Overview and status of novel primary containers

Developing Countries Vaccine Manufacturers Network

18th Annual General Meeting—Vaccines: Inspiring Innovation

September 25–28, 2017, Seoul, South Korea

Sarin Zehrung, PATH
September 25, 2017

Novel Primary Container and Packaging Technologies: Product Development Research and Market Use

lopting new container technology for low and middle income vaccine mark

Current vaccine market use – glass vial or ampoule (+ delivery syringe) – prefilled syringe (high income markets)

olymer tube/preformed technology

Photo: PATH

e Lameplast tube.

Photo: Merck

Photo: World Health Organization

RotaTeq® and ROTARIX tubes.

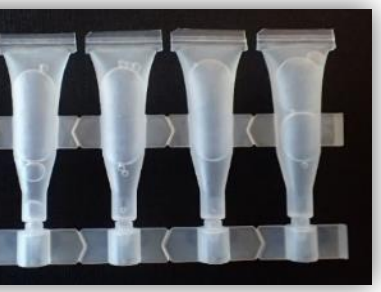


Photo: PATH

ast tubes in strip format.

Photo: EuBiologics

Euvichol® (oral cholera).

Photo: Serum Institute of India

Institute of India (rotavirus).

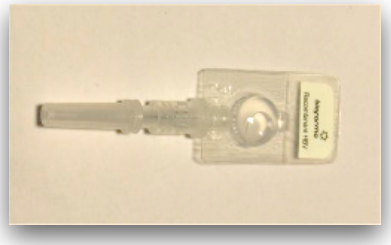


Photo: Bio Farma

Bio Farma Indonesia

Description

- Preformed tubes such as those produced by Lameplast a 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 fil A heat-sealing step provides closure after filling.
- CPAD preformed technology: BD Uniject™.

Technology status – vaccines

- Preformed tubes used for Merck RotaTeq® and GSK ROT WHO prequalified vaccines.
- Bio Farma – Uniject™ market use for hepatitis B and tet toxoid vaccines (WHO prequalified).
- Serum Institute of India (rotavirus), EuBiologics (cholera other manufacturers are adopting the tube container.
- Lameplast is currently developing lower cold chain volur design (reduced spacing between tubes).

tion: GSK, GlaxoSmithKline.

ow-fill-seal technology

scription

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.

chnology 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.

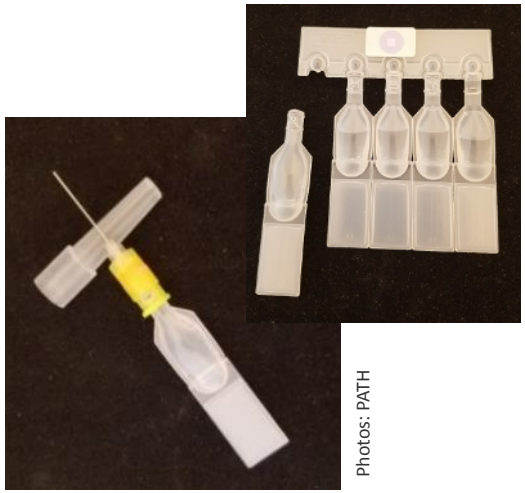
apiject-Rommelag collaboration: parenteral injection–capable design in development (K6 Apiject CPAD).

Maropack/GSK: BFS filling feasibility.

Photo: Rommelag

Example of BFS container with an insert (septum).

GSK BFS design for oral deliver



Photos: PATH

apiject single-dose parenteral injection–capable design.

Global Good ampoule desig

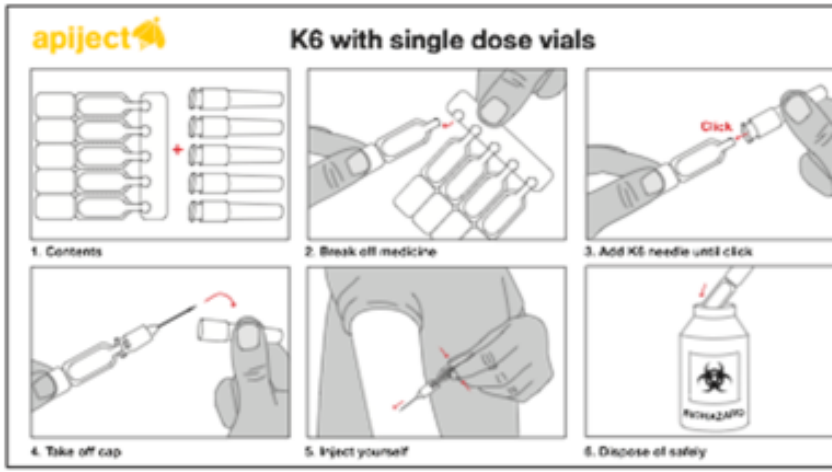
tions: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; GSK, GlaxoSmithKline; LAIV, live attenuated influenza vaccine; MMD, multi-monodose; VVM, vaccine vial monitor.

