Rotavirus liquid vaccine in plastic ampoules
A success story

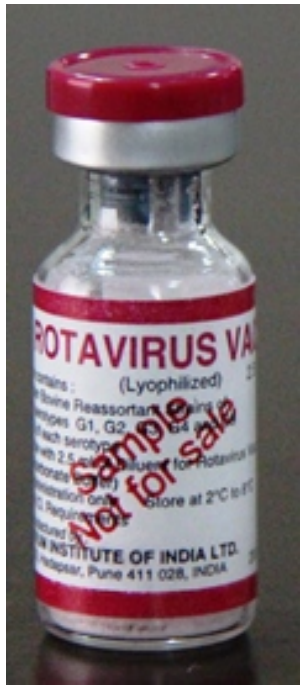
Workshop on New packaging technologies

DCVMN – 11 May 2022

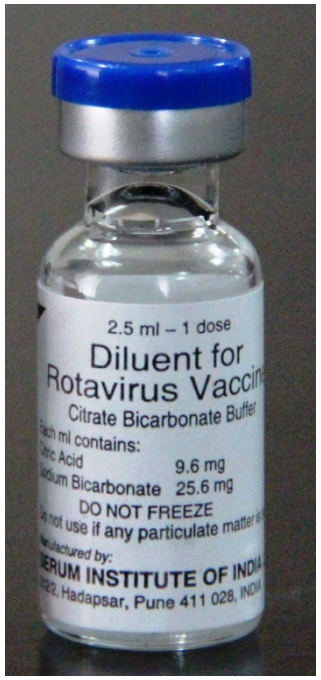
Scope

- What we had to start with in the Rota space
- Basis of change to new packaging
- Elements of the journey to implement change
- Final comparisons

What we had - Single dose, Lyophilized



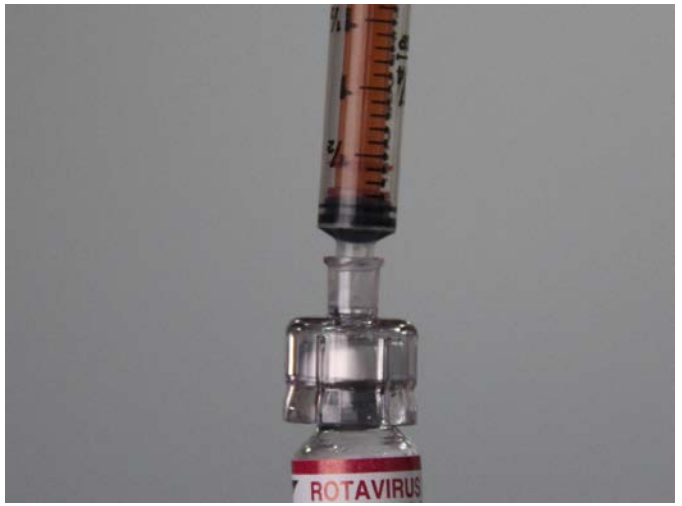
Single dose Lyophilized vaccine in a 40 mm high vial



Diluent of citrate – bicarbonate buffer in a 40 mm high vial

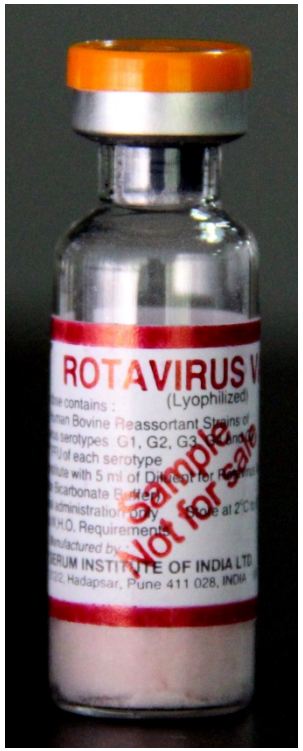
3 mL Oral syringe (Needle will not fit)

