

VACCINE PACKAGING WITH BLOW/FILL/SEAL TECHNOLOGY: DEVICES, VACCINE COMPATIBILITY AND ECONOMIC CONSIDERATIONS

Developing Countries Vaccine Manufacturers' Network

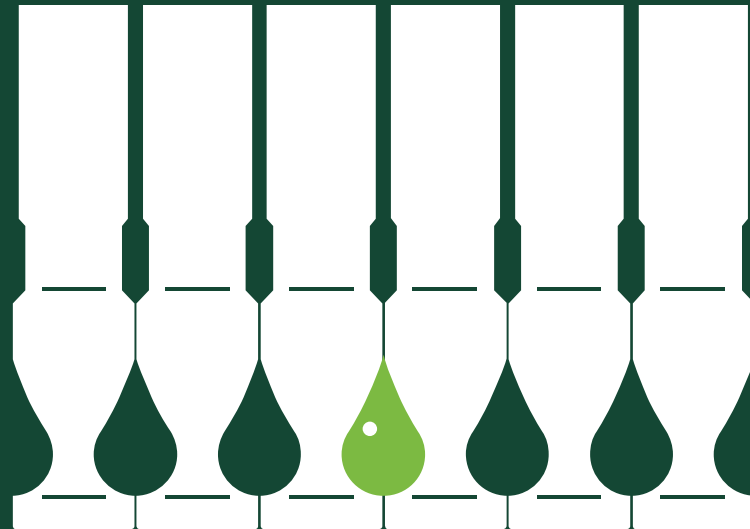
19th Annual General Meeting

29th October-1st November 2018

Kunming, China

Tim Kram, General Manager,
Rommelag USA, Inc.

Dr. Otto Schubert, Sr. Consultant
Rommelag CMO



ROMMELAG BLOW/FILL/SEAL ASEPTIC TECHNOLOGY



PRESENTATION OVER VIEW

- 1. General Introduction to Blow/Fill/Seal
Advanced Aseptic technology**
- 2. Blow/Fill/Seal, a world wide technology**
- 3. Vaccines and Blow/Fill/Seal**
- 4. Next steps**