Geoff McDonald
General Manager
GSK Australia
0:01 / 2:19
CC
HD

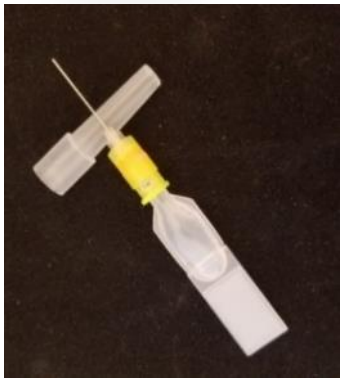
biject blow-fill-seal

insert instructions

apiject



0.5 ml



5. option 2 (health care worker giving injection)

FS trial filling: Maropack and GSK

HOW WE WORK

GRANT

CK Print

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: $715,789
Term: 23
Topic: Family Health: Nutrition, Vaccine Development
Program: Global Health
Grantee Location: Zell Lu

Image: Maropack AG.

act:

Prasad (Bill & Melinda Gates Foundation)
Prasad@gatesfoundation.org

Kram (Rommelag/Maropack)
kram@rommelag.com

Fill your product in Blow-Fill-Seal

We are opening our facility to groups interested in trialling their product in BFS

Defined by the FDA as **"advanced aseptic processing,"** BFS is fast becoming the future choice for innovative liquid products.

Advantages of BFS

- Lower unit cost compared to glass
- Sterile unit dose presentation
- Easy end-user disposal
- Smaller carbon footprint compared to glass
- Unbreakable
- Bottle shaped to enable better product delivery
- Bottle shape can be linked to branding
- All liquids suitable, e.g. eye-drops, injections, etc.

BFS containers are lighter and more space efficient than glass alternatives reducing freight and storage costs.

Biologicals and vaccines are our speciality.

Contact Philip Leslie at GSK Boronia
philip.r.leslie@gsk.com
+61418340097

We will fill your product in one day at minimal cost!

1. We set up the machine to run a sterile trial with your pr
2. You send us your product in a 5 litre bag supplied by us
3. We send back 1,000-2,000 BFS containers filled with y product – you are welcome to witness the filling proces
4. We provide you with GMP documentation

Photo courtesy of Rommelag

This trial will enable
- Assess compatibilit polymer & BFS pro
- Run stability trials
- Perform E+L studie

Optional extras:
- Help with E+L testi
- Flow wrapping the containers
- Formulation
- Quality testing
- Stability testing
- Suitable products c have clinical trials r as a next step

