New Vaccine Delivery Technologies

Developing Country Vaccine Manufacturers Network Annual General Meeting

Buenos Aires, Argentina

Darin Zehrung – PATH

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New and alternative delivery and packaging technologies

- Improved ease of vaccine delivery, efficacy, cost-effectiveness, and safety are areas of focus.
- Impact on cold chain volume is a key consideration.
- Some are compatible with existing vaccine formats (e.g., vials or ampoules).
- Others are integrated with vaccine formulations (e.g., combination products).
- Developers include industry, academic, and nonprofit research groups.

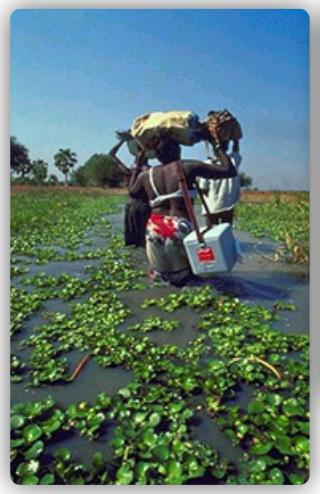


Photo: WHO

Photos: UNICEF

Microarray patch (MAP) technology

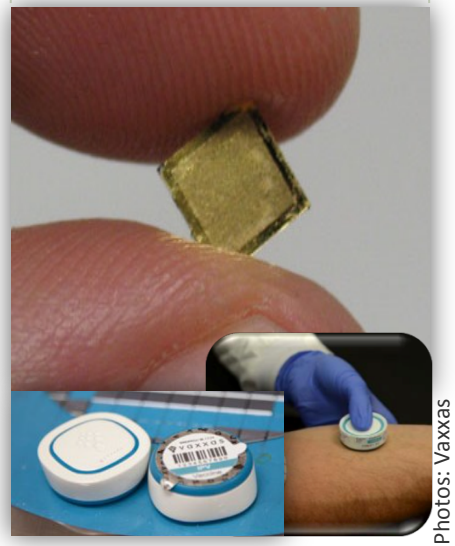
Description

- Patches consist of hundreds of tiny projections that deliver solid vaccine into the skin.
- Coated MAPs and dissolving MAPs are the leading types for vaccine delivery.
- An integrated applicator may be required to allow for consistent delivery (penetration through stratum corneum).

Status

- Research is ongoing with IPV, MR, influenza, and rotavirus vaccines.
- BMGF/WHO GPEI funding – IPV, MR (future).
- PATH manufacturing and delivery cost analysis.

Vaxxas



Photos: Vaxxas

Coated MAP

Georgia Tech

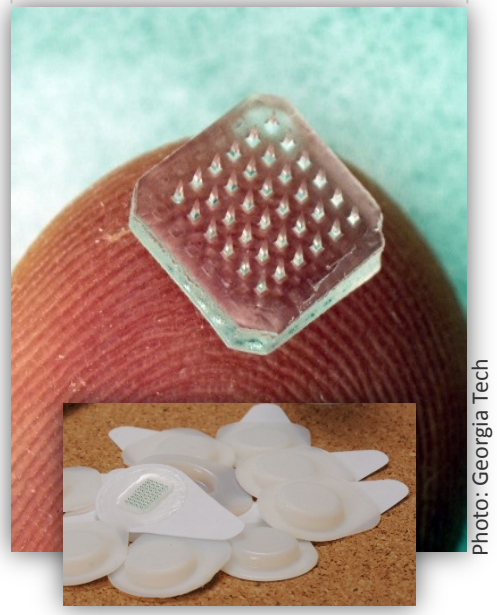


Photo: Georgia Tech

Dissolving MAP

Abbreviations: MAP, microarray patch; IPV, inactivated polio vaccine; MR, measles rubella; BMGF, Bill & Melinda Gates Foundation; WHO, World Health Organization; GPEI, Global Polio Eradication Initiative.

