ONLINE WEBINAR

# VACCINE WASTAGE REDUCTION - VACCINE PACKAGING

DCVMN INTERNATIONAL
Developing Countries Vaccine Manufacturers Network International

ROMMELAG

**MR. TIM KRAM**
Managing Director - Rommelag USA Inc

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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**
23 October, 2023

**REGISTER USING LINK**

# 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


State vaccine store (Nigeria)

Cold box vaccine transfer (Nepal)

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 (Prevnar 13) | 4 | 3.5 |
| PCV-13 (Prevnar 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, multi-dose containers can only be used for a few hours before remaining vaccine must be disposed of
- 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.

**Vaccine wastage numbers WHO uses for coverage planning**

| 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

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

World Health Organization

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

# GLASS SUPPLY CHAIN AND MANUFACTURING COMPLEXITY

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

unfolded ampoule card

folded ampoule card


| 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 (Prevnar 13) | 4 | 3.5 |
| BFS Ampoules (foil pack of 5 single doses) | 1 | ~3 |
| PCV-13 (Prevnar 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 |

# BFS PROCESS AND BENEFITS

- Blow Fill Seal (BFS) Process
- Simple process - Inputs are plastic pellets (LDPE) and 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**

# ROMMELAG CMO

## 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

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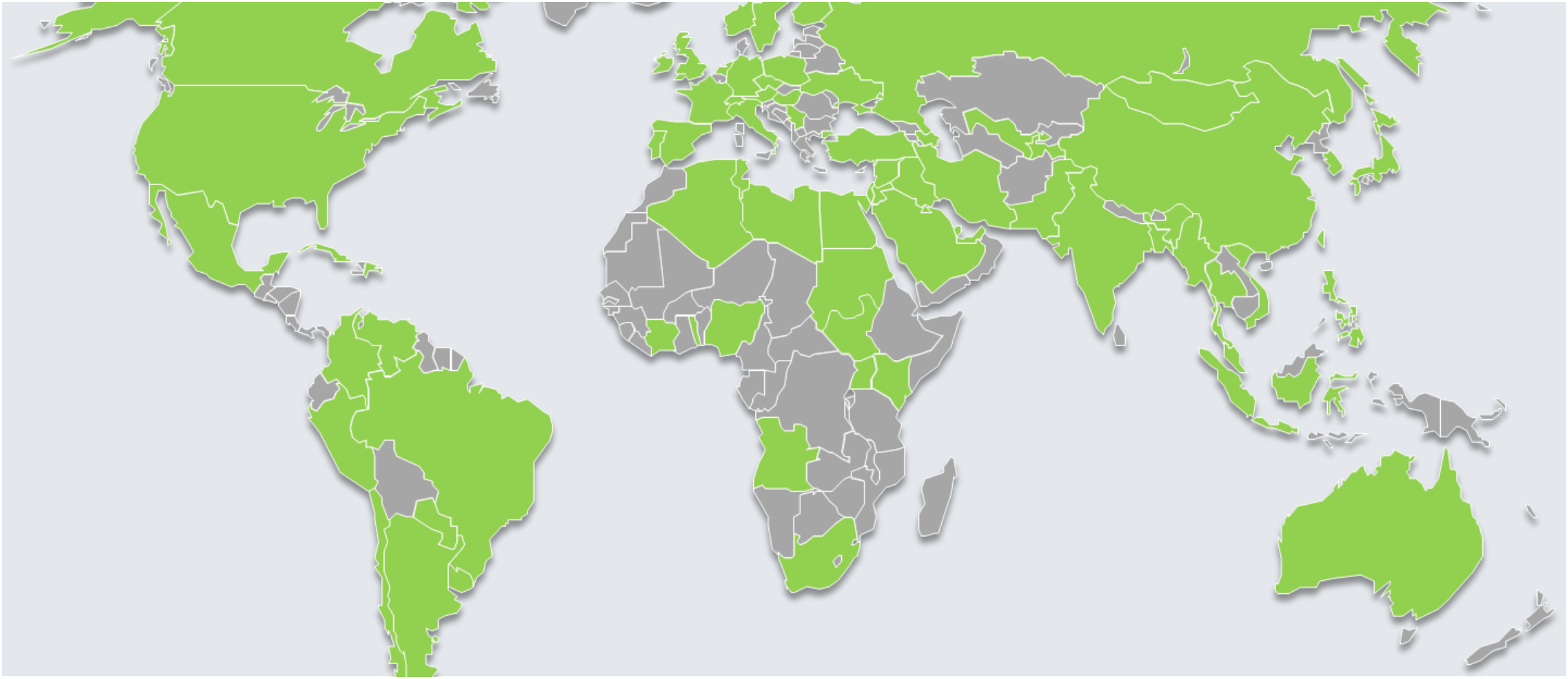
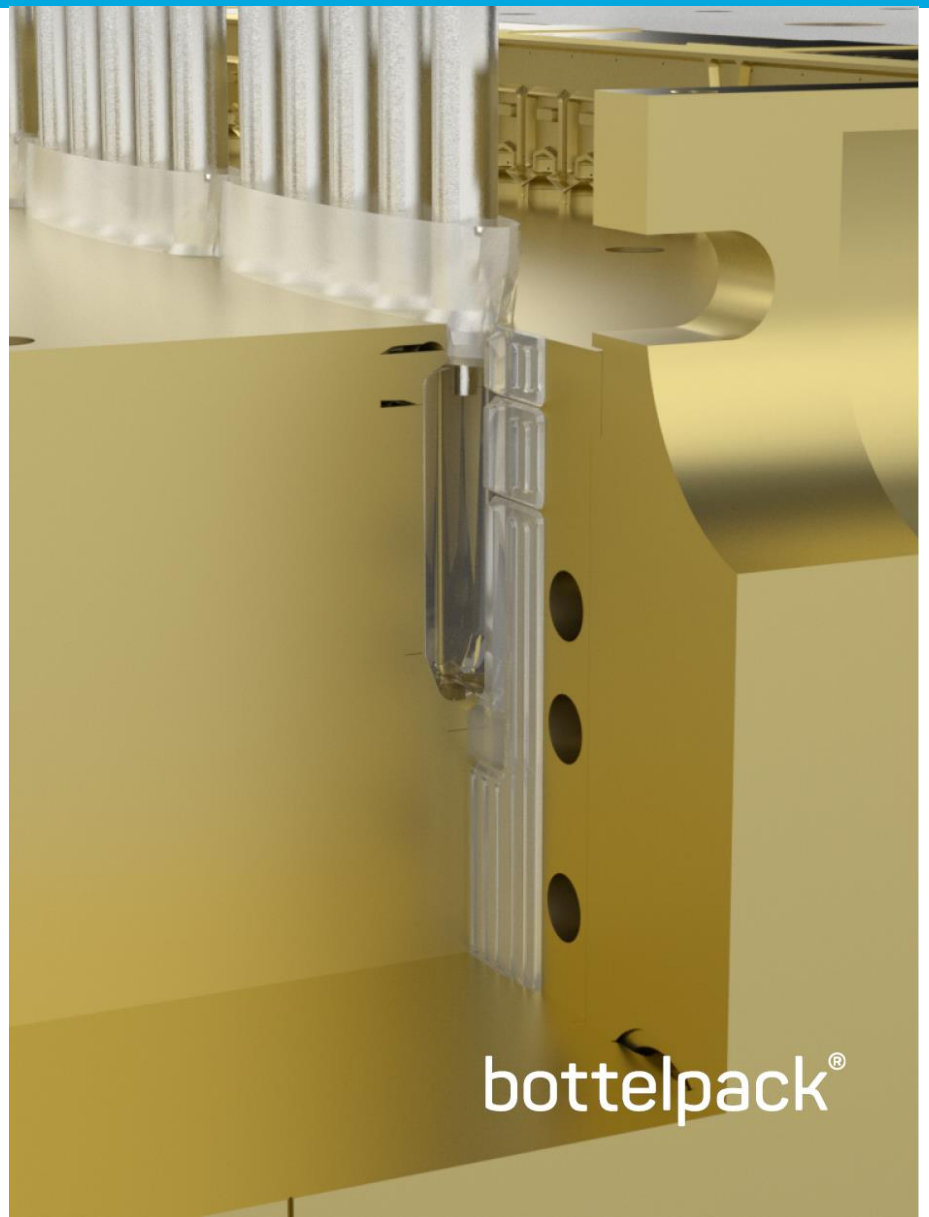