We are GSK's Blow-Fill-Seal Centre of Excellence

Want to trial your product in BFS?
Contact us soon to schedule your trial

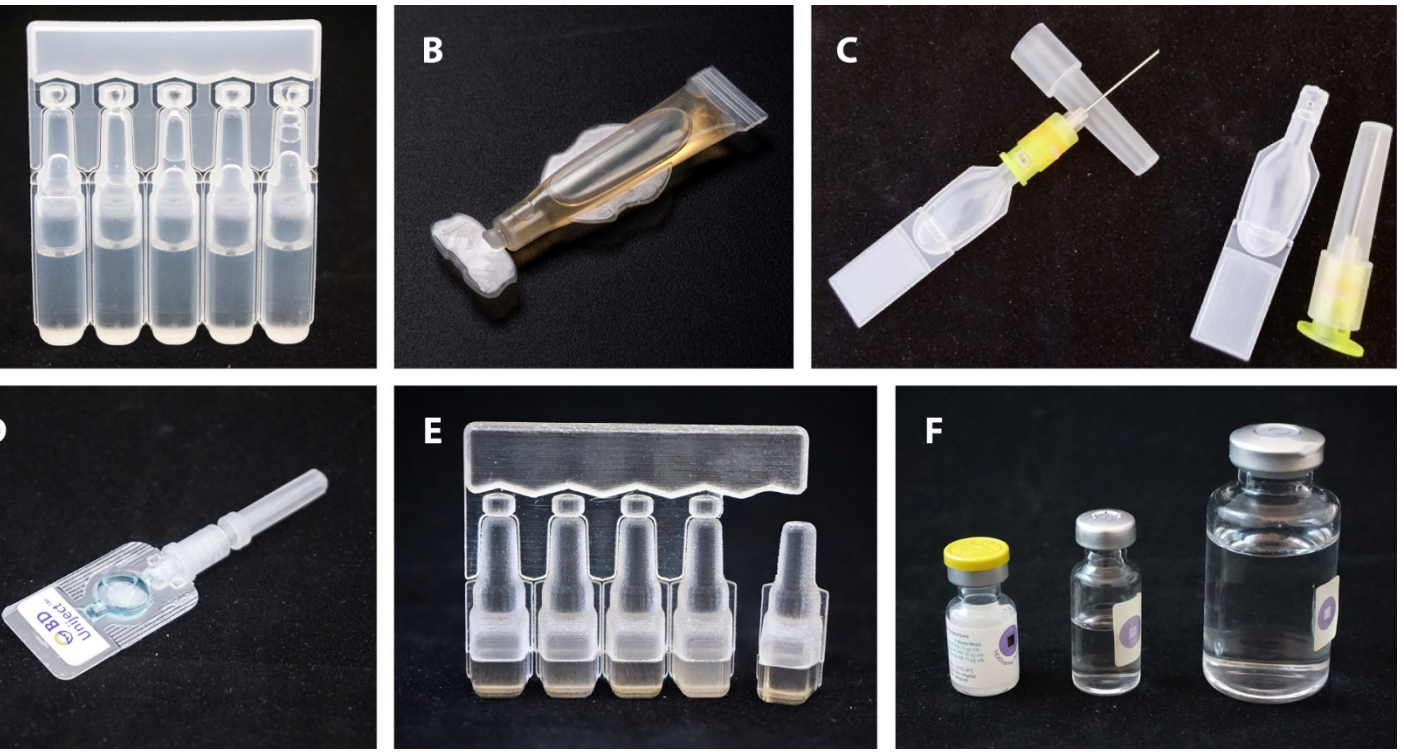
Images: GS

Contact: Phillip Leslie (GSK Boronia)
Philip.R.Leslie@gsk.com

tions: 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.