Microarray patch (MAP) technology considerations

Cost	• Depends on production volume and vaccine application.
Packaging	• Will require protective packaging, to protect from moisture ingress and mechanical damage to microarray projections.
Fill-finish	• Requires the development of new filling and handling equipment. • Capital equipment costs potentially high compared to other filling technologies. • Aseptic process likely required from SRA perspective (cost implication).
Formulation compatibility	• Combination product – requires integration of formulation and delivery device (formed dissolvable or coated MAP).
Programmatic	• Cold chain impact dependent on thermostability of formulation and requirement for applicator. • House-to-house campaign use possible with technology.

Abbreviations: MAP, microarray patch; SRA, Stringent Regulatory Authority.

Blow-fill-seal (BFS) technology

Description

- BFS technology is a method of producing liquid-filled containers that are formed, filled, and sealed in a continuous, automated system.
- Advanced aseptic process for packaging of sterile pharmaceutical products.

Status

- Evaluation of LAIV and rotavirus vaccine delivery has occurred with this technology.
- GSK Rotarix BFS development—MMD 5-dose conjoined strip (single VVM), 10 strips per secondary package (cold chain volume reduction).
- BMGF grants:
  - maropack AG grant (vaccine filling at BFS facility).
  - BFS for Oral or Injectable Vaccines: RFP (due Nov. 10).

Photo: rommelag

Example of BFS container with an insert (septum).

Photo: PATH

PATH/Rommelag MMD BFS design for oral delivery.

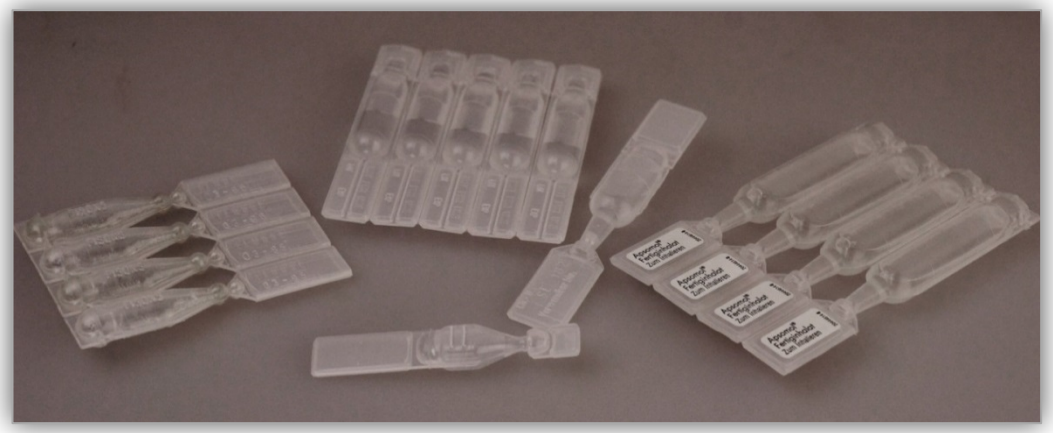


Photo: rommelag

Examples of small-volume containers with relatively large labeling tabs.

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Abbreviations: BMGF, Bill & Melinda Gates Foundation; LAIV, live attenuated influenza vaccine; GSK, GlaxoSmithKline; MMD, multi-mono dose; VVM, vaccine vial monitor; RFP, request for proposal .

Blow-fill-seal (BFS) technology considerations

Cost	• Potential for lower per-unit cost. • Water-filled BFS containers currently available.
Packaging	• May require foil pouch to protect from oxygen or volume loss (water vapor transmission).
Fill-finish	• Requires new filling equipment, or purchasing from supplier/contractor. • Capital equipment costs are high compared to other filling technologies. • BFS is considered an advanced aseptic process by the FDA and can be situated in a class C environment (no need for isolators). • Testing must be conducted to ensure dosage form is not adversely affected by heat introduced during filling process.
Formulation compatibility	• Will need to determine compatibility of formulation (including adjuvant) with polymer material (generally polypropylene or polyethylene). • Only suitable for liquid presentations (currently).
Programmatic	• Easy disposal (polyolefin based). • Can be used as a delivery device as well (for oral delivery or parenterally with integrated needle design).