# BFS Basics

# BLOW/FILL/SEAL BASICS

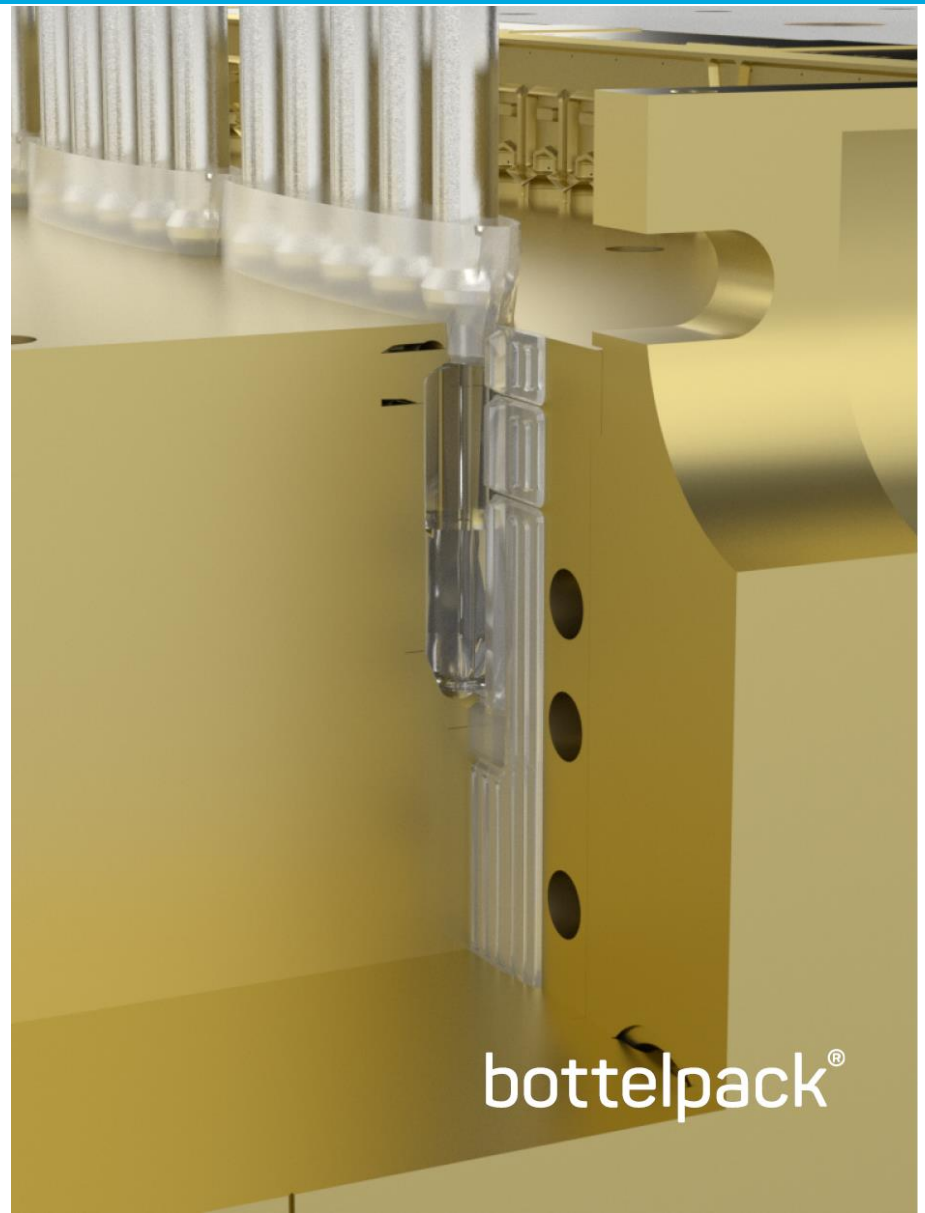
## FORM



# BLOW/FILL/SEAL BASICS

ROMMELAG ENGINEERING

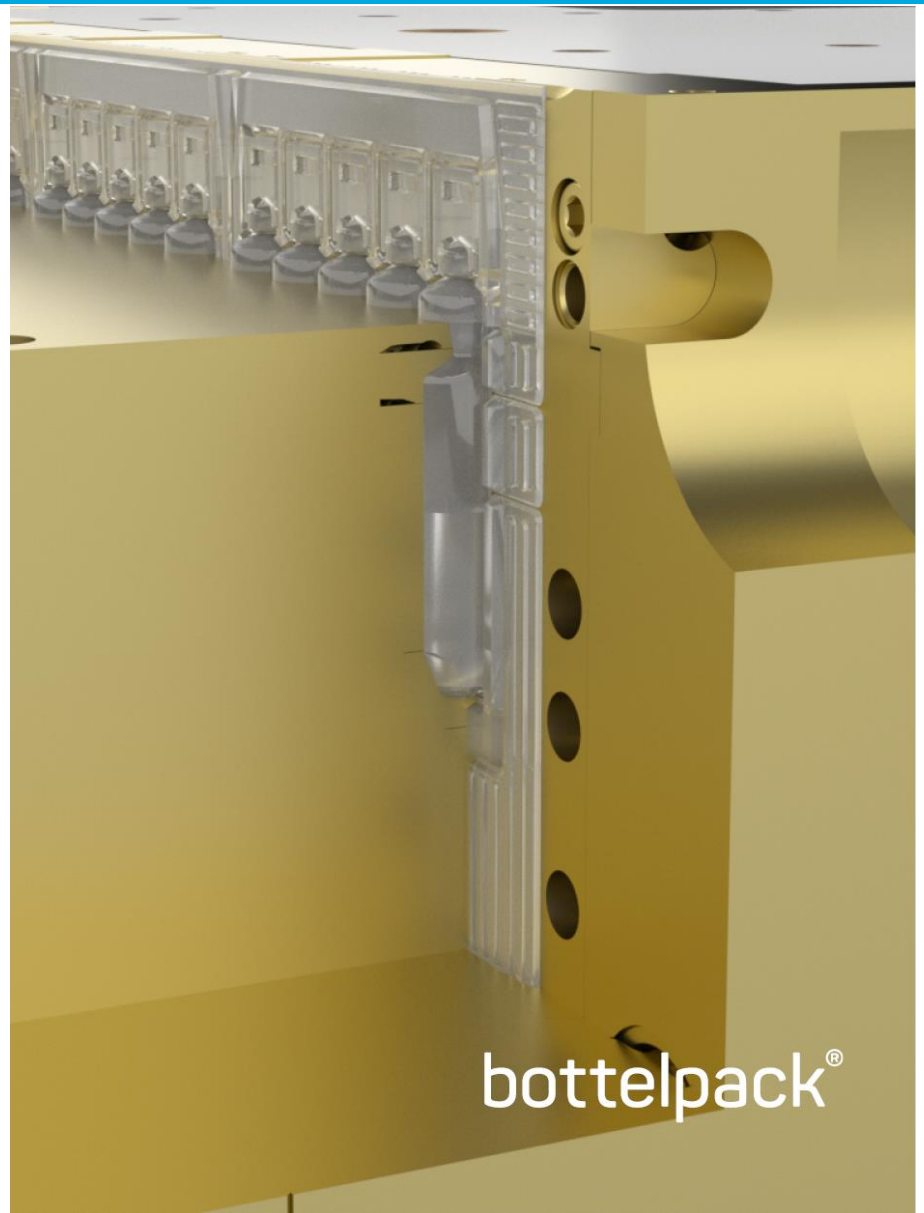
## FORM

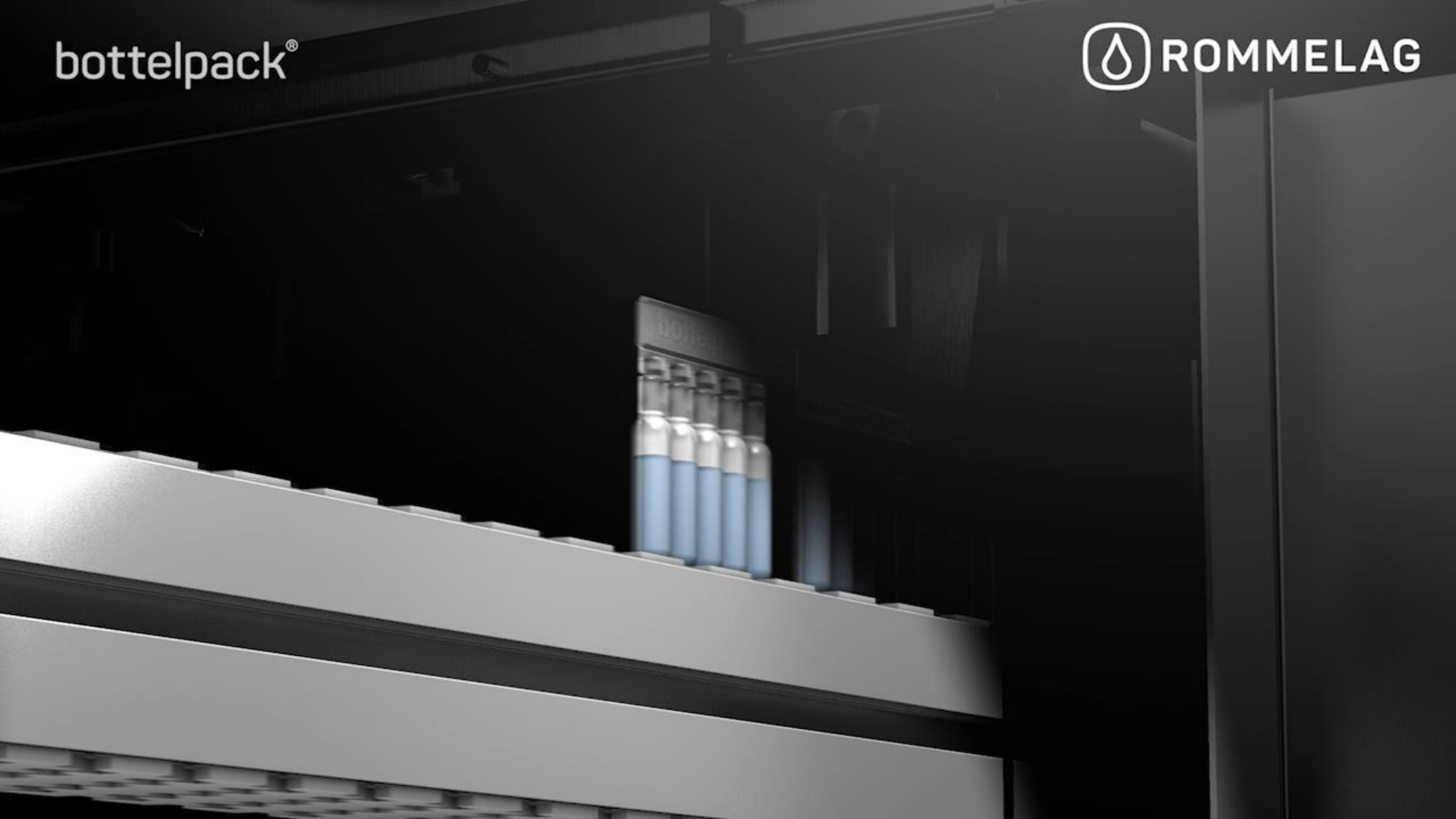


# BLOW/FILL/SEAL BASICS

ROMMELAG ENGINEERING

## FORM

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# LINKS TO VIDEO

- **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**

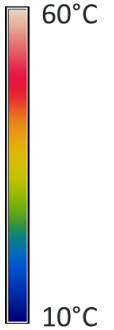
# OPTIMIZING BFS FOR VACCINE TESTING (AND MANUFACTURING)

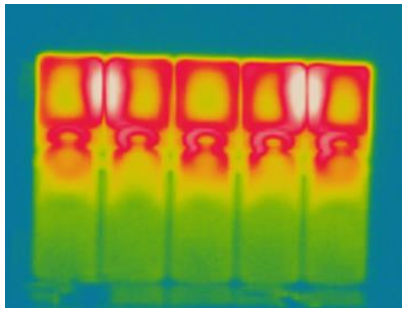
New Horizons work with Rommelag to optimize for TESTING vaccines