ROMMELAG BLOW/FILL/SEAL TECHNOLOGY

TIM KRAM

Commitment to Aseptic Fill/Finish Technology



Innovators
Blow/Fill/Seal
Technology

850 People



Contract
Manufacturing
utilizing
Blow/Fill/Seal
950 People

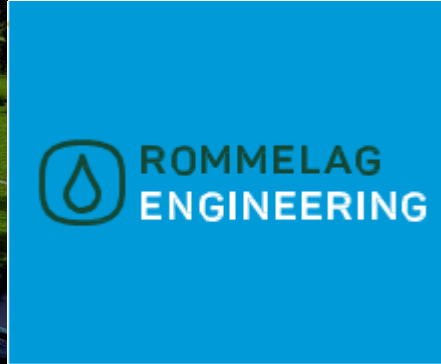
Bill and Melinda Gates
foundation grant

Develop New Delivery
Systems

Bill and Melinda Gates
foundation grant

Test Vaccines for
Compatibility



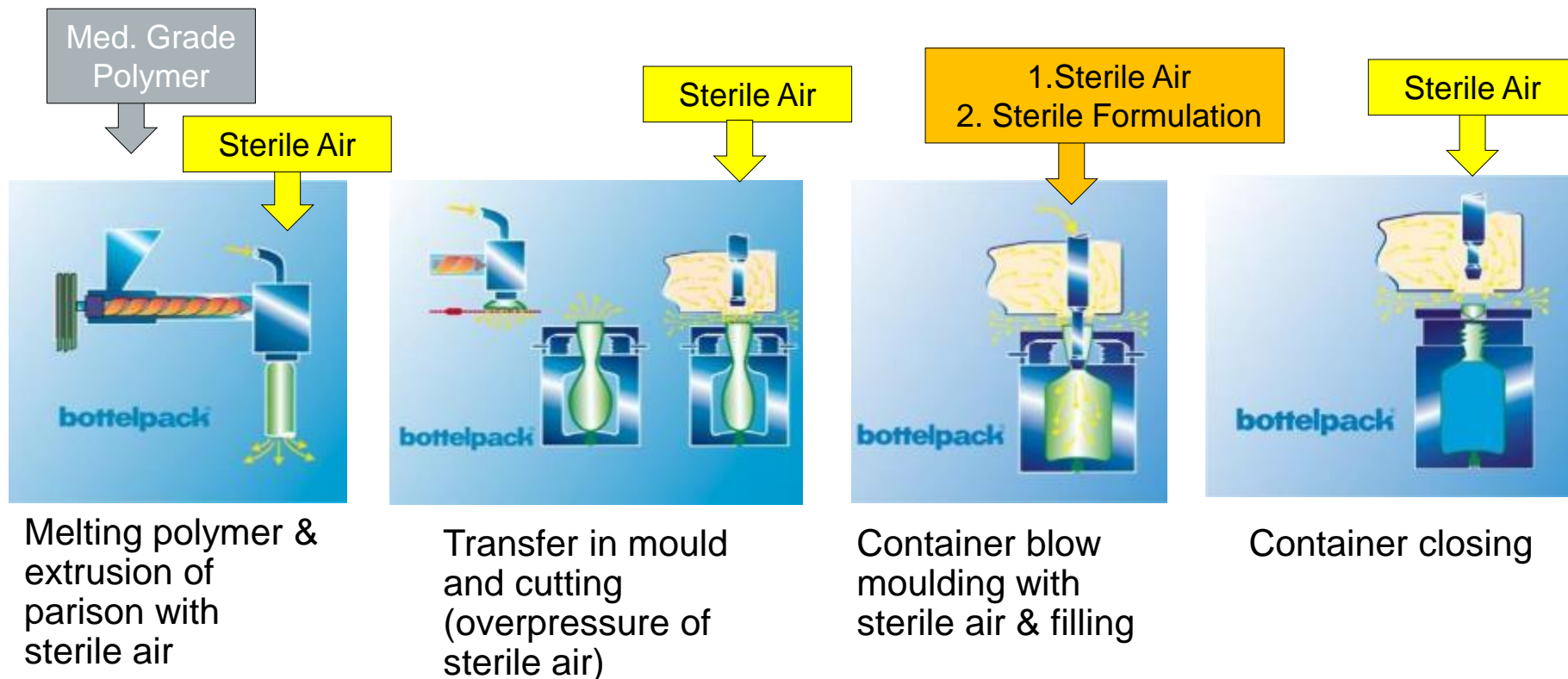