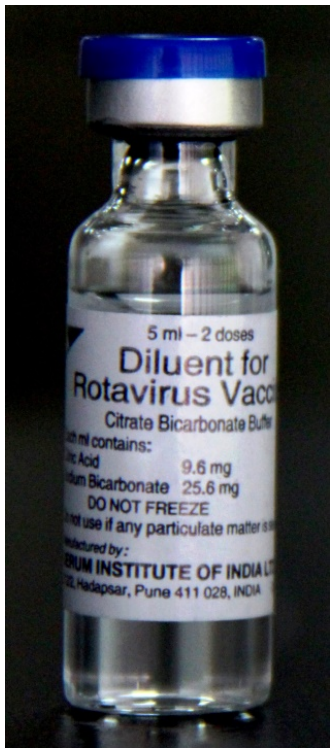
An adapter to enable the transfer of diluent and vaccine.

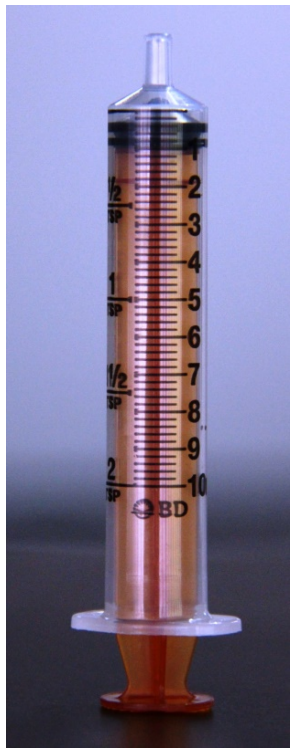


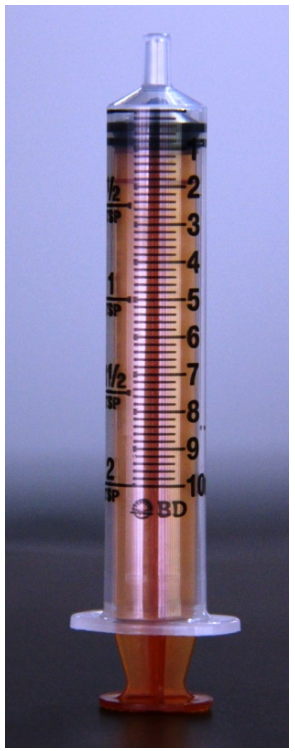
Reconstitution of the vaccine.

What we had -Two dose, Lyophilized



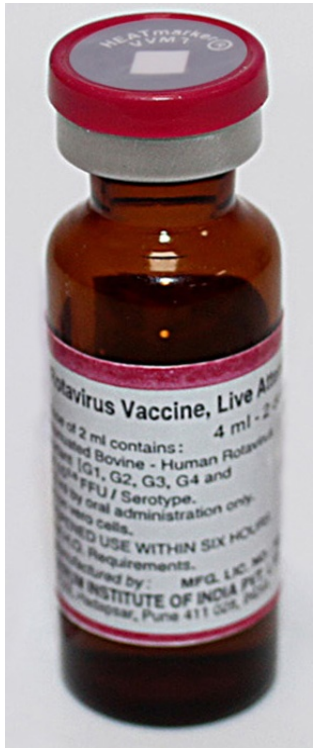


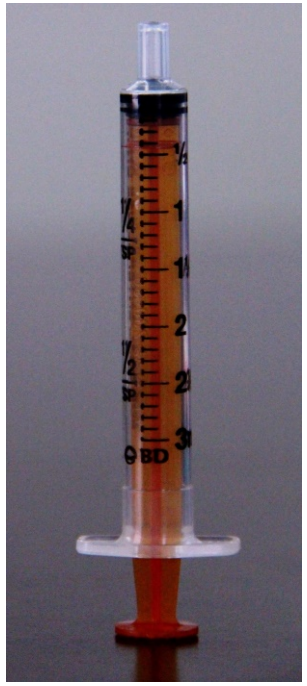




As compared to 1 dose Lyophilized	Vials are taller – 50 mm
	2 syringes of 6 mL
	(To be able to transfer 5 mL diluent)
	Vial adapter
Mainstay of the procurement by UNICEF	
Presently we are seeing a switch from 2 dose Lyo to 2 dose liquid	

