

ONLINE WEBINAR

VACCINE WASTAGE REDUCTION - VACCINE PACKAGING

 **DCVMN**
INTERNATIONAL
Developing Countries Vaccine
Manufacturers Network International

 **ROMMELAG**



MR. TIM KRAM

Managing Director -
Rommelag USA Inc



DR. MATTHEW PETERS

Engineering and Business
Development - New
Horizons, a division of
Global Health Labs, Inc.

Conventional glass packaging of vaccines can complicate downstream vaccine logistics systems – from wasted cold chain space to management of empty vials. Many of these issues can be directly addressed with novel packaging designs, all of which are practically accessible with flexible Blow/Fill/Seal (BFS) fill/finish technology. In this webinar, we show how ampoule designs can dramatically reduce cold chain space while reducing wastage in the field and how BFS processes have evolved to handle temperature-sensitive materials and other unique aspects of vaccine formulations (e.g. BSL2, suspensions).



TIME

14:00 - 15:00 CEST



DATE

30 July 2024

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OPTIMIZING VACCINE LOGISTICS IN DEVELOPING COUNTRIES – VACCINE PACKAGING SOLUTIONS

- Introductions
- **Logistics** challenges with glass packaging of vaccines
 - Distribution, cold chain space, wastage
 - Manufacturing
- Plastic packaging solutions
- Commercial Blow Fill Seal (BFS) processes to deliver these solutions
- BFS process – how does it work
- Derisking BFS processes for use with vaccines
- Next steps



INTRODUCTIONS – MATTHEW PETERS

- New Horizons – a Division of Global Health Labs
- Nonprofit fully funded by Gates Ventures
- Engineer/Business Development
- Leads several projects to solve vaccine delivery problems in LMIC

- mpeters@nhgh.org

INTRODUCTIONS – TIM KRAM

- Rommelag USA
- Managing Director

- Tim.Kram@rommelag.com

GLASS VACCINE PACKAGING ISSUES (IN DEVELOPING COUNTRIES)

- Vaccine distribution logistics issues:
 - Cold chain space
 - Wastage
 - Counterfeiting
- Manufacturing logistics:
 - Raw material supply chain
 - Local manufacturing difficult or not possible
 - Lessons from COVID-19 vaccines



Cold box vaccine transfer (Nepal)



State vaccine store (Nigeria)



Off-grid clinic (DRC)



Outreach (Syria, India)

COLD CHAIN STORAGE SPACE

- Vaccine distribution systems are stressed
 - Cold chain equipment is expensive
 - A lot of the equipment functions poorly
 - More vaccine doses needed as populations grow
 - More vaccine types are being added (e.g. HPV, COVID, RSV)
- Multi-dose glass vials help, but introduce new problems (e.g. wastage)
- Routine vaccines may one day be out of the cold chain (due to reformulation, use microarray patches, etc.) but that day is still far away

Rotarix vaccines take up most of the space in this refrigerator – the only one in this Kenyan clinic.



Cholera vaccine campaign staff in Bangladesh sacrifice icepacks for vaccines to accommodate 11 mL/dose packaging

Vaccine Cold Chain Volumes in Secondary Packaging per WHO
(<https://extranet.who.int/pqweb/vaccines/prequalified-vaccines>)

Vaccine	Doses per vial	(cm ³ /dose)
DTP-HepB (Serum Institute)	20	2.1
IPV (Imovax)	10	2.4
IPV (Serum Institute)	10	3.4
PCV-13 (Pevnar 13)	4	3.5
PCV-13 (Pevnar 13)	1	12
Rota (Rotarix)	5	12
IPV (IPV Vaccine SSI)	1	12.9
DTP-HepB-HI (Serum Institute)	1	14
HPV (Gardasil)	1	15
Rota (Rotarix)	1	17

WASTAGE IN MULTI-DOSE VIALS

- Once tapped, most multi-dose containers can only be used for a few hours before remaining vaccine must be discarded
- Cold chain space savings from multi-dose vials is substantially offset by high wastage



Multi-dose RI vaccine vials in a clinic in Nairobi, Kenya.