- 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

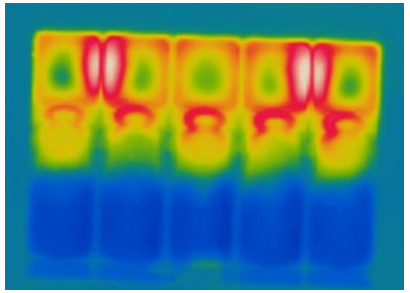
**5 L bulk tanks supports small volume test fills down to 1 L of product and is jacketed for product cooling. Transfer lines to filling machine are insulated to retain cooling.**

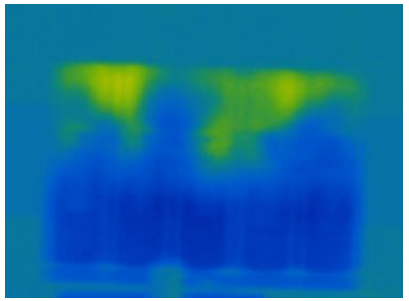
**No cooling on machine**

Hottest spot - 65°C



**Tank, filling mandrels, mold and punch tool cooling**

Hottest spot - 61°C



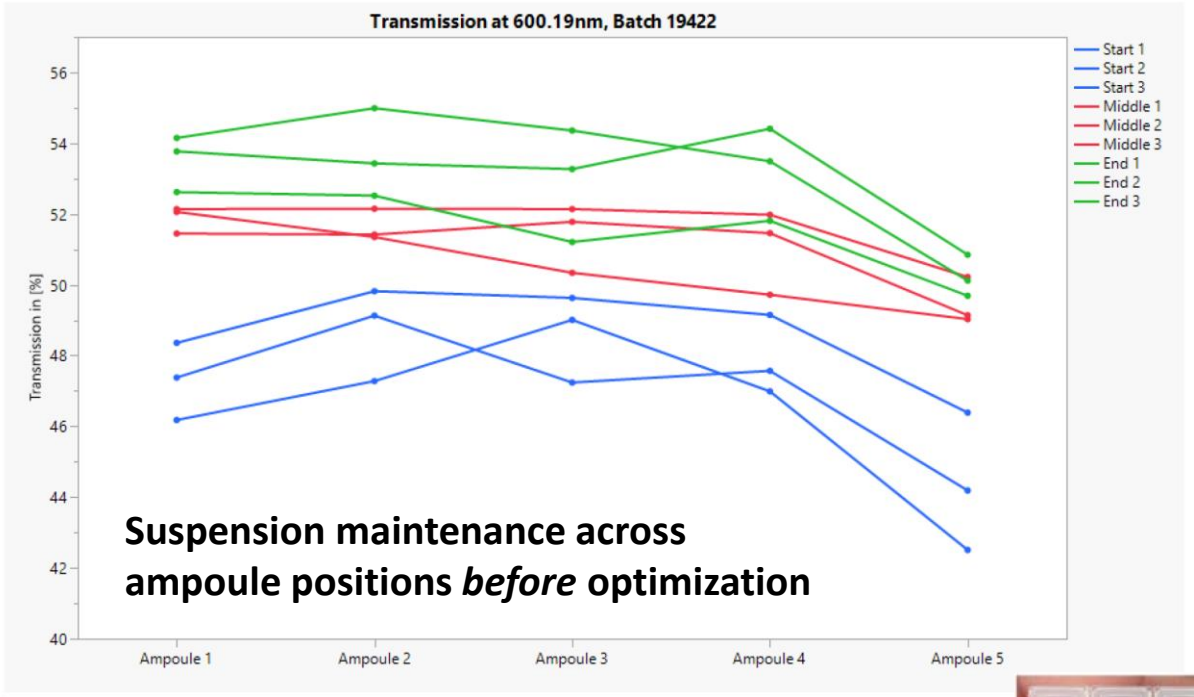
**Tank, filling mandrels, mold and punch tool cooling with post-fill cooling tunnel activated**