What we have Liquid – 2 dose and 1 dose



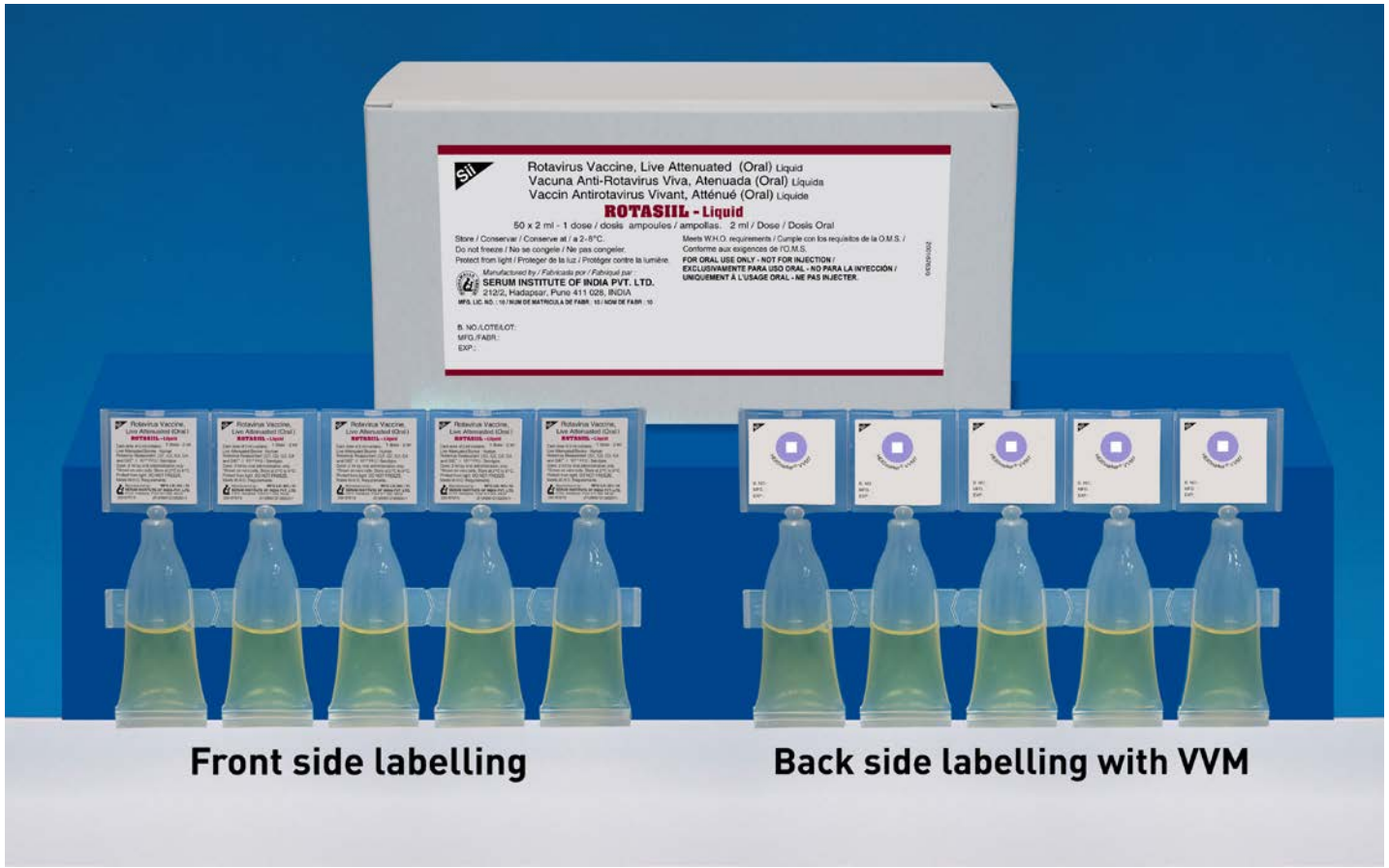


As compared to 2 dose Lyophilized, the 2-dose liquid has

- No diluent
- 2 syringes of 3 mL (Not 6 mL)
- Vial adapter

As compared to 1 dose Lyophilized, the 1-dose liquid has no diluent, rest are identical

