New Vaccine Delivery Technologies
Developing Country Vaccine Manufacturers Network Annual General Meeting
Buenos Aires, Argentina

Darin Zehrung – PATH
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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.
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.
- PATH manufacturing and delivery cost analysis.

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

<table>
<thead>
<tr>
<th><strong>Cost</strong></th>
<th>Depends on production volume and vaccine application.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Packaging</strong></td>
<td>Will require protective packaging, to protect from moisture ingress and mechanical damage to microarray projections.</td>
</tr>
</tbody>
</table>
| **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. |
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).
## Blow-fill-seal (BFS) technology considerations

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

**Abbreviations:** BFS, blow-fill-seal; FDA, U.S. Food and Drug Administration.
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).
### 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:
  - Dual chamber frangible seal (Hilleman Laboratories – rotavirus vaccine).
  - Neopac Fleximed® Easymix (laminate film).

<table>
<thead>
<tr>
<th>Container type</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual-chamber vials</td>
<td>Eulysis Single Vial System, Pfizer Act-o-Vial®</td>
</tr>
<tr>
<td>Dual-chamber prefilled syringe or cartridge</td>
<td>Vetter Lyo-ject® (Ompi), LyoGo</td>
</tr>
<tr>
<td>Dual-chamber (or three-chambered) frangible seal: polymer tubes or device</td>
<td>Aktivax, Neopac Fleximed® Easymix</td>
</tr>
</tbody>
</table>
# Reconstitution technology considerations

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

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

- Disposable syringe jet injector (PharmaJet Tropis)

- Hollow microneedle (NanoPass MicronJet)

Abbreviation: ID, intradermal; HCW, health care worker; fIPV, fractional inactivated polio virus; AD, auto-disable.
<table>
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<th></th>
<th>ID adapter</th>
<th>Disposable syringe jet injector</th>
<th>Hollow microneedle</th>
</tr>
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<tbody>
<tr>
<td><strong>Cost</strong></td>
<td>• Devices are generally more expensive than AD needle and syringe delivery.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fill-finish</strong></td>
<td>• Vial-based presentation (future potential for prefill).</td>
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<tr>
<td><strong>Programmatic</strong></td>
<td>• Specific to Helm AD syringe (future co-packaging).</td>
<td>• Storage of injectors (central or local).</td>
<td>• Requires pairing with low-deadspace, AD-capable syringe to minimize vaccine wastage and prevent reuse.</td>
</tr>
</tbody>
</table>
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](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.

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.
# 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

- **Evaluation criteria (scoring tool)**
  - **Efficacy**
  - **Effectiveness**
  - **Safety**
  - **Availability**
  - **Cost**
  - **Other factors**

- **Priority vaccines**
  - V1, V2, V3, V4, V5, V6

- **Key vaccine technologies**
  - T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11

- **Technology pairing and filtering out of nonviable pairs**

- **Deep qualitative evaluation**

- **Deep quantitative analyses**
  - Health impact
  - Systems costs
  - Other quantitative analyses
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.

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

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