Novel Primary Container and Packaging Technologies: PATH Cost Analysis

ost analysis: Delivery technology overview



Photos: PATH

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

Oral vaccine packaging

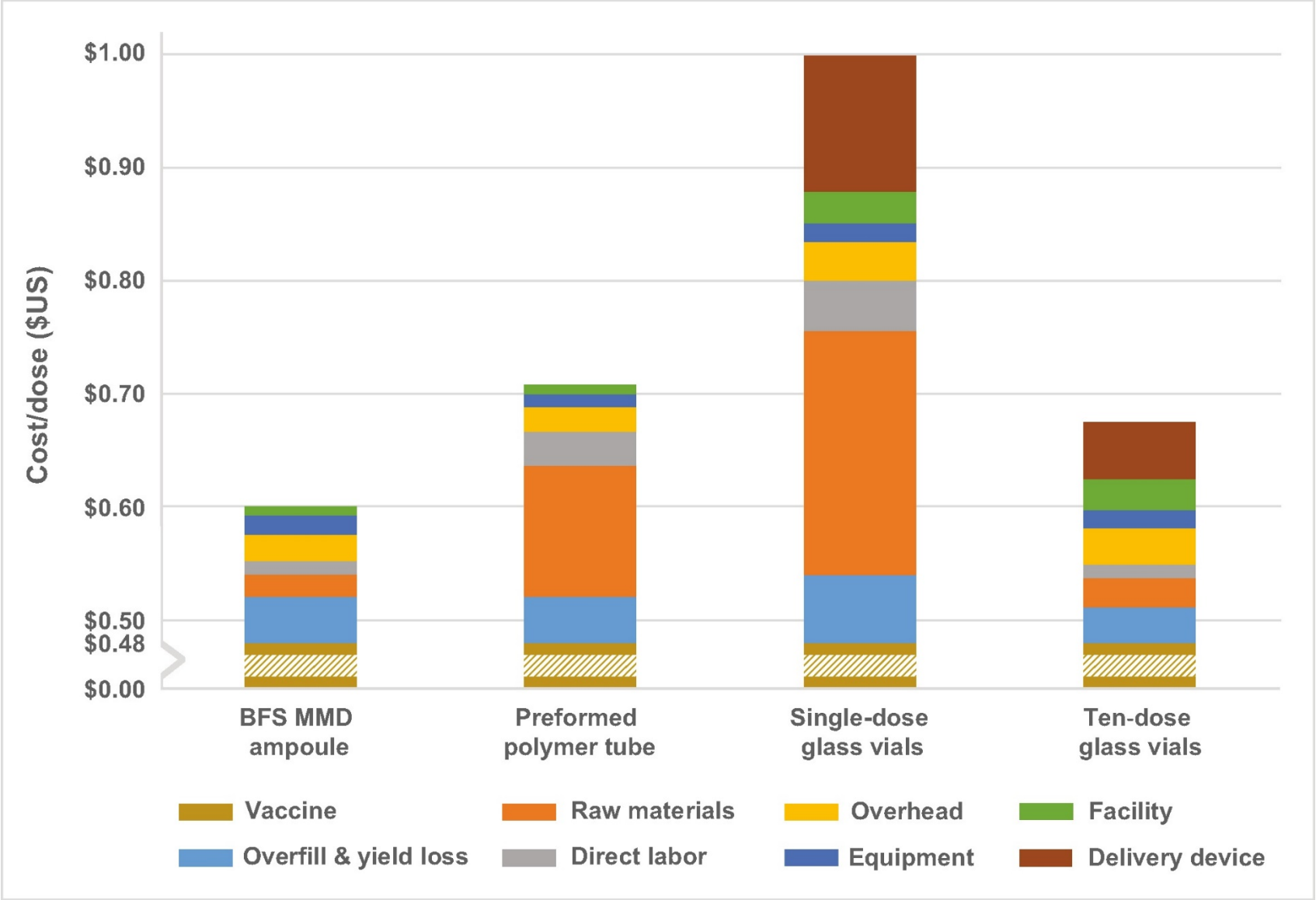
- Glass vials
  - Single-dose
  - Ten-dose
- BFS MMD ampoules
- Preformed polymer tubes

Parenteral vaccine packaging

- Glass vials
  - Single-dose
  - Ten-dose
- BFS MMD ampoules
- BFS CPAD
- Preformed CPAD

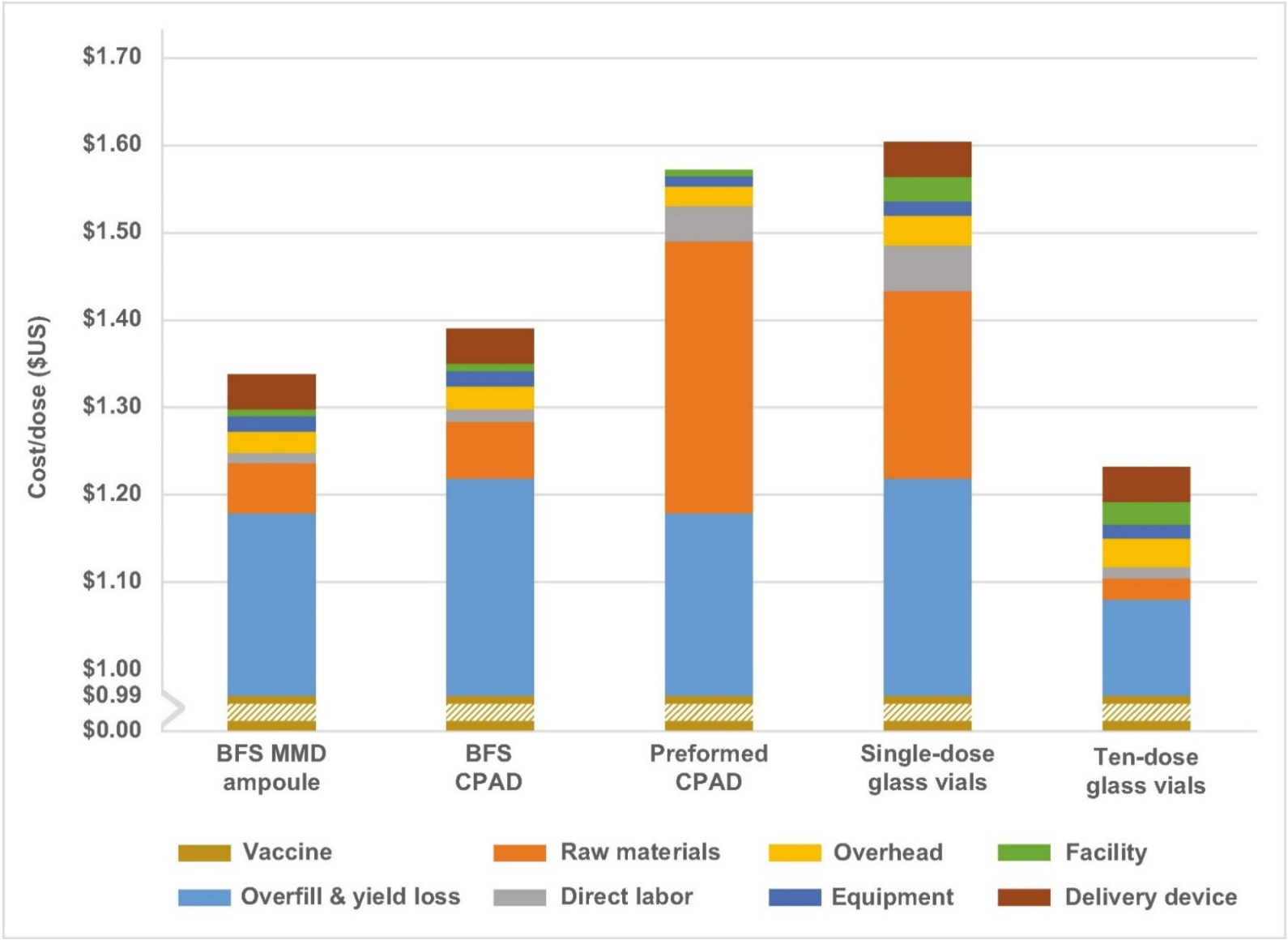
ions: BFS, blow-fill-seal; CPAD, compact, prefilled, autodisable device; MMD, multi-monodose.

