

#### **VACCINE WASTAGE REDUCTION - VACCINE PACKAGING**

### SOLVING PROBLEMS WITH BFS PACKAGING

#### DCVMN AGM SÃO PAULO **OCTOBER 2024**





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#### VACCINE LOGISTICS CHALLENGES IN DEVELOPING COUNTRIES

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

# Vaccine packaging can play a part in addressing these problems

Vaccines arrive from out of country





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. vaccine 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 <sup>3</sup> /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, 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.

Vaccine wastage numbers WHO uses for coverage planning				
Vialpresentation	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.w source/immunization/tools/revising-wastage-concept-n	ho.int/docs/defau ote.pdf?sfvrsn=30	lt- e43557 4		

#### ar 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 S. 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





"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 <u>Riley Griffin</u> 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	(cm³/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
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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
- Capital costs are comparable if not better than glass packaging
- Operation costs are less than glass packaging

#### ROMMELAG ENGINEERING



#### THE HOME OF BLOW FILL SEAL TECHNOLOGY



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**Inventor of BFS** technology

1964 Start

- German and Swiss ٠ facilities
- Currently 1000 people ٠
- 30-50 machines per year ٠

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#### 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



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#### ROMMELAG CMO



#### **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





ROMMELAG ENGINEERING

# **BFS Basics**

Presentation Topic

25-05-22



### **BLOW/FILL/SEAL BASICS**



FORM



### **BLOW/FILL/SEAL BASICS**



FORM



### **BLOW/FILL/SEAL BASICS**



FORM



#### LINKS TO VIDEO



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

#### OPTIMIZING BFS FOR VACCINE TESTING (AND MANUFACTURING)

Equipment installed at Rommelag CMO is optimized to test vaccines for compatibility with BFS:

- 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

Filling mandrels Ampoule mold set

Punch



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



## CONCLUSIONS AND NEXT STEPS

- BFS process is ready to package vaccines
- Packaging concepts for more off-the-shelf packaging solutions direct injection, drop size regulation, etc. – continue to be developed
- 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

## THANK YOU

- Rommelag "Silver" Booth
- Questions

## SUPPLEMENTARY SLIDES

## AMPOULE CARD FOLDING MACHINE

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



WWWWWWWWWWWW

unfolded ampoule card



Unfolded 5-ampoule card just before picking



folded ampoule card



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

#### 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



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