Rota 1 dose in plastic ampoule: No accessories. Where we went



Basis of change

Serum Institute was successful in creating a vaccine that was heat stable. (Storage conditions: at or below 25°C for 30 months)

However, the market feedback was – though heat stable, a liquid, ready to administer format was preferred

Basis of change

The need for a container that doubled up as an administering device meant that a plastic container was appropriate.

This meant buying new dedicated equipment – a major change in the working strategy of Serum Institute – to work with vial lines that are easy to interchange with other products.

Though such an approach would decrease the fungibility of the line, Serum decided to go ahead with the decision to switch to a plastic container

The main elements of the journey

Stability in plastic	Select the method of manufacturing	Container Design
Worked out the sterilization approach – Overkill vs Bioburden	Small scale for tox and clinics: Hired equipment with low footprint	Design line for final commercial facility

Stability in plastic

- Based selection on plastic used in IV Fluid industry:
  Cleanest plastic as Terminal sterilization and large volume dose make this the highest risk application.
- Established compatibility:
  Filled product in pre-formed kits available with Rommelag made from Low Density Polyethylene (LDPE).
- Ensured compatibility with more than 1 source:
  Purell and Sabic

Select Method of manufacturing - options

The Rommelag / Weiler type equipment where plastic containers were created within the filling equipment, then filled with product and then sealed. (Blow-Fill-Seal)

The IMA / TM s.r.l type equipment where plastic containers were purchased sterile from Lameplast / Bisio Projetti, then filled with product and then sealed.