ost of good sold: Rotavirus vaccine



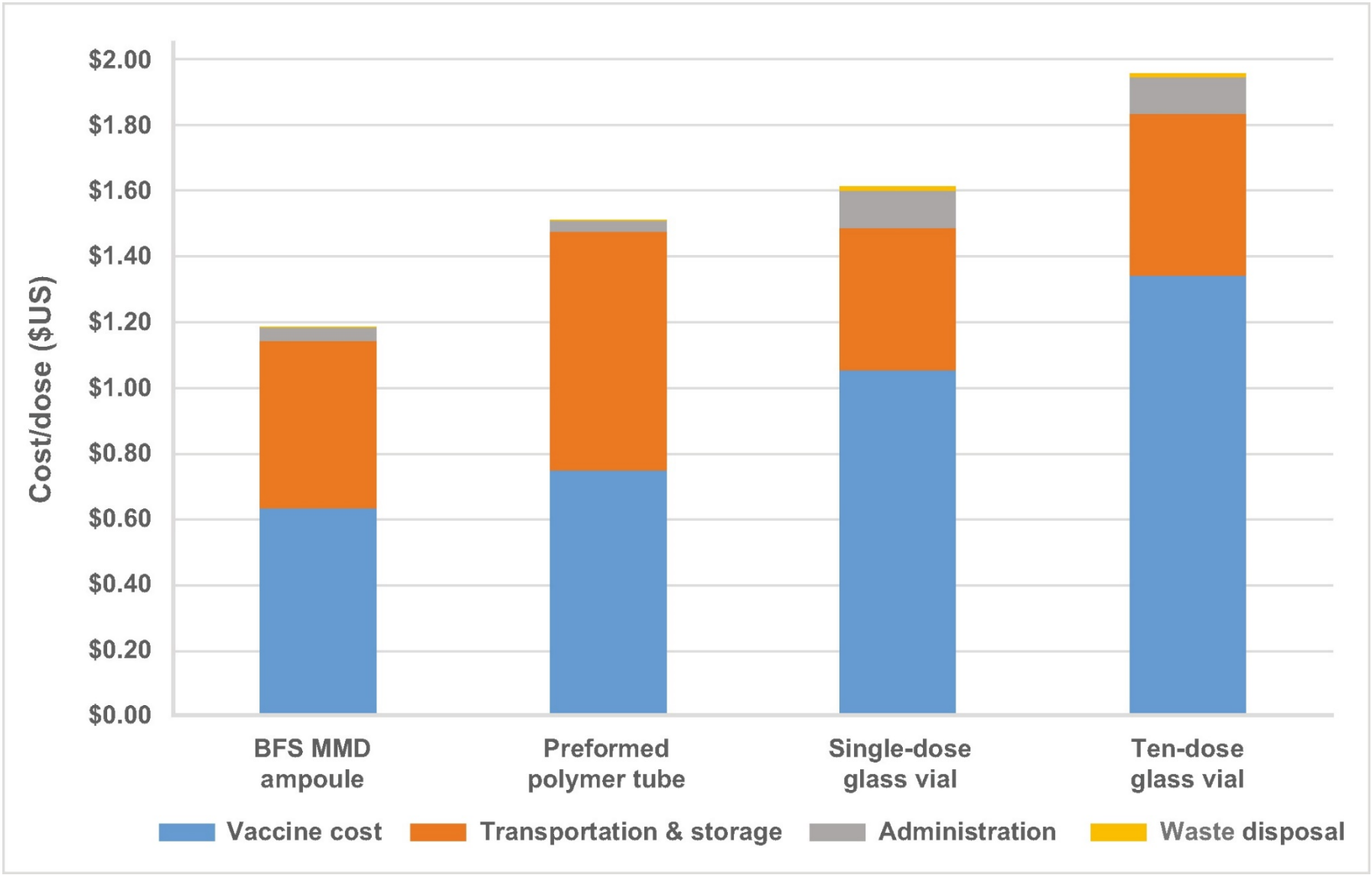
ions: BFS, blow-fill-seal; MMD, multi-monodose.