Vial presentation	Routine	Campaigns
Single Dose	5%	5%
2 or 5-dose, regardless of MDVP	10%	10%
10 or 20-dose: if opened vial can be re-used in subsequent sessions	25%	15%
10 or 20-dose: if opened vial must be discarded at end of session or maximum in 6 hours from the time the vial was opened	40%	15%
20-dose or more: if opened vial must be discarded at end of session	50%	20%

From WHO April 8, 2019 Concept Note: https://www.who.int/docs/default-source/immunization/tools/revising-wastage-concept-note.pdf?sfvrsn=30e43557_4

nbc NEWS June 6, 2022, 1:27 AM PDT
By Joshua Eaton

The U.S. has wasted over 82 million Covid vaccine doses

Vaccine providers say declining demand, large minimum orders and multidose vials make it hard to avoid waste while still offering shots to anyone who wants them.

Sept. 23, 2021, 1:30 AM PDT
By Joshua Eaton

The U.S. is discarding millions of Covid vaccines. One cause: Multi-dose vials.

The federal government is working with Covid-19 vaccine manufacturers to reduce the number of doses per vial, amid growing concerns about wasted vaccines.

COUNTERFEITING VACCINES IN GLASS VIALS



CBS NEWS

WORLD

Thousands get fake COVID vaccine shots in alleged scam in India

BY ARSHAD R. ZARGAR
JULY 5, 2021 / 11:50 AM / CBS NEWS

"scammers are...accused of filling used, empty bottles of real vaccine with the saline solution and administering the shots to anyone who showed up at the events."

Indian police investigate whether scammers gave thousands of shots of salt water instead of vaccine.

Fourteen people have been charged with conspiracy and forgery, the latest example of fraud undermining India's pandemic response.

The New York Times



By Hari Kumar

July 4, 2021



"An estimated 1 in 10 medical products in low- and middle-income countries is substandard or falsified."

Bloomberg

By [Riley Griffin](#)

June 25, 2020 at 2:00 AM PDT

Fear of Vial Shortage for Covid Vaccines Prompts Flurry of Deals

- CEPI secures production for 100 million multidose glass vials
- Move follows similar deals made by companies, U.S. government

The Telegraph

By Sarah Newey, GLOBAL HEALTH SECURITY CORRESPONDENT

19 January 2022 • 10:49am

Plastic pouches to replace glass vials as Covid vaccine manufacturing ramps up in Africa

The Institut Pasteur de Dakar aims to produce 300m doses a year, and will use plastic pouches to package the shots rather than glass vials

NON-GLASS PACKAGING INNOVATIONS – SOLVING PROBLEMS WITH AMPOULE DESIGNS

- The work shown here is a set of PROOF of CONCEPT designs to address critical vaccine logistics issues associated with glass packaging
- Vaccine manufacturers can tweak designs as needed to solve other problems – such as accessing vaccine contents, labeling needs, etc.
- Blow Fill Seal process allows these designs and others to be readily produced (i.e. cost effective)

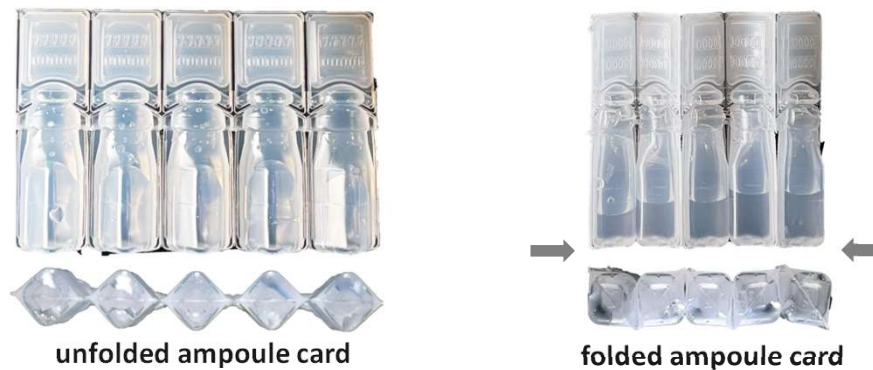


The initial design concept for this work functions like a standard glass ampoule



FOLDING MULTI-MONODOSE (MMD) AMPOULES

Folding single-dose ampoules reduce cold chain space to multi-dose levels



Vaccine	Doses per vial	(cm ³ /dose)
DTP-HepB (Serum Institute)	20	2.1
IPV (Imovax)	10	2.4
IPV (Serum Institute)	10	3.4
PCV-13 (Pevnar 13)	4	3.5
BFS Ampoules (foil pack of 5 single doses)	1	~3
PCV-13 (Pevnar 13)	1	12
Rota (Rotarix)	5	12
IPV (IPV Vaccine SSI)	1	12.9
DTP-HepB-HI (Serum Institute)	1	14
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BFS PROCESS AND BENEFITS