Select method of mfg - The decision

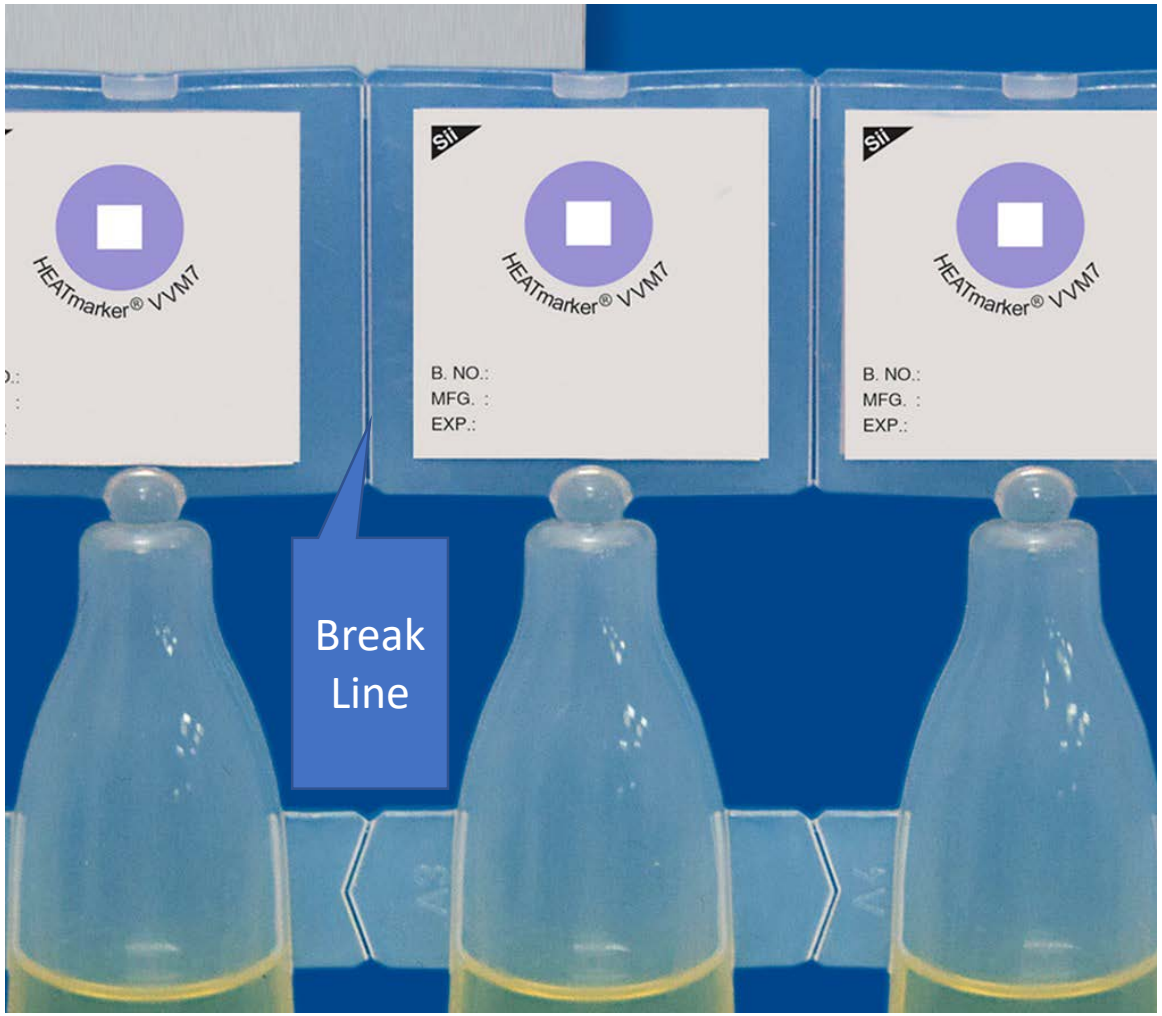
Based on 3 factors, Serum Institute **opted for the approach of using pre-formed containers**:	No high temperature exposure of the product during the formation of the container which has to be hot enough to seal it after filling
	Floor loading factor which is lower (there was no vacant facility with the higher loading factor)
	Ability to hire and retrofit small scaled down versions of the equipment for the preparation of clinical batches, pending the commercial facility getting ready

Container design

Labeling on body or on Twist off tab. We opted for labeling on the tab as plastic is permeable and we did not want to work to prove that the label/ink adhesive would not migrate.