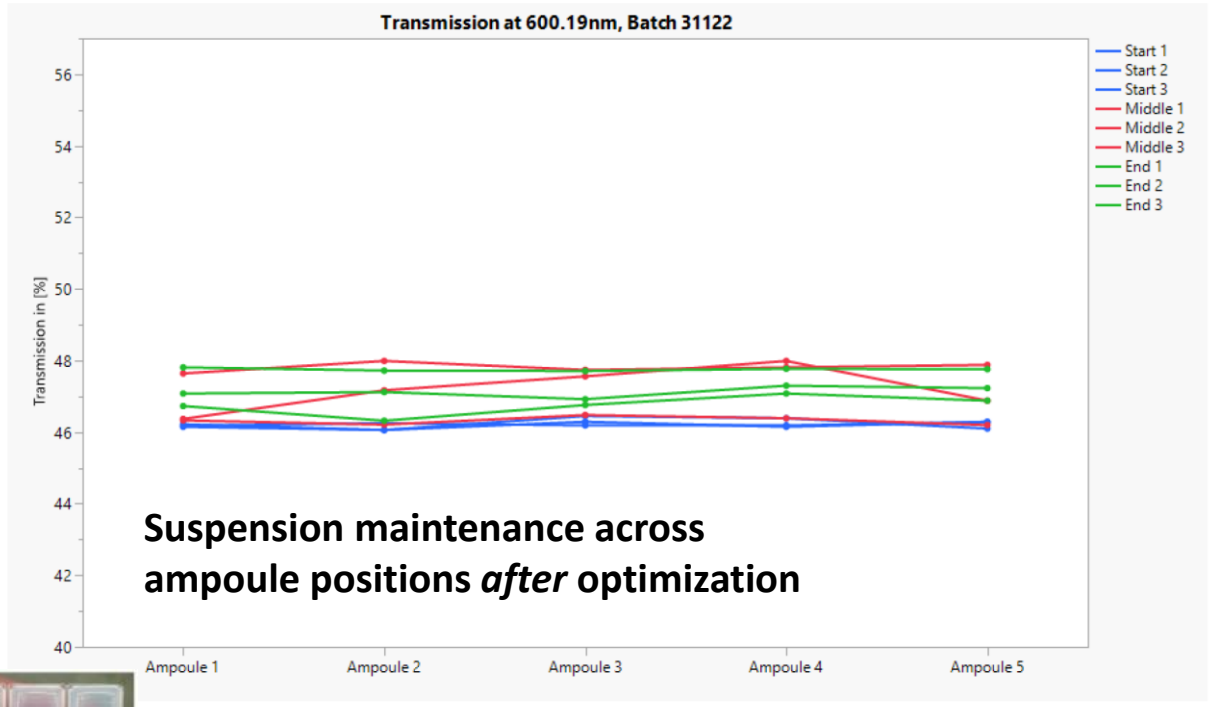
Hottest spot - 25°C

**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

## 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]

[a]Rheumatology and Internal Medicine, Miami Research Associates, Miami, FL, USA. [b]Internal Medicine, Benchmark Research, Metairie, LA, USA. [c]Vanda Pharmaceuticals, Inc., Washington, DC, USA. [d]i3Statprobe, Clarksburg, MD, USA. [e]Comparative Effectiveness Research, GlaxoSmithKline, Research Triangle Park, NC, USA. [f]Clinical 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