Abbreviations: BFS, blow-fill-seal; FDA, U.S. Food and Drug Administration.

Polymer tube (injection molded) technology

Photo: PATH

A single Lameplast tube.

Photo: Merck

Photo: WHO

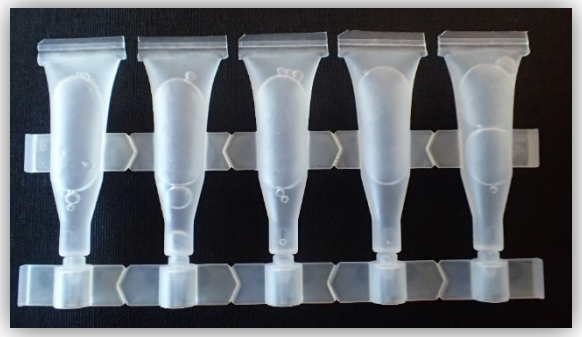

Photo: PATH

Lameplast tubes in strip format.

Photo: Eubiologics

Euvichol® (oral cholera)

Description

- Injection-molded tubes such as those produced by Lameplast and Rexam are generally made from polyethylene or polypropylene in either single units or strips.
- Tubes are left open at the end opposite the nozzle for filling. A heat-sealing step closes the tube after filling.
- Used for Merck RotaTeq® and GSK Rotarix® vaccines.

Status

- Rotavirus and cholera manufacturers adopting tube technology.
- Lameplast currently developing lower cold chain volume design (reduced spacing between tubes).

Abbreviation: GSK, GlaxoSmithKline.

Polymer tube (injection molded) technology considerations

Cost	• Low cost. • Water-filled, injection-molded containers are currently available.
Packaging	• May require pouching to protect from oxygen or loss of solvent.
Fill-finish	• Requires new filling equipment, and purchasing sterile, empty containers from supplier/contractor. • Filling equipment is relatively low cost and does not have a large footprint. • Various container shapes and sizes are possible.
Formulation compatibility	• Will need to determine compatibility of formulation with polymer material (generally polypropylene or polyethylene).
Programmatic	• Easy disposal. • Can be used as a delivery device as well (for oral delivery).

Reconstitution technology

Description

- Improve the ease and safety of delivering reconstituted vaccines and pharmaceuticals by physically integrating the dry product and the diluent.
- Some integrated reconstitution technologies also include a delivery feature, while others require use of a separate syringe for delivery.

Status

- Technologies in use for pharmaceuticals, others are still in development. Examples include:
  - Act-O-Vial®: Pfizer's Solu-Cortef and Solu-Medrol (glucocorticoids).
  - Dual chamber frangible seal (Hilleman Laboratories – rotavirus vaccine).
  - Neopac Fleximed® Easymix (laminate film).

Container type	Examples
Dual-chamber vials	 Photos: PATH Eulysis Single Vial System  Photos: PATH Pfizer Act-o-Vial®
Dual-chamber prefilled syringe or cartridge	 Photos: Vetter Vetter Lyo-ject® (Ompi)  Photos: LyoGo LyoGo
Dual-chamber (or three-chambered) frangible seal: polymer tubes or device	 Photos: PATH Aktivax  Photos: Neopac Neopac Fleximed® Easymix

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Reconstitution technology considerations

