Poster #72

Feasibility Evaluation of Blow Fill Seal Process and Compatibility with Aluminum Phosphate Adjuvanted Recombinant RSV F Nanoparticle Vaccine

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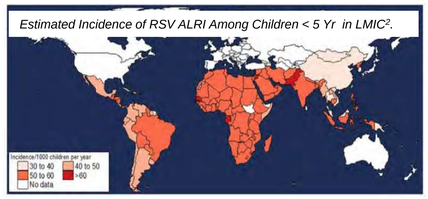
INTRODUCTION

Respiratory syncytial virus (RSV) is one of the common causes of childhood acute lower respiratory tract infections (ALRI) in infants and young children worldwide.

In a 2015 analysis, six million estimated episodes of RSV-severe ALRI occured in children younger than 5 years of age in low-income and middle-income countries (LMIC). The overall RSV-ALRI mortality was estimated to be as high as 118,200. In children younger than six months, 1.4 million hospital admissions and 27,300 in-hospital deaths were due to RSV-ALRI[1].

ResVax (Pre-fusogenic RSV F nanoparticle vaccine) is currently being assessed in the Prepare™ (Phase 3) trial for the protection of infants via maternal immunization in healthy third trimester pregnant women.

To ensure cost effective and cold chain efficient vaccine for LMIC, a novel product presentation is needed in contrast to conventional glass vials and syringes.



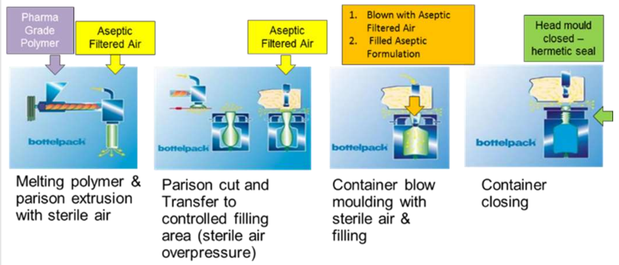
CONCLUSIONS

- Product uniformity can be achieved using the BFS technology.
- The stability profile of RSV F nanoparticle vaccine in BFS under accelerated and intended storage conditions appears comparable to the profile in glass vials and syringes.
- The result of this feasibility assessment provides data to enable a potential cost-effective product presentation of the RSV F nanoparticle vaccine for WHO pre-qualification pathway.

REFERENCES

1. Shi T *et. al.* Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet 2017 390(10098): 946-958.
2. PATH The global respiratory syncytial virus burden 2017. https://www.path.org/publications/detail.php?i=2810; accessed Feb 2018
3. PDA Technology Report No. 77: The Manufacture of Sterile Pharmaceutical Products Using Blow-Fill-Seal Technology 2017.

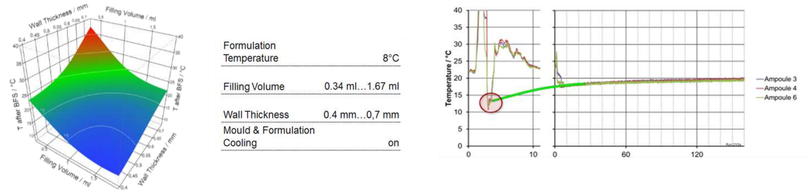
BLOW-FILL-SEAL (BFS) TECHNOLOGY



Estimates	2mL Vial	1mL Standard Pre-filled syringe	Blow-Fill-Seal containers
Relative Fill Process & Components Cost	Medium	High	Low
Relative Product loss (process, container & use)	High	Low	Low
Primary container weight	6-7 g	6-7 g	1 g
Cold Chain Volume	~20 cm^3/10 doses	~60 cm^3/10 doses	~10 cm^3/10 doses

- BFS technology[3] has been a robust method to produce aseptic pharmaceuticals since the late 1960's.
- In the past, the technology was not generally feasible for protein based biopharmaceuticals and vaccines due to elevated process temperature.
- Drivers to use BFS technology for vaccines include high throughput production, single inventory supply chain (only resin; no vial or syringe components), and a lower storage volume requirement.

Advances in Controlling BFS Process Temperature Enable Application for Protein Based Biopharmaceuticals and Vaccines



The data above show the temperature profiles within the mould and inside the ampoule. The BFS process with cooling shows that temperature can be controlled within a range that is acceptable for proteins.

FEASIBILITY ASSESSMENT OF ALUMINUM PHOSPHATE ADJUVANTED RSV F VACCINE WITH BLOW-FILL-SEAL

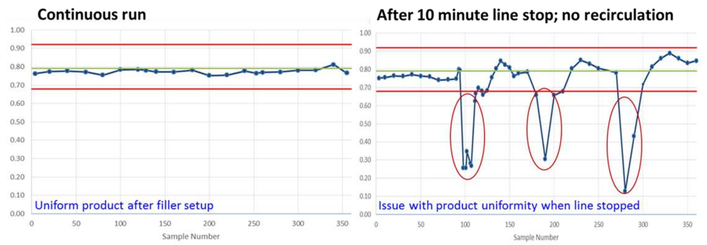
Objective

- Evaluate BFS technology for product compatibility and process feasibility with aluminum phosphate adjuvanted RSV F nanoparticle vaccine.
- Enable data driven decision for potential cost effective product presentation for WHO pre-qualification pathway.