- Blow Fill Seal (BFS) Process
- Simple process - Inputs to BFS machine are plastic pellets (LDPE) and bulk vaccine bulk
- Systems are sterile, GMP, and BSL2
- Well established with WFI and other pharma products (including some vaccines), leachables understood
- Molds to form ampoules are readily modified to specific needs of vaccines
- Costs are comparable if not better than glass packaging

THE HOME OF BLOW FILL SEAL TECHNOLOGY

- **1964 Start**
- **Inventor of BFS technology**
- **German and Swiss facilities**
- **Currently 1000 people**
- **30-50 machines per year**



CONTRACT MANUFACTURING

- **1974 Start**
- **German and Swiss facilities**
- **Currently 900 people**
- **+40 BFS systems**
- **+1 billion containers made per year**
- **0.1 to +1000 mL fill range**
- **Aseptic liquids and suspensions**
- **Terminally sterilized products: IV**
- **Gels, creams, topicals**

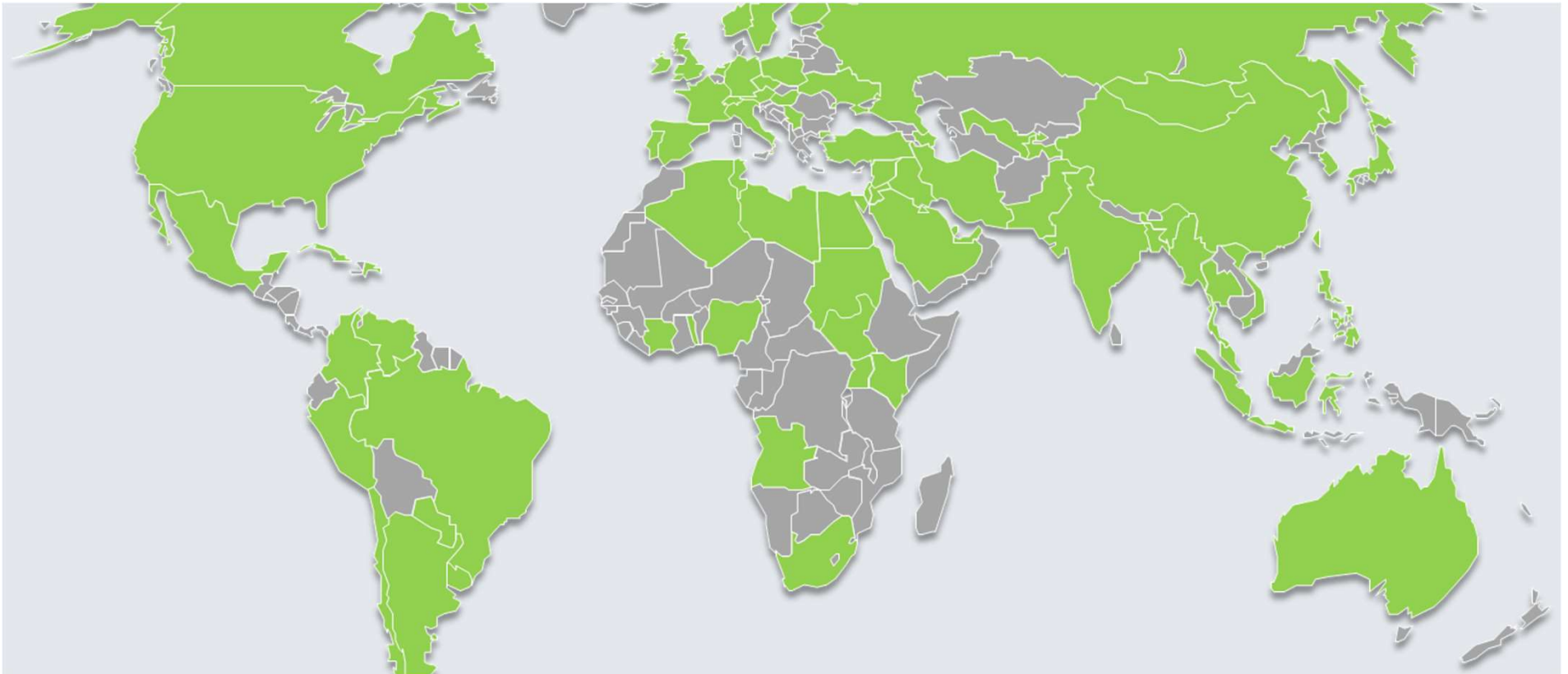


BSL-2 FACILITY ZELL SWITZERLAND

- **2012 opening**
- **Modular design:**
 - Module 0 – base function
 - Module 1 – test BFS unit
 - Module 2 and 3 ready to build expansions
- **Validated for biologics and vaccines**
- **Small batch capability**
- **Disposables option (filling system)**
- **Open facility design**

