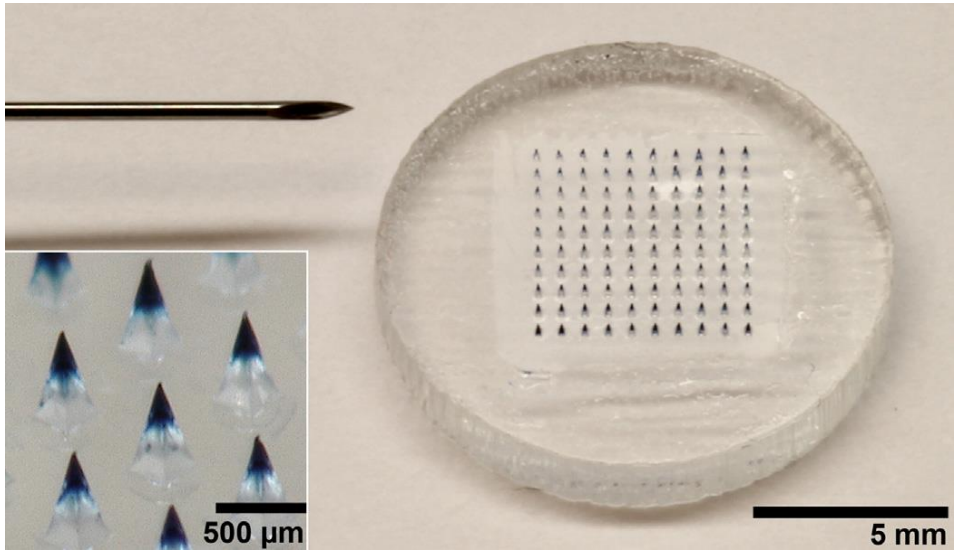

Fig. 1. Microneedle patch for measles vaccination. A microneedle patch is shown next to a 25-gauge hypodermic needle. The patch contains 100 solid microneedles made of water-soluble excipients that encapsulate measles vaccine for delivery to the skin. The inset photo shows a magnified view of the microneedles. To facilitate imaging, the microneedles encapsulated dye (trypan blue) instead of vaccine.*

*Chris Edens, Marcus L. Collins, James L. Goodson, Paul A. Rota, Mark R. Prausnitz. Measles vaccination of nonhuman primates using a microneedle patch. *Vaccine.* 2015; doi:10.1016/j.vaccine.2015.02.074.

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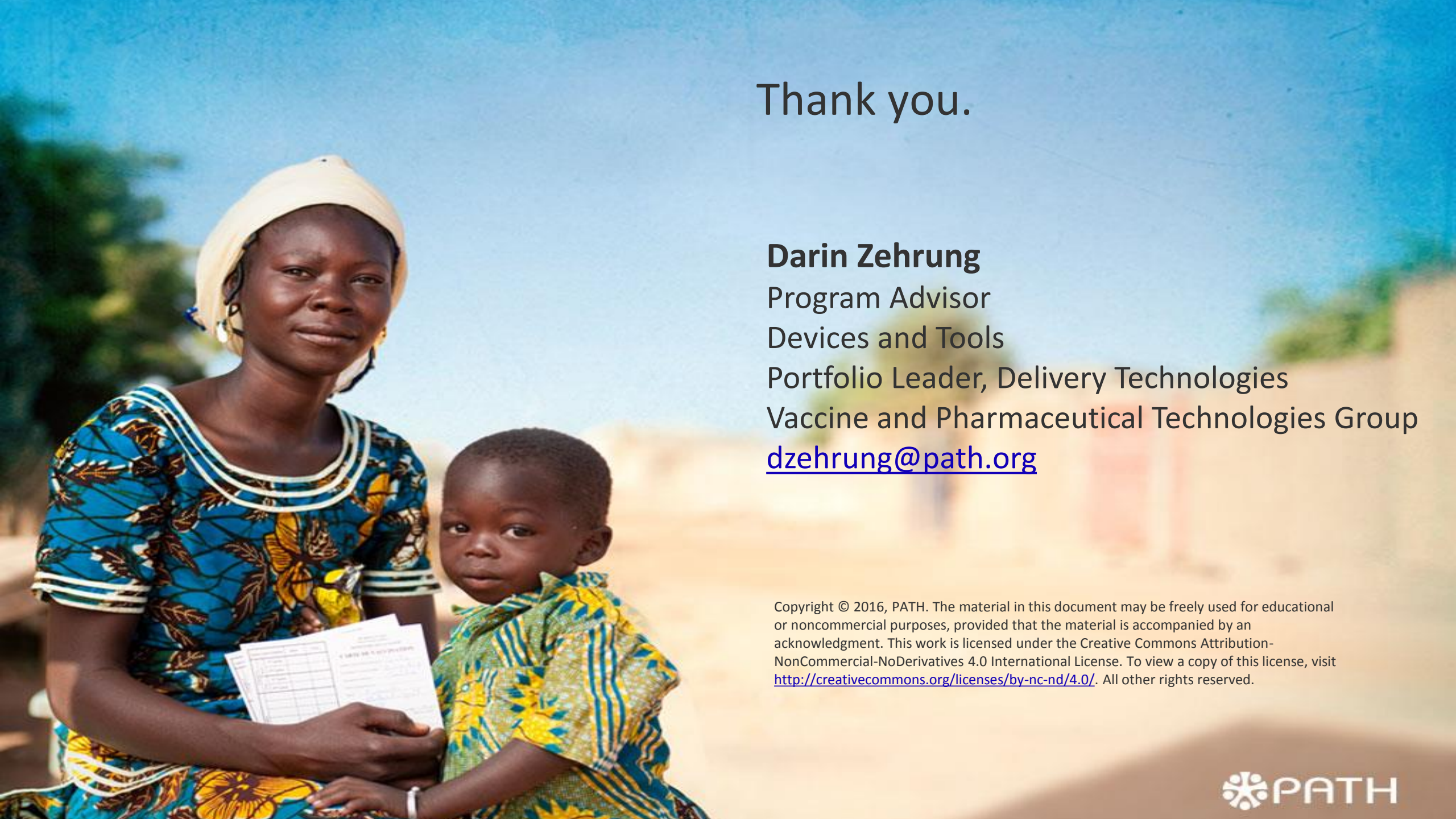

Thank you.

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