ost of good sold: Inactivated poliovirus vaccine



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

otal cost of delivery: Rotavirus vaccine



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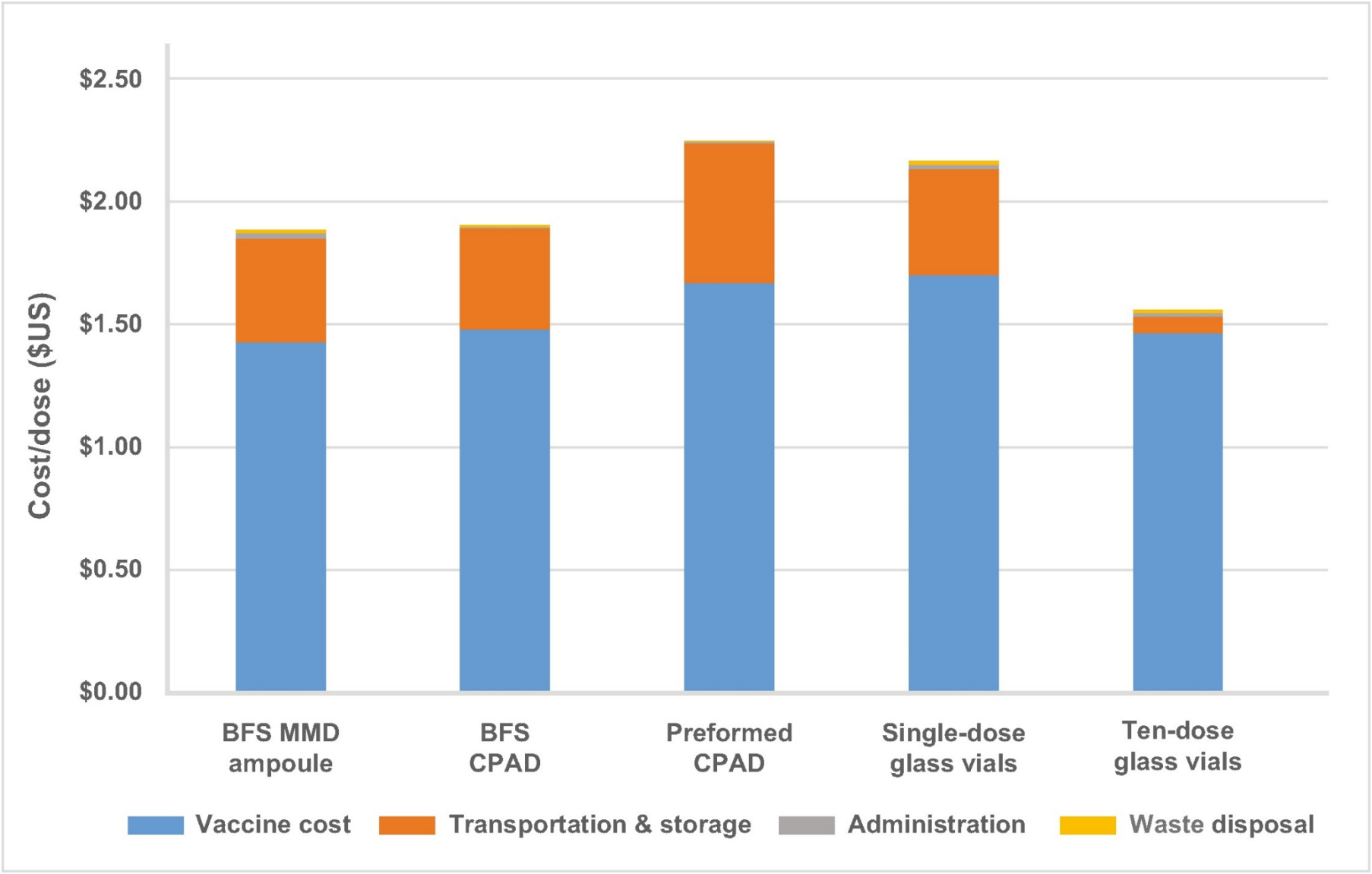
otal cost of delivery: Inactivated poliovirus vaccine