	Dual-chamber vials	Dual-chamber prefilled syringe or cartridge	Dual-chamber frangible seal: foil sachet, polymer or device
Cost	• Integrated reconstitution devices are generally more expensive than liquid-only presentations.		
Packaging	• Generally made from glass (impermeable) and elastomer to separate components. SVS uses a polymer cup.	• Glass (impermeable) with elastomer stoppers.	• Tubes made from polymers (semipermeable). Neopac tubes use laminated film (PP/SiOx/ Aclar(PCTFE)/PP). • Pouches utilize foil/laminate.
Fill-finish	• May be possible to fill and lyophilize using standard equipment.	• Dry components can be lyophilized in-situ. • Ready to fill format (tub/trays - Ompi EZ-fill).	• Potentially not compatible with in-situ lyophilization (powder must be milled or spray-dried and then filled into container).
Formulation compatibility	• Similar profile to glass vials.	• Similar profile to glass vials.	• Need to confirm compatibility with container components/ materials.
Programmatic	• Reduces the number of separate components supplied and logistical complexity. • Can simplify reconstitution (mixing) process and reduce risk of errors. • Cold chain volume may increase compared to separate containers for liquid and dry powder.		

Abbreviation: SVS, single vial system; PP, polypropylene; SiOx, silicon oxide; PCTFE, polychlorotrifluoroethylene (Aclar)

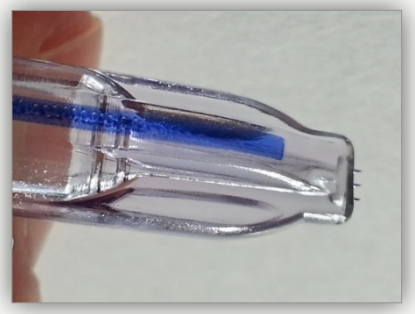
Intradermal delivery technology

Description

- Increased ease of use for ID delivery by HCWs (compared to Mantoux).
- Enables use of fractional doses of vaccine (e.g., IPV).
- Potential for house-to-house delivery (campaigns).
- Compatible with existing vaccine vial/ ampoule presentation—no reformulation.

Status

- Tropis – WHO prequalification.
- Polio eradication (ID fIPV):
  - ID adapter (4M units with AD syringe).
  - Tropis (5,000 injectors, 5M syringes).

Technology examples	
Intradermal adapter (West/Helm)	 Photo: PATH  Photos: West
Disposable syringe jet injector (PharmaJet Tropis)	 Photo: PharmaJet
Hollow microneedle (NanoPass MicronJet)	 Photos: NanoPass

Abbreviation: ID, intradermal; HCW, health care worker; fIPV, fractional inactivated polio virus; AD, auto-disable.

Intradermal technology considerations

	ID adapter	Disposable syringe jet injector	Hollow microneedle
Cost	• Devices are generally more expensive than AD needle and syringe delivery.		
Fill-finish	• Vial-based presentation (future potential for prefill).	• Vial-based presentation (future potential for prefill).	• Vial-based presentation (future potential for prefill).
Formulation compatibility	• Similar profile to glass vials.	• Similar profile to glass vials.	• Similar profile to glass vials.
Programmatic	• Specific to Helm AD syringe (future co-packaging).	• Storage of injectors (central or local).	• Requires pairing with low-deadspace, AD-capable syringe to minimize vaccine wastage and prevent reuse.

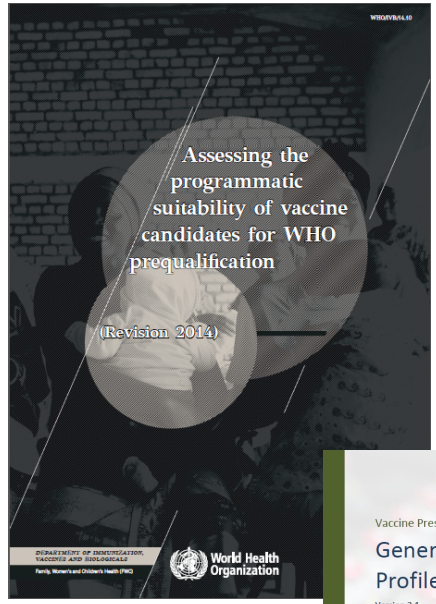
Abbreviation: AD, auto-disable.