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BLOW/FILL/SEAL BASICS

BLOW-FILL-SEAL (BFS) PROCESS

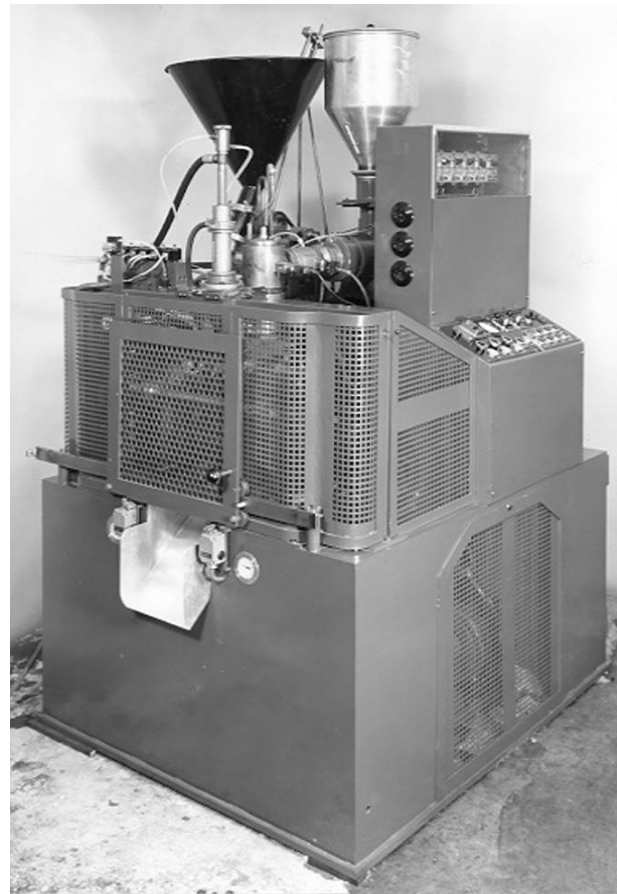
Blow/Fill/Seal Process: 4-13 seconds



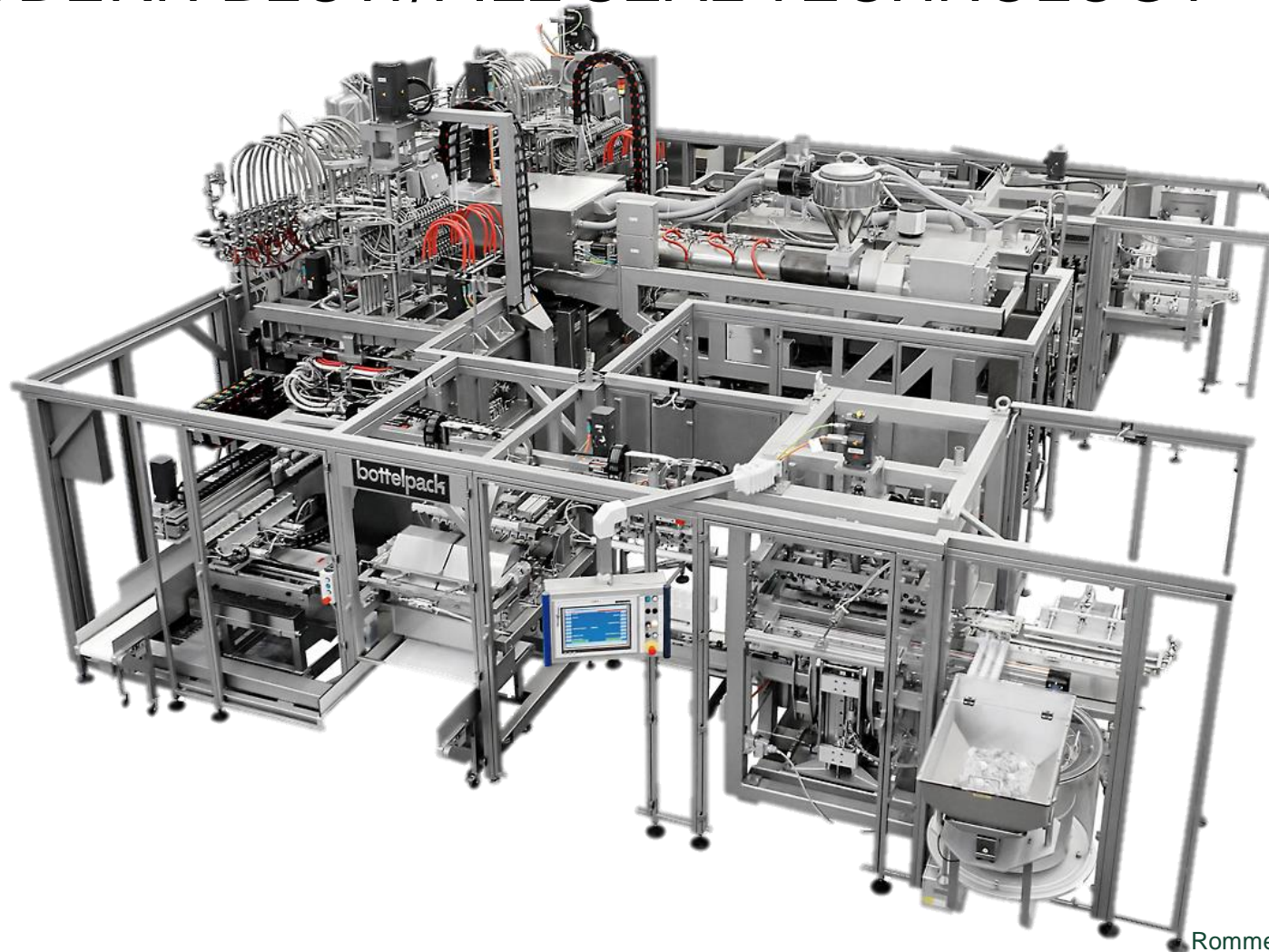
VIDEO SHOWING BFS PROCESS 430



1962 – GERHARD HANSEN AND BLOW FILL SEAL



MODERN BLOW/FILL SEAL TECHNOLOGY



WHY BFS TECHNOLOGY

ASEPTIC RISK REDUCTION

- Operators = Contamination Sources

“Blow-fill-seal (BFS) technology is an automated process by which containers are