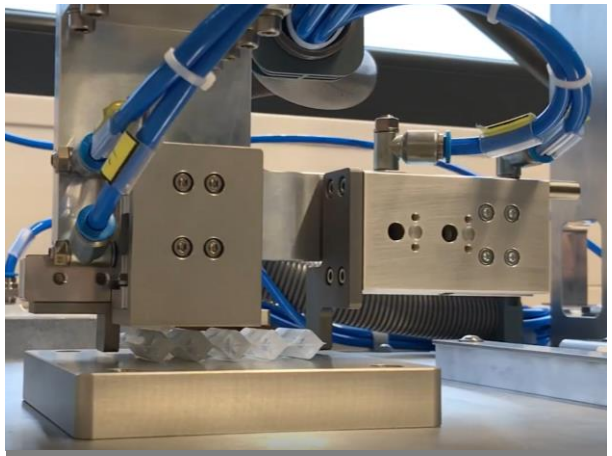
unfolded ampoule card

folded ampoule card

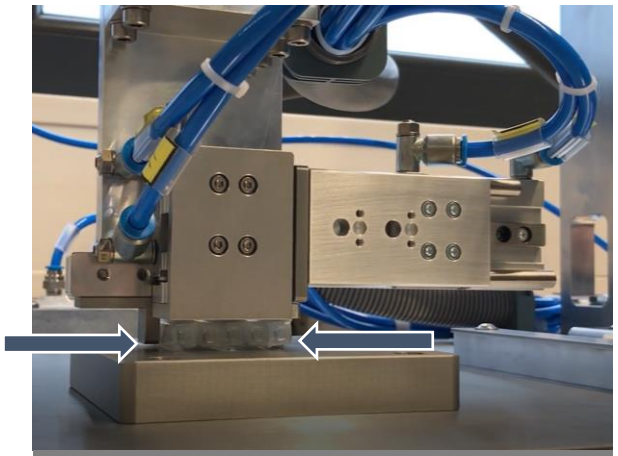
***Ampoule folding picker arm* unit:**

- 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

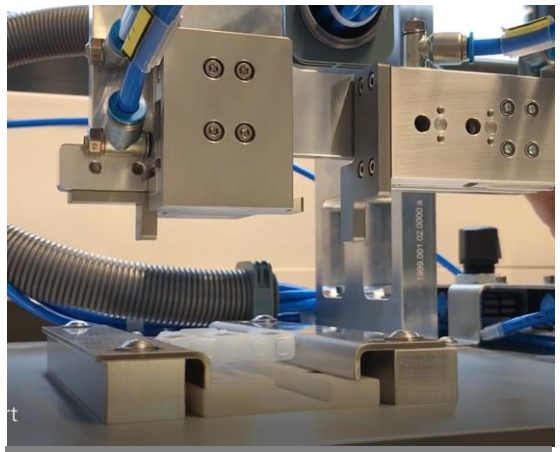


Unfolded 5-ampoule card just before picking



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

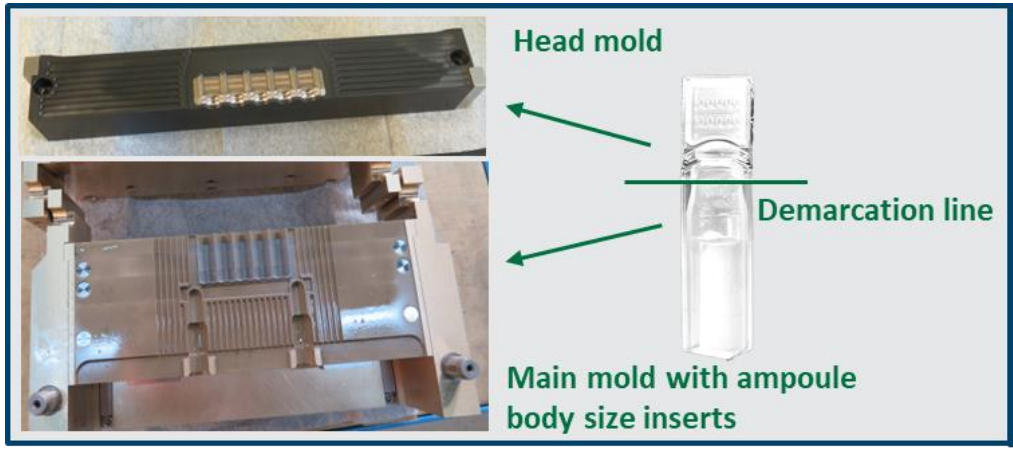
- Labeling and VVM
- Needs product to drive regulatory discussions with WHO
- Clarity on labeling could reduce packaging size
- Overwrap and boxes lock in cold chain space savings

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




GMP mold hardware generates ampoule details via head and body inserts that can be swapped with minimal effects on cooling and other process optimization features validated in previous insert configurations.

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