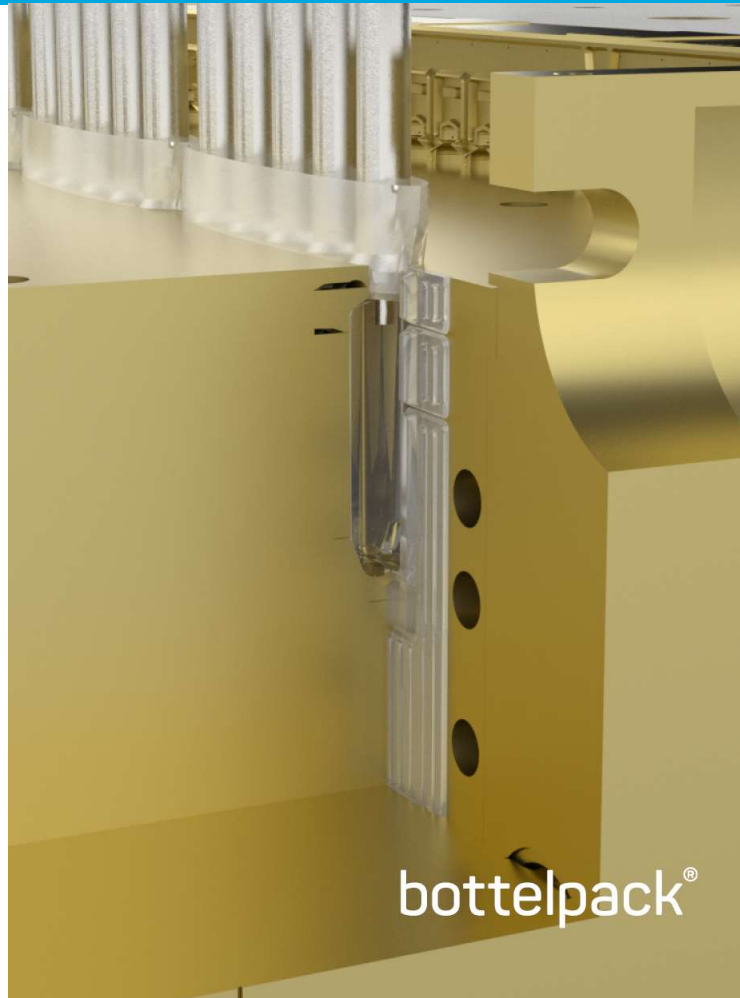


WORLD WIDE PRESENCE

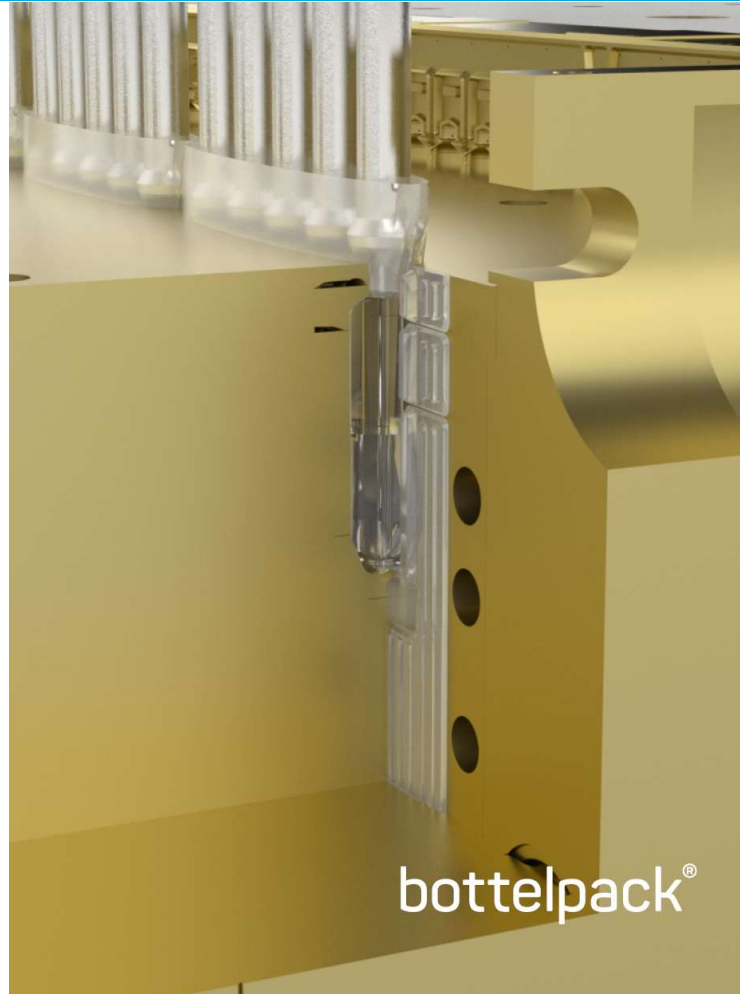


BFS Basics

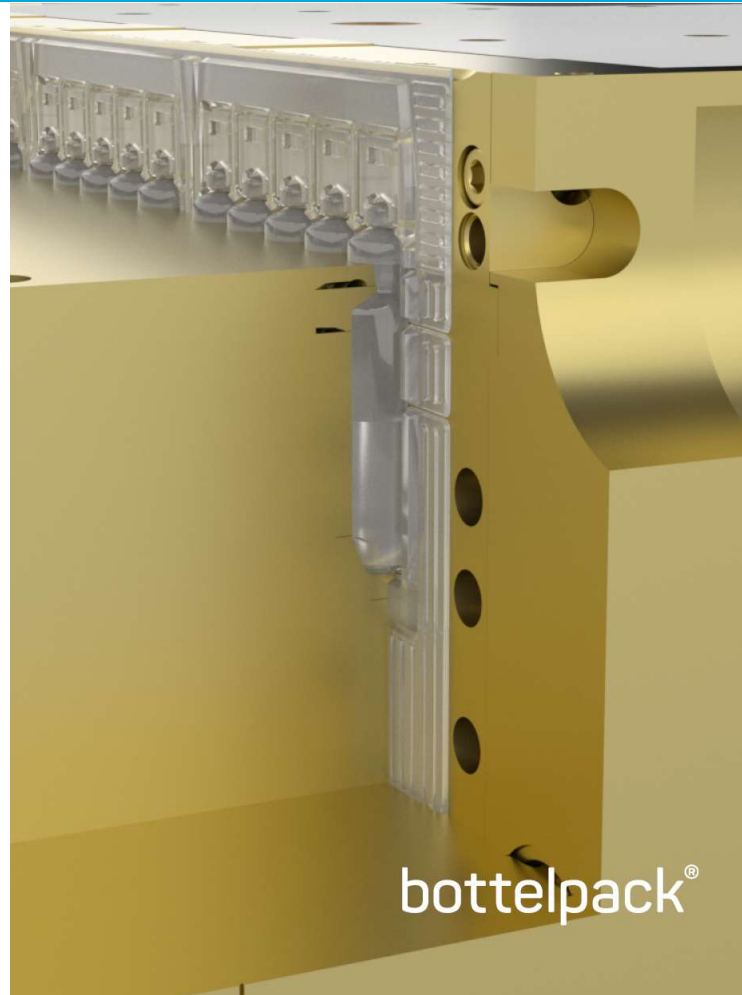
FORM



FORM



FORM



bottelpack®

 ROMMELAG



- **Company general-**
- <https://www.rommelag.com/en/technologies/blow-fill-seal>
- **321M BFS machines showing individual systems –**
- <https://www.youtube.com/watch?v=PNN69NxT3Oc>
- **Rotary BFS technology**
- <https://www.youtube.com/watch?v=K7awm57wgiY>
- <https://www.youtube.com/watch?v=djYqnMipKS8>

OPTIMIZING BFS FOR VACCINE TESTING (AND MANUFACTURING)

New Horizons work with Rommelag to optimize for TESTING vaccines

- Hardware (e.g. molds) for BFS machine in GMP/BSL2 facility capable of producing material suitable for use in clinical trials
- Front end optimized to test laboratory batches of bulk vaccine as small as 1 L
- Optimized CoolBFS – multiple layers of cooling systems added to remove all process heat exposure to vaccines
- Product flow through system optimized to maintain adjuvant suspensions during fill

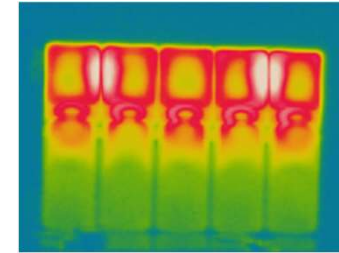
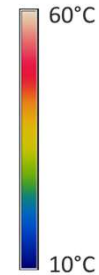
BFS COOLING TO PROCESS VACCINES IS NOW VALIDATED



5 L bulk tanks supports small volume test fills down to 1 L of product and is jacketed for product cooling. Transfer lines to filling machine are insulated to retain cooling.