formed, filled, and sealed in a continuous operation. This manufacturing technology includes economies in container closure processing and **reduced human intervention...”¹.**

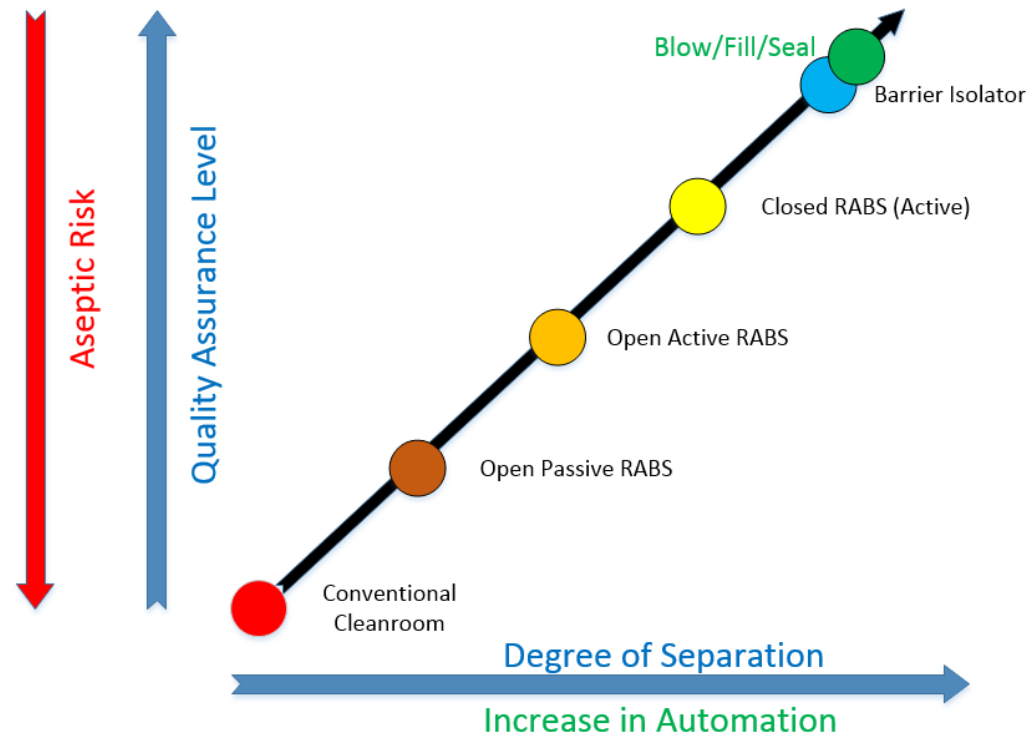


¹FDA *Guidance for Industry, Sterile Drug Products Produced by Aseptic Processing*
— *Current Good Manufacturing Practice*, 2004, Appendix 1, APPENDIX 2: BLOW-
FILL- SEAL TECHNOLOGY

ASEPTIC RISK REDUCTION – ADVANCED ASEPTIC PROCESSING

The FDA view...