WHO Programmatic Suitability for Prequalification (PSPQ) and Generic Preferred Product Profile (gPPP)

WHO Programmatic Suitability for Prequalification

- Defines characteristics that determine programmatic suitability of vaccine candidates for prequalification.
  - E.g., presentation, labeling, packaging.
- WHO Secretariat assesses vaccine candidates based on PSPQ guidelines.

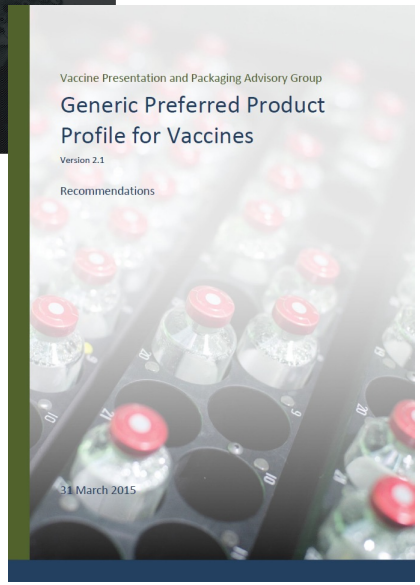
http://apps.who.int/iris/bitstream/10665/148168/1/WHO_IVB_14.10_eng.pdf?ua=1



Generic Preferred Product Profile

- The Generic Preferred Product Profile for Vaccines provides additional recommendations on formulation, presentation, packaging, and labeling of vaccines to ensure programmatic suitability in developing countries.
- Many of these consensus recommendations have been or will be integrated into the PSPQ.

http://www.who.int/immunization/policy/committees/VPPAG_Generic_PPP_and_Workplan.pdf?ua=1



Abbreviation: WHO, World Health Organization; PSPQ, Programmatic Suitability for Prequalification; gPPP, Generic Preferred Product Profile .

IPAC Delivery Technology Working Group – recent activities

- MAPs
  - Measles-Rubella preferred product characteristics / target product profile.
- Alternative prefill containers
  - BFS (vial/ampoule, integrated needle).
  - Cartridge (parenteral delivery).
- Technology evaluation tools:
  - Vaccine Technology Prioritization Framework.
  - Vaccine Technology Impact Assessment.

Photo: Georgia Tech

Photo: ©Rommelag

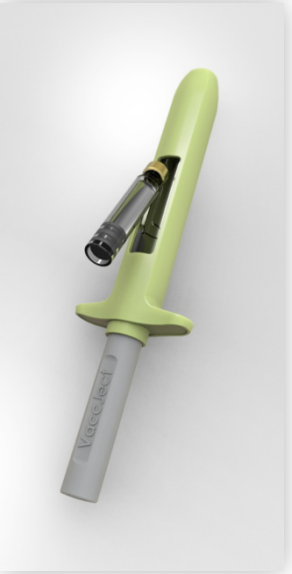


Photo: Duoject

Abbreviations: IPAC, Immunization Practices Advisory Committee; WHO, World Health Organization; MAP, microarray patch; BFS, blow-fill-seal;.

Vaccine 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**.