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

Next Generation Packaging + Delivery Technologies: Vaccine Research and Development

ass cartridge and ampoule technology

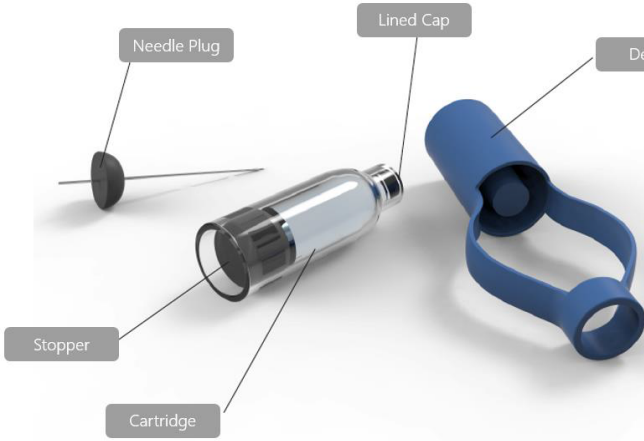
escription

- 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).

echnology 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.

Photos: Duoject/PnuVax

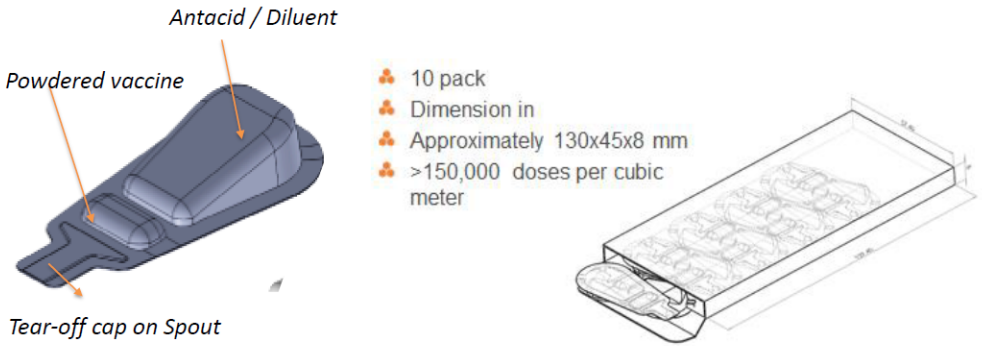


tions: LMIC, low- and middle-income country; PCV, pneumococcal conjugate vaccine.

tegrated reconstitution technology

scription

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



Milled Lyophilized Powder and Diluent in a two component pack

chnology 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).

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

ansdermal microarray patches (MAPs) for pharmaceutical deliver

scription

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).

chnology status – vaccines + drugs

IPV, MR, influenza, rotavirus, tetanus toxoid, and other vaccines evaluated.