- BFS, Isolators, cRABS
- Increased Quality
- Decreased Aseptic Risk
- Isolators and RABS increase separation
- BFS automation reduces contamination sources



COMPARING RISK: BLOW/FILL/SEAL TO CONVENTIONAL GLASS SYSTEMS

Conventional Glass	Blow/Fill/Seal Plastic
Glass Breakage	Robust container
Silicone contamination	Silicone not required
Preformed container, stopper, cap	Newly Created Container
Transport to facility	N/A
Storage – days/months prior to fill	N/A
Decontamination step	N/A
Aseptic filling	Aseptic filling
Capping in classified area	N/A
Known particle contamination	Very low particle load (10x <)
Multiple integrated systems	Single automated system

TRADITIONAL INJECTION METHODS WITH BFS



COMMON APPLICATIONS



Large Volume Parenterals LVP



Injectables - Small Volume Parenterals SVP



Respiratory Care Products, Inhalations



Multi-dose Ampoules
Unit-dose Ampoules



Eye Care, Nose Care, Ear Care,
Contact Lense Cleaning



Ointments, Enemas, Gels

COMMON BFS PRODUCTS



COMMERCIAL CONTAINERS FOR INJECTABLE PRODUCTS

LUER CONNECTION FOR SYRINGE

Rommelag CMO

- <1 mL
- Advanced Aseptic
- Other designs being developed
- Glass ampoule replacement



HISTORY OF BLOW/FILL/SEAL WITH VACCINES

VACCINE COMPATIBILITY – NASAL LAV VACCINE

2007-2010

Results: Q/LAIV-BFS was immunologically noninferior to T/LAIV because the upper bounds for all four 95% confidence intervals (CIs) for post-dose strain-specific GMT ratios were less than the predefined margin of ≤ 1.5 . Secondary immunogenicity outcomes, solicited symptoms, and AEs were also comparable.

Post Dose Ratio of Geometric Mean Titers (GMTs) of Hemagglutination Inhibition (HAI) Antibody

Strain	Q/LAIV		T/LAIV		GMT Ratio (T/LAIV / Q/LAIV)	
	N	GMT	N	GMT	Ratio	95% CI
A/H1N1	1176	8.1	586	7.7	0.95	0.87, 1.03
A/H3N2	1176	8.3	586	7.7	0.93	0.85, 1.00
B Yamagata	1176	60.3	294	54.1	0.90	0.79, 1.02
B Victoria	1176	27.4	292	26.7	0.97	0.87, 1.10

H1N1 & H3N2 data from 2 T/LAIV arms were combined for analysis

Conclusion: The immunogenicity and safety of Q/LAIV-BFS, as defined in this study, were comparable to those of T/LAIV in adults.

This study was sponsored by MedImmune.

VACCINE COMPATIBILITY – ORAL ROTA LAV

2012

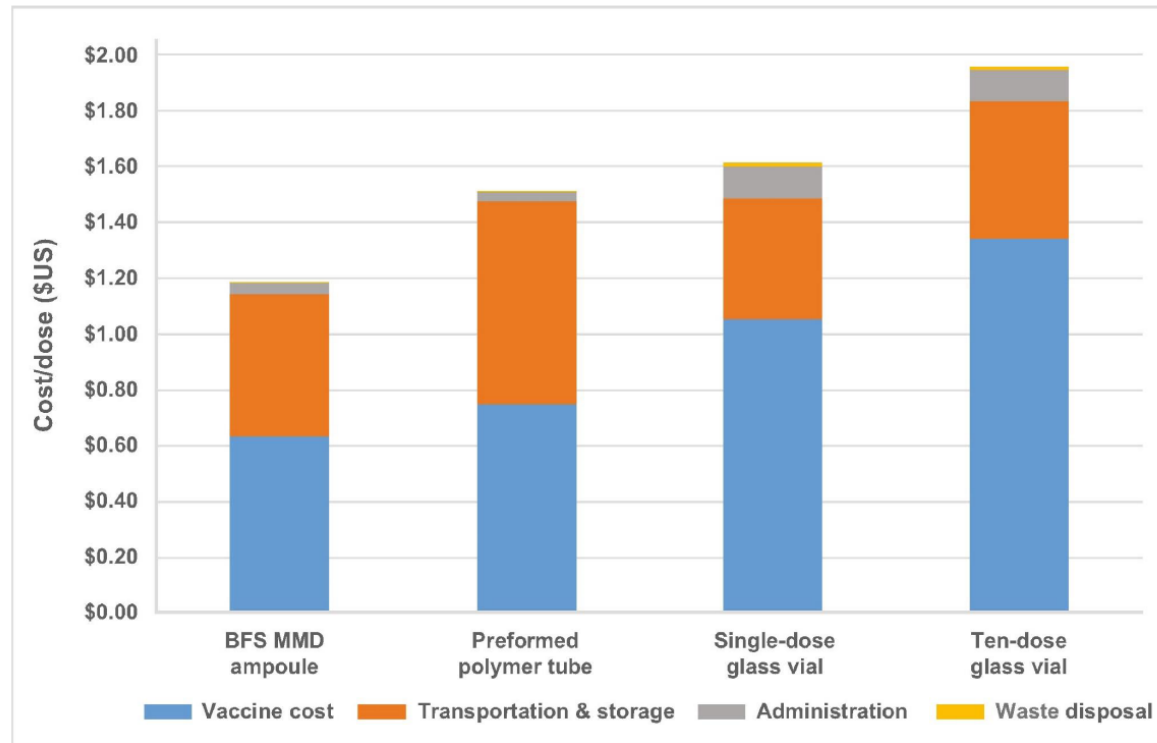
- Multiple vaccines tested
- Statistically no difference between BFS and existing packaging
- Existing prefilled plastic tube
- GSK Australia converting to BFS