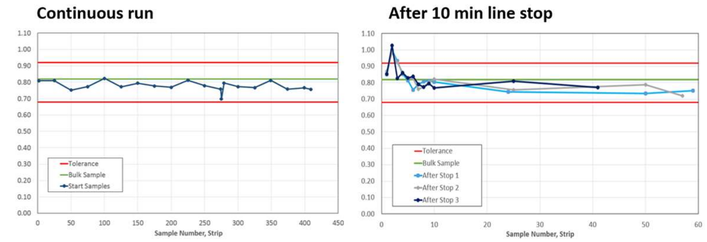
Process Control Challenge with Aluminum Phosphate Adjuvanted Product

To avoid product uniformity issues aluminum phosphate particles need to be continuously mixed in a product holding tank and continuously recirculated in the fill line.

Process Control for Fill Uniformity with BFS Technology Is Feasible



Fill Uniformity Further Improved with Recirculation Loop



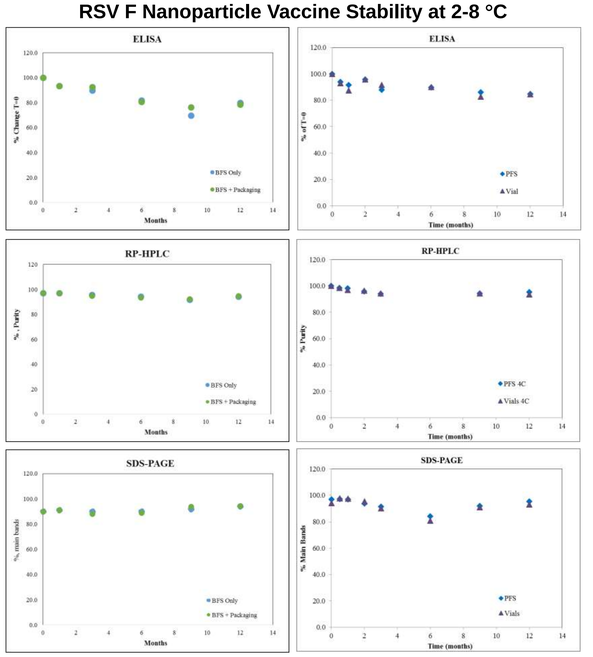
Stability Testing with and without Moisture/Gas Barrier Secondary Packaging

Temp	Test	Time 0	1M	3M	6M	9M	12M	18M	24M
2-8°C	ELISA		x	x	x	x	x	x	x
	A280		x	x	x	x	x	x	x
	Appearance		x	x	x	x	x	x	x
	SDS PAGE		x	x	x	x	x	x	x
	RP-HPLC		x	x	x	x	x	x	x
25°C	ELISA		x	x					
	A280		x	x					
	Appearance		x	x					
	SDS PAGE		x	x					
	RP-HPLC		x	x					
37°C	ELISA		x						
	A280		x						
	Appearance		x						
	SDS PAGE		x						
	RP-HPLC		x						

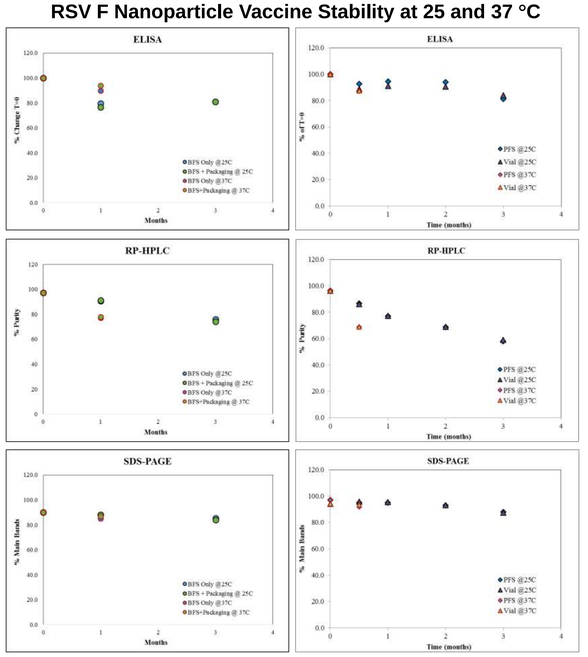
Limited water loss even if BFS containers were not stored in gas / moisture barrier secondary packaging

Storage Conditions	Water Loss per Month
2-8 °C	0.03%
25 °C	0.39%
37 °C	1.35%

RSV F Nanoparticle Vaccine Stability at 2-8 °C



RSV F Nanoparticle Vaccine Stability at 25 and 37 °C



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Conflict of Interest Disclosure: YHL, EO, RH, SB, KP, EW, and TH are employees of Novavax, Inc. TK is an employee of Rommelag USA Inc. SG and YS are employees of Maropack AG. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter of materials discussed in the poster apart from those disclosed.