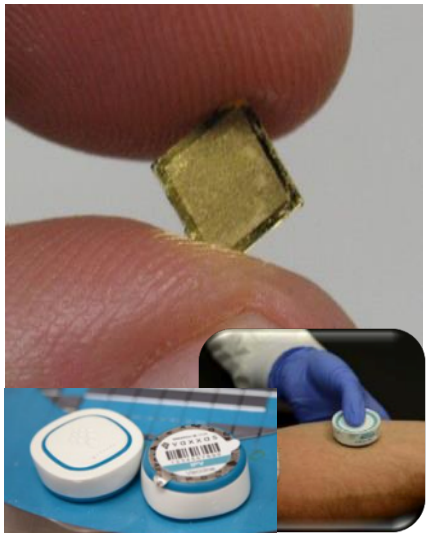
Essential medicines research: ARVs, contraceptives, antimalarials, antibiotics.

Influenza clinical studies completed: presentation/ publications (Georgia Tech, Vaxxas, CosMED).

PATH and AMP field evaluations: programmatic suitability.

MR TPP: potential future WHO WG.

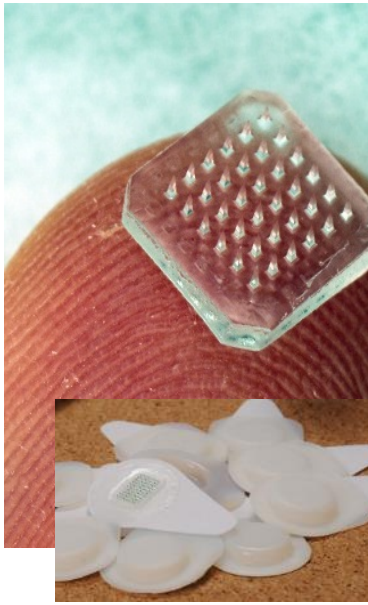
Vaxxas Nanopatch™



Photos: Vaxxas

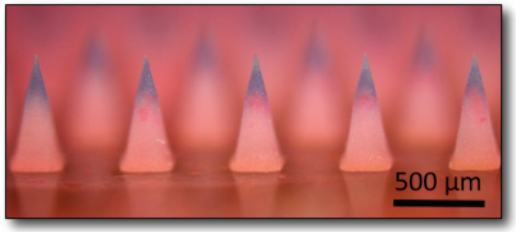
Coated microarray

Micron Biomedi



Dissolving microar

Vaxess MIMIX™

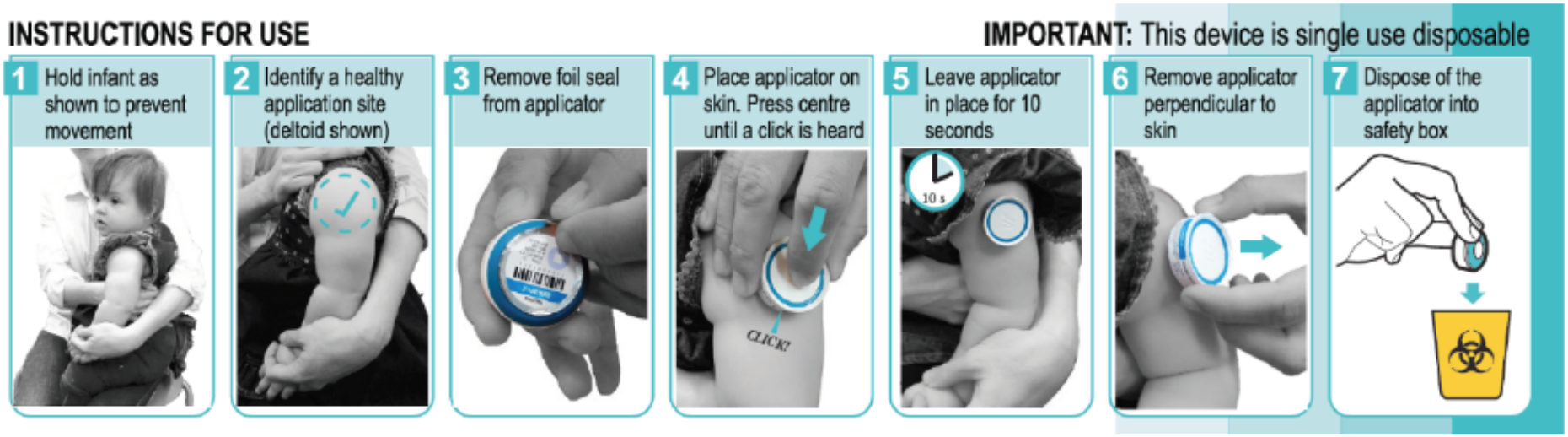


Photos: Vaxess

Dissolving, controlled-release microarray

ns: 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 Organi

anopatch™ with applicator



Photos: Vaxxas

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