GlaxoSmithKline Australia VP and General Manager Geoff McDonald in the new vaccine facility. Picture Aaron Francis

PATH DEVELOPED PRODUCTION COSTS

Total cost of delivery – Rotavirus vaccine



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Abbreviations: BFS, blow-fill-seal; MMD, multi-mono-dose.



BILL AND MELINDA GATES FOUNDATION GRANTS

VACCINES: WHY BLOW FILL SEAL

Container development grant

- Single dose per container:

- No preservatives
- Low wastage
- Low breakage
- Small cold chain footprint

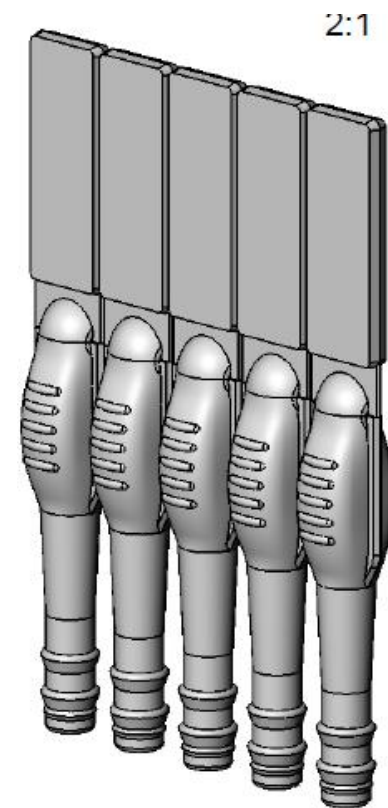
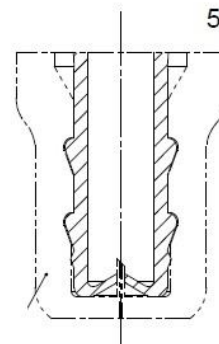
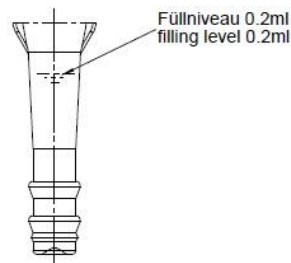
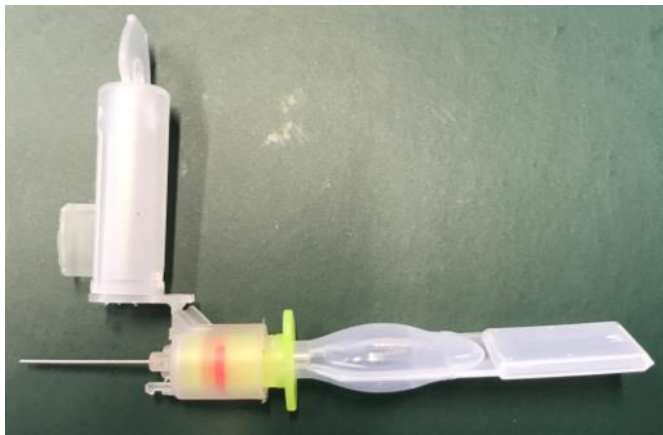
- Low Cost of Goods