Visual inspection station (in front of machine)



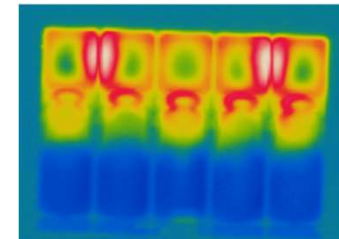
No cooling on machine

Hottest spot - 65°C

Filling mandrels

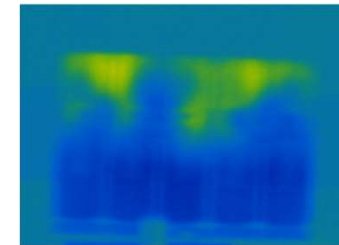
Ampoule mold set

Punch tool



Tank, filling mandrels, mold and punch tool cooling

Hottest spot - 61°C



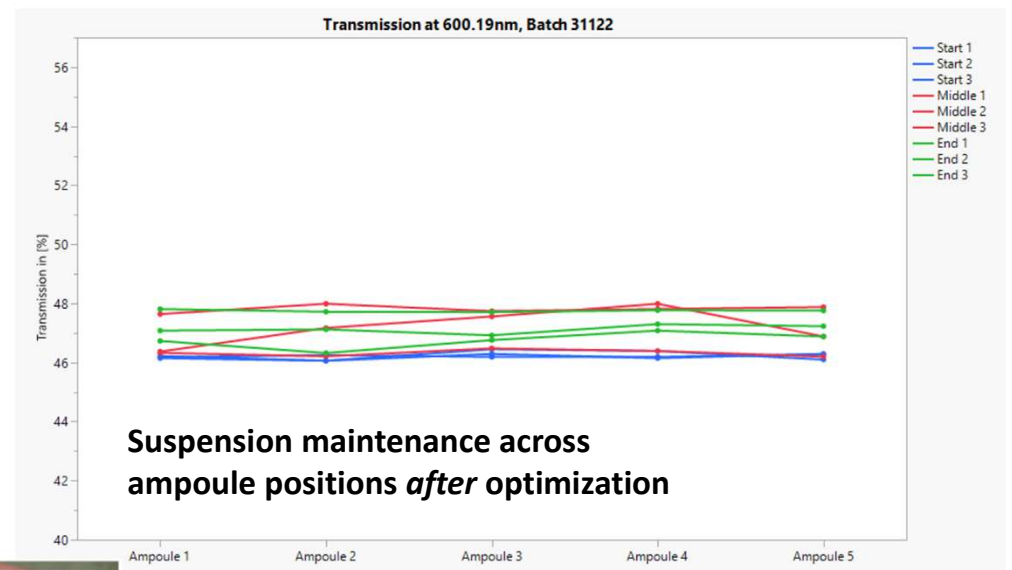
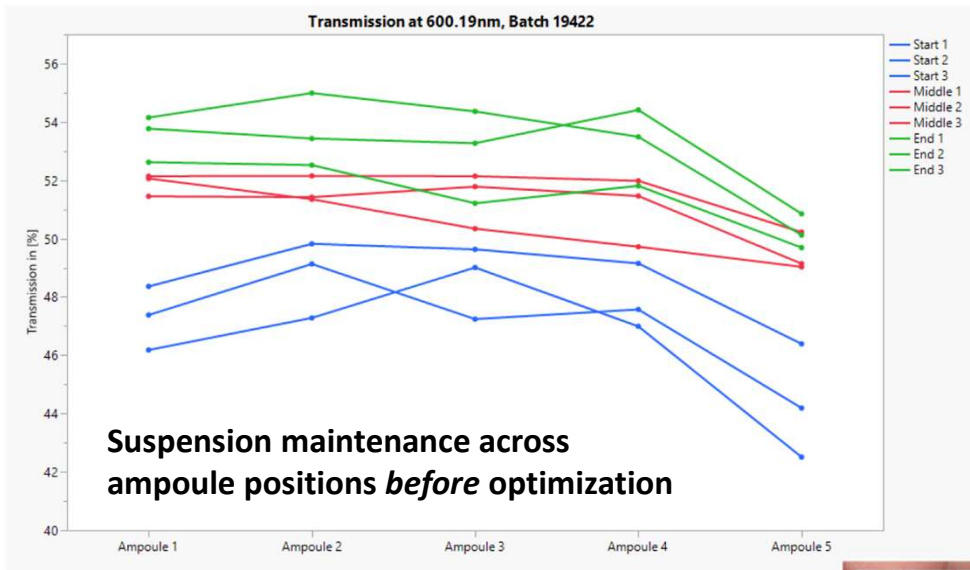
Tank, filling mandrels, mold and punch tool cooling with post-fill cooling tunnel activated

