Novel primary containers and delivery technologies

13th International Rotavirus Symposium
August 29 – 31, 2018
Minsk, Belarus

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Program Leader, Devices & Tools
Novel Primary Container and Delivery Technologies: Market Use and Product Development Research
### Current rotavirus vaccine delivery and packaging

<table>
<thead>
<tr>
<th>Company</th>
<th>Vaccine Name</th>
<th>Description</th>
<th>Doses per course</th>
<th>VVM</th>
<th>Cold chain volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bharat</td>
<td>ROTAVAC</td>
<td>Frozen liquid in a 1, 5, or 10 dose glass vial. Vaccine delivered using an oral poliovirus vaccine (OPV) dropper affixed to the vial after opening (5 x 0.1-mL drops).</td>
<td>3</td>
<td>VVM2</td>
<td>~3 cm³ per dose</td>
</tr>
<tr>
<td>Merck</td>
<td>RotaTeq®</td>
<td>All-in-one liquid vaccine. Preformed single-dose LDPE tube in individual foil pouch</td>
<td>3</td>
<td>No VVM</td>
<td>46.3 cm³ per dose</td>
</tr>
<tr>
<td>GSK</td>
<td>Rotarix®</td>
<td>All-in-one liquid vaccine. Preformed single-dose LDPE tube loose in cardboard carton</td>
<td>3</td>
<td>VVM14</td>
<td>17.1 cm³ per dose</td>
</tr>
</tbody>
</table>
Polymer tube/preformed technology

Description

• Preformed 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 provides closure after filling.

• CPAD preformed technology: BD Uniject™.

Technology status – vaccines

• Preformed tubes used for Merck RotaTeq® and GSK Rotarix® WHO prequalified vaccines.

• Bio Farma – Uniject™ market use for hepatitis B vaccine (WHO prequalified).

• Serum Institute of India (rotavirus), EuBiologics (cholera), and other manufacturers have adopted the tube container.

• Lameplast is currently developing lower cold chain volume design (reduced spacing between tubes).

Abbreviations: CPAD, compact prefilled auto-disable device; WHO, World Health Organization.
Blow-fill-seal technology

Description

- Blow-Fill-Seal (BFS) technology is a method of producing liquid-filled containers that are formed, filled, and sealed in a continuous, automated system.
- It is an advanced aseptic process for packaging sterile pharmaceutical products.

Technology status – vaccines

- 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).
- Global Good design: low cold chain volume ampoule.
- Maropack: BFS filling feasibility (BMGF supported).

Abbreviations: BMGF, Bill and Melinda Gates Foundation; CPAD, compact prefilled auto-disable device; LAIV, live attenuated influenza vaccine; MMD, multi-monodose; VVM, Vaccine Vial Monitor.
ApiJect BFS

Phase 1 – BFS Container + Needle Hub
Factory pre-attached

Inkjet expire date and lot number on back side
Press bubble to inject vaccine
Sterile gas such as Nitrogen
One-way AD valve prevents refill or drawback

Multi-fold drug label required information. Vaccine Vial Monitor on back side
All plastic elements. Filled via low-heat BFS process
Vaccine/antigen reservoir (storilo fill) 0.1 mL to 3.0 mL
K6 Needle Hub field-attached or pre-attached

Phase 2 – BFS Container + Needle Hub + RFID
Factory pre-attached

Drug label booklet on top of NFC chip
NFC chip is embedded at time of manufacture. Unique electronic ID #

Abbreviations: AD, auto-disable; BFS, blow-fill-seal; NFC, Near Field Communications; RFID, Radio-Frequency Identification
Novel primary containers and delivery technologies

Next Generation Packaging + Delivery Technologies: Vaccine Research and Development
Integrated reconstitution technology

Description

- Improves the ease and safety of delivering reconstituted vaccines and pharmaceuticals by physically integrating the dry product and the diluent.

Technology status – vaccines

Hilleman Laboratories’ IRAD.

- Dual-chamber, frangible-seal reconstitution technology for oral delivery.
- Heat-stable rotavirus vaccine with potential for CTC/outside cold chain use (4 months at 45°C).
- Human factors evaluation of IRAD design (India).
- Completion of Phase I/II (adults/infants) study: International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b).


https://www.gatesfoundation.org/How-We-Work/General-Information/Grant-Opportunities/Dual-Chamber-Injection-Device-RFP
Transdermal microarray patches (MAPs) for pharmaceutical delivery

Description

- Patches consist of tiny projections that deliver solid vaccine into the skin. Some platforms require an applicator for delivery (integrated or separate).
- Potential for enhanced thermostability (CTC use) and controlled release delivery (schedule reduction).

Technology status – vaccines + drugs

- IPV, MR, influenza, rotavirus, tetanus toxoid, and other vaccines evaluated.
- Essential medicines research: ARVs, contraceptives, antimalarials, antibiotics.
- Influenza clinical studies completed: presentation / publications (Georgia Tech, Vaxxas, CosMED).
- PATH and AMP field evaluations: programmatic suitability.
- WHO MR WG.
- PATH MAP Center of Excellence (vaccines, essential medicines, diagnostics).
Novel Primary Container and Delivery Technologies: PATH Cost Analysis
Cost analysis: Delivery technology overview

Oral vaccine packaging
- Glass vials
  - Single-dose
  - Ten-dose
- BFS MMD ampoules
- Preformed polymer tubes

Parenteral vaccine packaging
- Glass vials
  - Single-dose
  - Ten-dose
- BFS MMD ampoules
- BFS CPAD
- Preformed CPAD

A. BFS MMD ampoules for oral vaccines;
B. Preformed polymer tube;
C. BFS CPAD;
D. Preformed CPAD;
E. 3D-printed resin model of BFS MMD ampoules for parenteral vaccines;
F. Glass vials (left to right: 2R/31 mm single-dose vial for oral and parenteral vaccines, 4R ten-dose vial for parenteral vaccine, and 20R ten-dose glass vial for oral vaccines).


Abbreviations: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.
Cost of good sold: Rotavirus vaccine

Abbreviations: BFS, blow-fill-seal; MMD, multi-monodose.
Total cost of delivery: Rotavirus vaccine

Abbreviations: BFS, blow-fill-seal; MMD, multi-monodose.
Cost of good sold: Inactivated poliovirus vaccine

Abbreviations: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.
Abbreviations: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.
Summary of COGS and cold chain analysis

- The manufacturing cost for **single-dose BFS** is US$0.20; for **BFS MMD** the cost per dose is $0.18.
- Manufacturing cost per dose for a **10-dose glass vial** is $0.14.
- **MMD packaging improved the packing efficiency** from the single container of BFS by a factor of 1.5.
- Addition of a foil overwrap could **more than double the cold chain volume of prefilled devices**.
- When the vaccine wastage and cold chain costs are included, **BFS MMD and 5-dose glass vials are the lowest-cost packaging types**.

Abbreviations: BFS, blow-fill-seal; COGS, cost of goods sold; MMD, multi-monodose.
# Acknowledgments

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<th>Duff and Phelps</th>
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<td>Stefanie Perella</td>
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<td>Marc Koska</td>
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<td>Jeff Sedita</td>
<td>Michael Berbari</td>
<td>Robyn Iqbal</td>
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<td>Matt Morio</td>
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<tr>
<td>Annie Rein-Weston</td>
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Thank you

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