- Vaccine compatibility



CPAD DEVELOPMENT GRANT

- **ApiJect Concept container**
 - Double needle design
 - Existing BFS container design



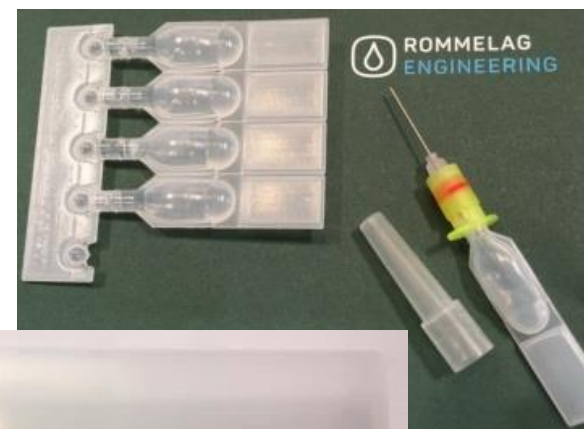
GLOBAL GOOD DESIGN – REDUCED CONTAINER SIZE OPTIMIZED FOR COLD CHAIN



GRANT TO DEVELOP NEW DELIVERY FORMS

Rommelag Engineering

- CPAD – Compact Auto Disable Device
- Replacement for single dose glass vial
- Rommelag Multi-Mono Dose Design



VACCINE COMPATIBILITY – INJECTABLE

Feasibility Assessment of Novavax RSV F vaccine with Maropack Cold BFS Process in Global Good Design Ampule

- Objective
 - Provide feasibility assessment on aluminum phosphate adjuvanted RSV F vaccine in BFS as a potential WHO product presentation, with funding from Bill and Melinda Gates Foundation to Rommelaag and Maropack.
- Scope
 - Primary: Evaluate aluminum phosphate adjuvanted RSV F vaccine compatibility/stability, potential leachables with BFS containers.
 - Stretch: Evaluate BFS fill system compatibility with recirculation system
- Outcome: Recommending further developing BFS as a potential WHO Product Presentation
 - RSV F vaccine stability profile in BFS similar to profiles in glass vials and syringes
 - Minimal concern on potential leachables in simulated leachable study
 - BFS fill process compatible with a recirculation system critical for uniformity control



VACCINE COMPATIBILITY – INJECTABLE

Feasibility Assessment of Novavax RSV F vaccine with Maropack Cold BFS Process in Global Good Design Ampule

- Feasibility study with Global Good BFS ampule design
 - 9 month/2-8 °C stability testing completed; continuing to 24 months
 - Stability profile in BFS, by ELISA, RP-HPLC, SDS-PAGE, similar to profiles in glass vial and PFS
- Further development of BFS container
 - Modify design to fit with WHO pre-qualified auto-disable syringes
 - Design target: similar use experience to glass vial
 - User Requirements Specification based on
 - Lesson learned from current BFS field study
 - WHO Generic Preferred Product Profile for Vaccines
 - Assessing programmatic suitability of vaccine candidates for WHO prequalification
 - WHO Immunization in Practice
 - WHO Cold chain preference & vaccine vial monitor implementation

INVENTPRISE VACCINE TESTING

Rommelag CMO

- Successful stability trial
 - Injectable vaccine
 - Containing adjuvant
-
- Supported by Global Good