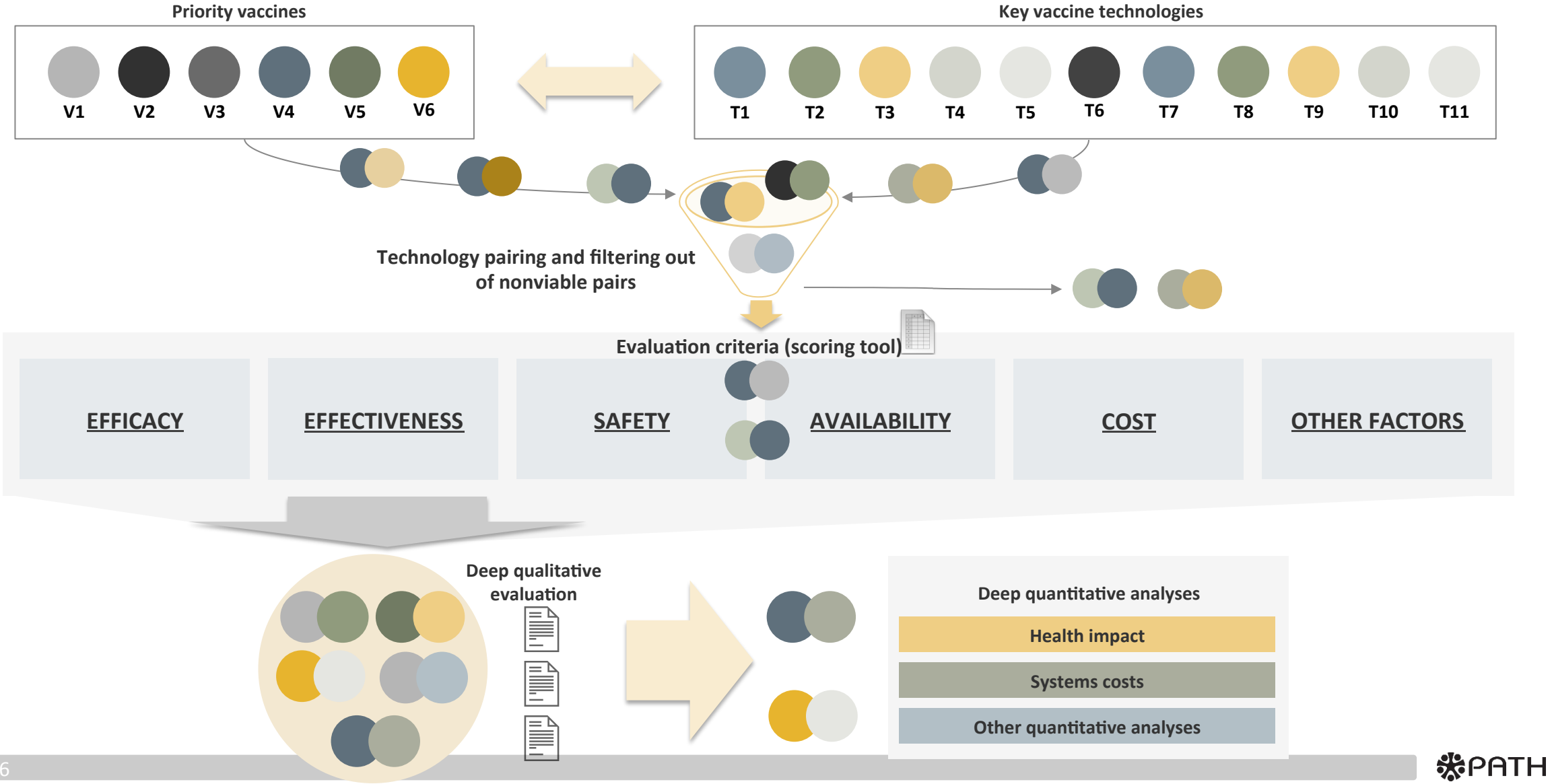
Approach

- 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 **high-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.

Vaccine technology prioritization: overview



Technology prioritization:
Vaccine Technology Impact Assessment Tool (V-TIA)

VACCINE TECHNOLOGY IMPACT ASSESSMENT TOOL

Commodity costs

* Vaccine purchase costs.
* Reconstitution and injection syringes purchase costs.
* Safety box purchase cost.

System costs

* Cold chain costs.
* Transport costs.
* Human resources costs for vaccine administration.

Health impact

* Number of children effectively immunized.
* Potential for increase in coverage.
* Potential for reduction in AEFI.

Abbreviation: V-TIA, Vaccine Technology Impact Assessment Tool (V-TIA); AEFI, adverse events following immunization.

Thank you.

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