Overview and status of novel primary containers

Developing Countries Vaccine Manufacturers Network

8th Annual General Meeting—Vaccines: Inspiring Innovation

September 25–28, 2017, Seoul, South Korea

Darin Zehrung, PATH

September 25, 2017
Novel Primary Container and Packaging Technologies: Product Development Research and Market Use
Adopting new container technology for low and middle income vaccine markets

- **Formulation suitability and compatibility**
  - Container + manufacturing process

- **Manufacturing scale readiness**
  - Further development required? (investment/time?)

- **Manufacturing and product costs**
  - Cost competitive?

- **Market introduction and use**
  - Time required to reach market/return on investment
  - Product differentiation?
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 and tetanus toxoid vaccines (WHO prequalified).

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

• Lameplast is currently developing lower cold chain volume design (reduced spacing between tubes).
Blow-fill-seal technology

Description

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.

apiject-Rommelag collaboration: parenteral injection–capable design in development (K6 Apiject CPAD).

Maropack/GSK: BFS filling feasibility.
0.5 ml

insert instructions
**BFS trial filling: Maropack and GSK**

**HOW WE WORK**

**GRANT**

**Maropack AG**

**Date:** March 2016

**Purpose:** to explore the value proposition and technical feasibility of blow-fill-seal for oral and injectable vaccines (IPV, Penta, HPV, PCV, Rota and Cholera), including other pipeline vaccines in development

**Amount:** 8715,780

**Term:** 23

**Topic:** Family Health: Nutrition, Vaccine Development

**Program:** Global Health

**Grantee Location:** Zell Lu

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**Abbreviations:** BFS, blow-fill-seal; GMP, good manufacturing practice; GSK, GlaxoSmithKline; HPV, human papillomavirus; IPV, inactivated poliovirus vaccine; PCV, pneumococcal conjugate vaccine; penta, pentavalent vaccine; rota, rotavirus.

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**Images:** GSK.
Novel Primary Container and Packaging Technologies: PATH Cost Analysis
Cost analysis: Delivery technology overview

Abbreviations: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.

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).

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
Cost of good sold: Rotavirus vaccine

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

Abbreviations: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.
Next Generation Packaging + Delivery Technologies: Vaccine Research and Development
Glass cartridge and ampoule technology

**Description**

- Widely utilized standard primary containers (example: dental pharmaceuticals).
- Low-cost, widely available technology.
- Potential for significant reduction in cold chain volume (20% less compared to 10-dose vial).

**Technology status – vaccines**

Two manufacturers are developing platforms for application in LMICs:

- Duoject/PnuVax: for PCV-13 application.
- Stevanato Group: glass cartridge and ampoule delivery designs.

Abbreviations: LMIC, low- and middle-income country; PCV, pneumococcal conjugate vaccine.
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 (9 months at 45°C).
- Human factors evaluation of IRAD design (India).
- Phase I/II (adults/infants): International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b).

Abbreviation: CTC, controlled temperature chain; IRAD, integrated reconstitution and administration device.
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.

MR TPP: potential future WHO WG.

**Abbreviations:**
- AMP, Agence de Médecine Préventive
- ARV, antiretroviral
- CTC, controlled temperature chain
- IPV, inactivated poliovirus vaccine
- MR, measles-rubella
- TPP, target product profile
- WG, working group
- WHO, World Health Organization
Nanopatch™ with applicator

Photos: Vaxxas

INSTRUCTIONS FOR USE

1. Hold infant as shown to prevent movement
2. Identify a healthy application site (deltoid shown)
3. Remove foil seal from applicator
4. Place applicator on skin. Press centre until a click is heard
5. Leave applicator in place for 10 seconds
6. Remove applicator perpendicular to skin
7. Dispose of the applicator into safety box

IMPORTANT: This device is single use disposable
Thank you