NEXT STEPS

Global Good next generation design

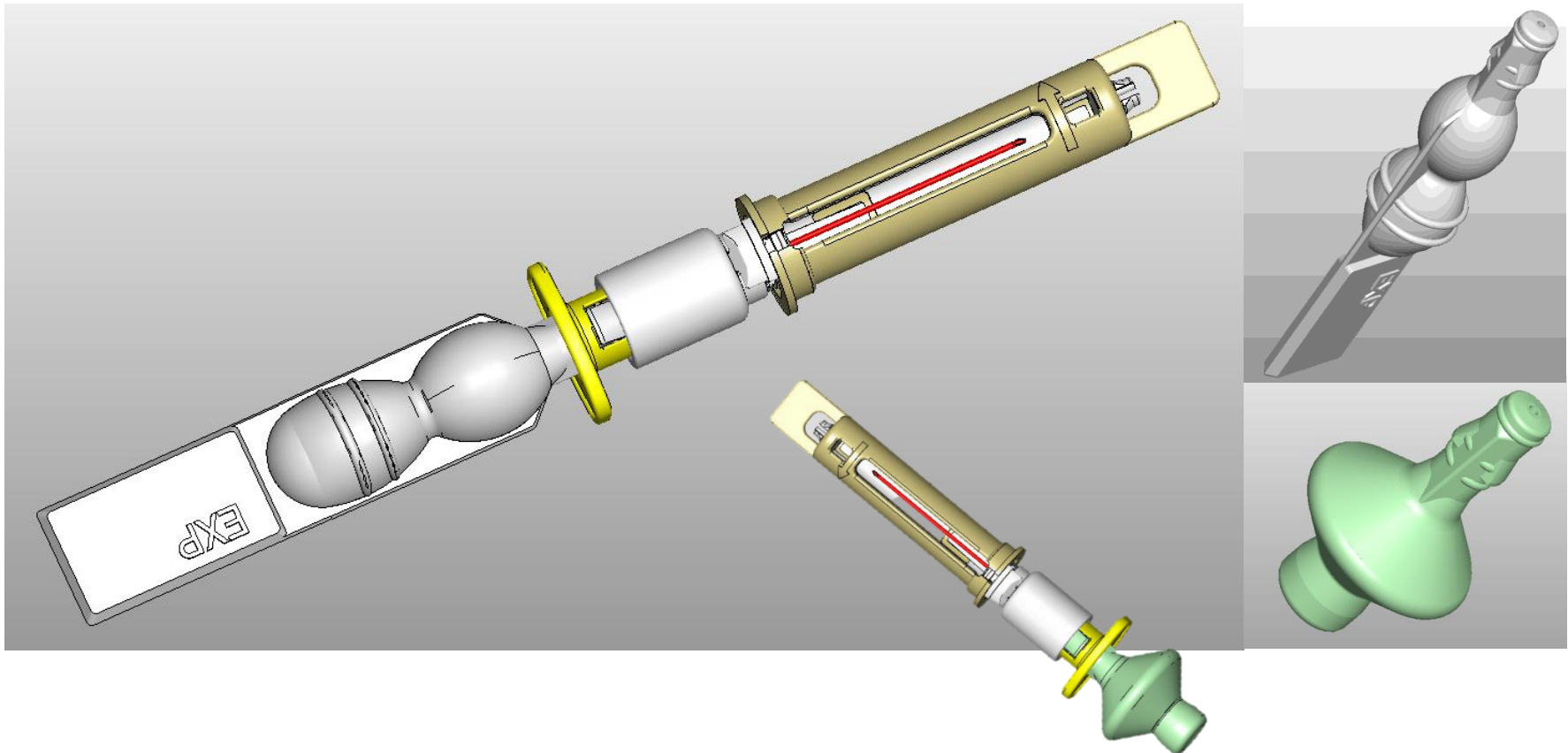
- cGMP system being built
- Capable of human trials
- Increased processing capability
- Cold chain capabilities
- Available to everyone



NEXT STEPS – NEW GRANT WORK

CPAD DEVICE – COMPACT AUTO DISABLE DEVICE

ApiJect development



NEXT STEPS

ROMMELAG CMO – DEDICATED TESTING SITE

FDA inspected facility

- Platform for trials
 - Clinical
 - Technical
- Dedicated biological facility
- Disposable filling system
- Commercial production capability



NEXT STEP



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