Hottest spot - 25°C

After active cooling steps, ampoules continue to cool as they are held upright during transfer to the visual inspection and leak testing stations

MANAGING ADJUVANT SUSPENSIONS

- Product suspensions are maintained throughout the filling system and across all ampoule positions
- Light-transmission assay monitors suspension behavior in real time at plant to make corrections during the fill if needed



VACCINE TRIALS TO DATE

- Live attenuated flu vaccine – nasal spray
- Multiple oral rotavirus vaccine products
- RSV vaccine
- Conjugated vaccines
- 2 more VVM 2 vaccines...

Immunogenicity of a quadrivalent Ann Arbor strain live attenuated influenza vaccine delivered using a blow-fill-seal device in adults: a randomized, active-controlled study*

Eric A. Sheldon,^a Robert Jeanfreau,^b Joseph A. Sliman,^{c,†} Supoat Charenkavanich,^{d,†} Matthew D. Rousculp,^{e,†} Filip Dubovsky,^f Raburn M. Mallory^f

^aRheumatology and Internal Medicine, Miami Research Associates, Miami, FL, USA. ^bInternal Medicine, Benchmark Research, Metairie, LA, USA. ^cVanda Pharmaceuticals, Inc., Washington, DC, USA. ^dStatprobe, Clarksburg, MD, USA. ^eComparative Effectiveness Research, GlaxoSmithKline, Research Triangle Park, NC, USA. ^fClinical Development, MedImmune, LLC, Gaithersburg, MD, USA.

Correspondence: Raburn M. Mallory, Clinical Development, MedImmune, LLC, One MedImmune Way, Gaithersburg, MD 20878, USA. E-mail: malloryr@medimmune.com

*Previous presentation: Data from this study were presented at the 48th Annual Meeting of the Infectious Diseases Society of America, October 21–24, 2010, Vancouver, British Columbia, Canada (Abstract No. 3671).

[†]At the time this study was conducted, Drs. Sliman, Charenkavanich, and Rousculp were employees of MedImmune, LLC, Gaithersburg, MD 20878, USA.

Trial registration: Clinicaltrials.gov identifier NCT00952705.

Accepted 08 September 2012. Published Online 14 October 2012.



AMPOULE CARD FOLDING MACHINE

Mechanized folding is a key component for mass-producible reduced-volume vaccine packaging process



unfolded ampoule card

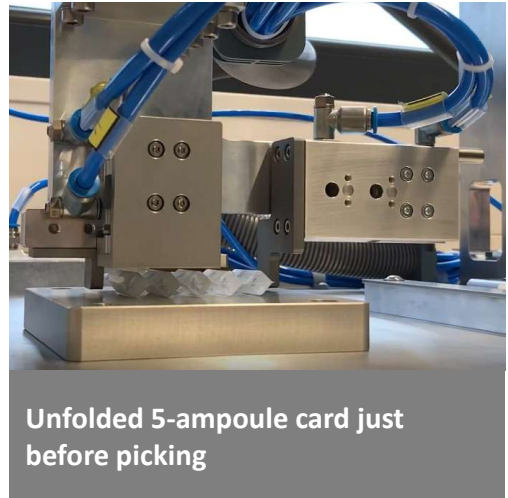


folded ampoule card

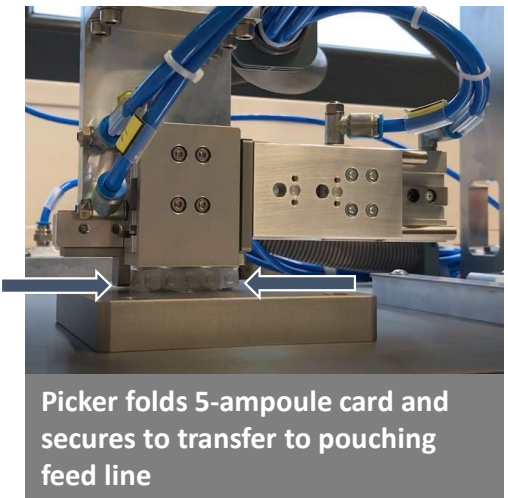
Ampoule folding picker arm unit:

- Grabs an unfolded card of 5 ampoules from one processing line
- Folds it
- Transfers folded ampoule card to the flow wrapper feed line

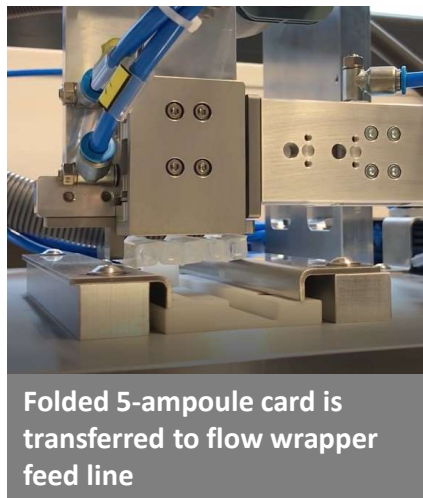
Ampoules are then held in folded state by rails as they proceed to flow wrapper/ foil-pouching machine



Unfolded 5-ampoule card just before picking



Picker folds 5-ampoule card and secures to transfer to pouching feed line



Folded 5-ampoule card is transferred to flow wrapper feed line



Rails on flow wrapper feed line maintain folded state until fully foil-pouched

SECONDARY PACKAGING

Secondary packaging solutions

- Labeling and VVM
- Needs product to drive regulatory discussions with WHO
- Clarity on labeling could reduce packaging size
- Overwrap and boxes lock in cold chain space savings



unfolded ampoule card

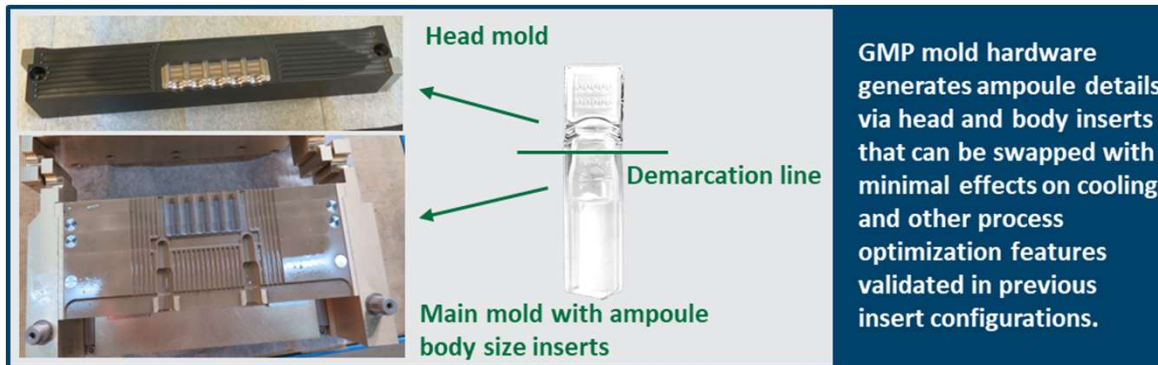


folded ampoule card



CONCLUSIONS AND NEXT STEPS

- BFS process is ready to package vaccines
- New Horizons and Rommelag will continue to develop packaging concepts for more off-the-shelf packaging solutions – direct injection, drop size regulation, etc.
- In field trials of packaging designs will continue
- There may be funding available to support trial fills
- Reach out to Tim Kram for more information



Testing water-filled *NH* BFS ampoules in Uganda. Photos from BMGF-funded PATH report "Programmatic and human factors evaluation of three blow-fill-seal parenteral vaccine container designs" submitted to Rommelag March 2018

CONTACT



Tim Kram
Managing Director

Rommelag USA Inc.
27905 Meadow Drive · Suite 9 · Evergreen CO 80439 · USA
T +1 303 674 8333 · M +1 720 308 9448 · F +1 303 670 2666
Home Office +1 303 697 2980
tim.kram@rommelag.com · www.rommelag.com