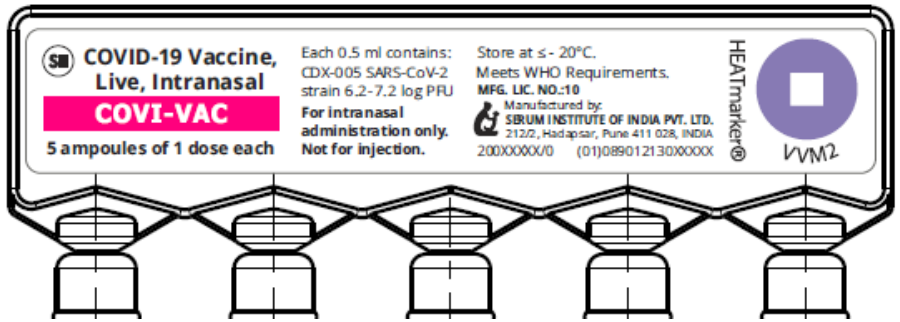
Container design- VVM

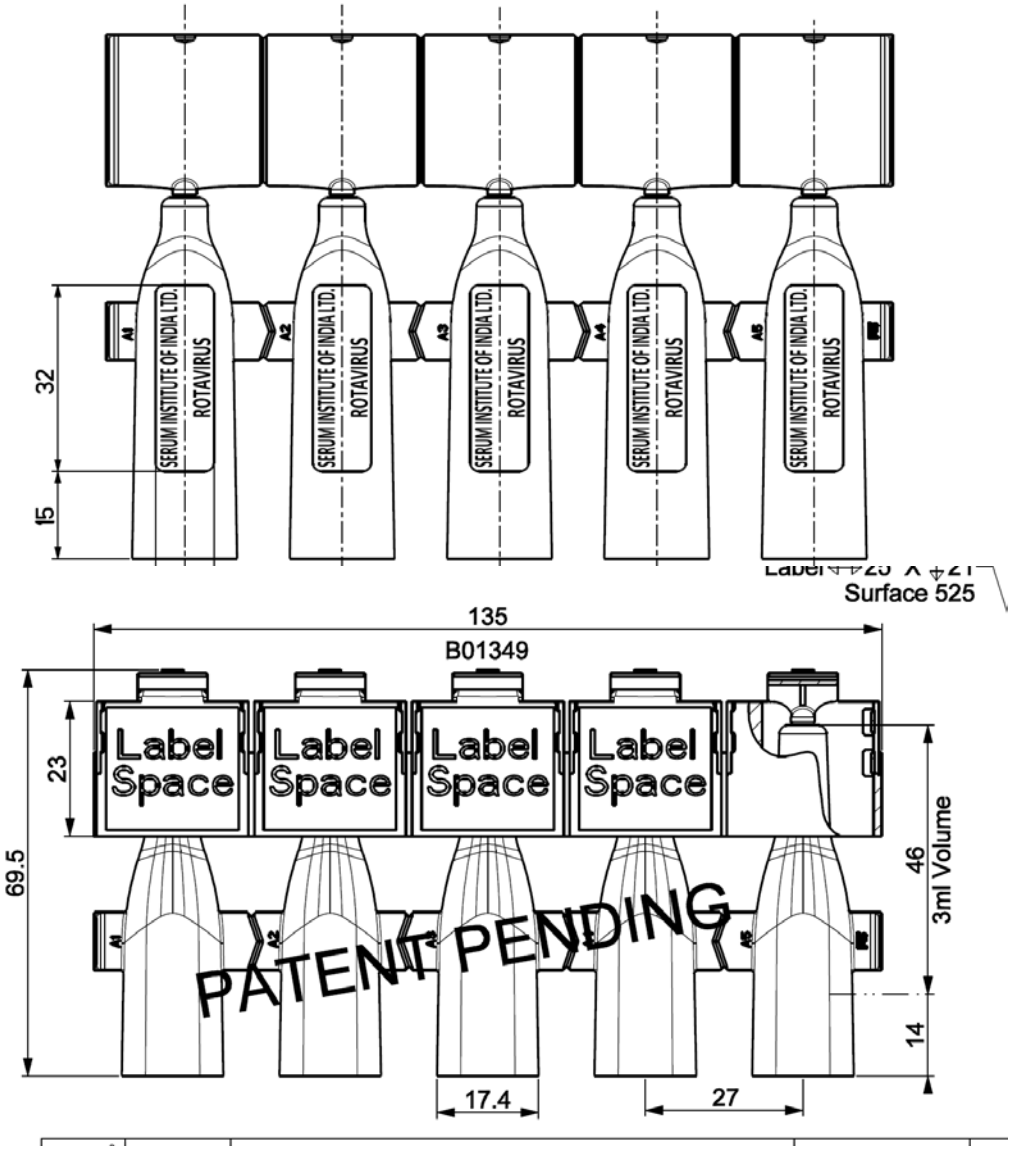
Rules state that every container should have a VVM. There was an option to put 1 VVM on a common tab to the strip of 5 plastic ampoules, with the ampoule being detached and opened at the same time so that it has to be used. We opted for individual tabs rather than common tab so that the product could be sold as a single ampoule in the trade market rather than a strip of 5 ampoules

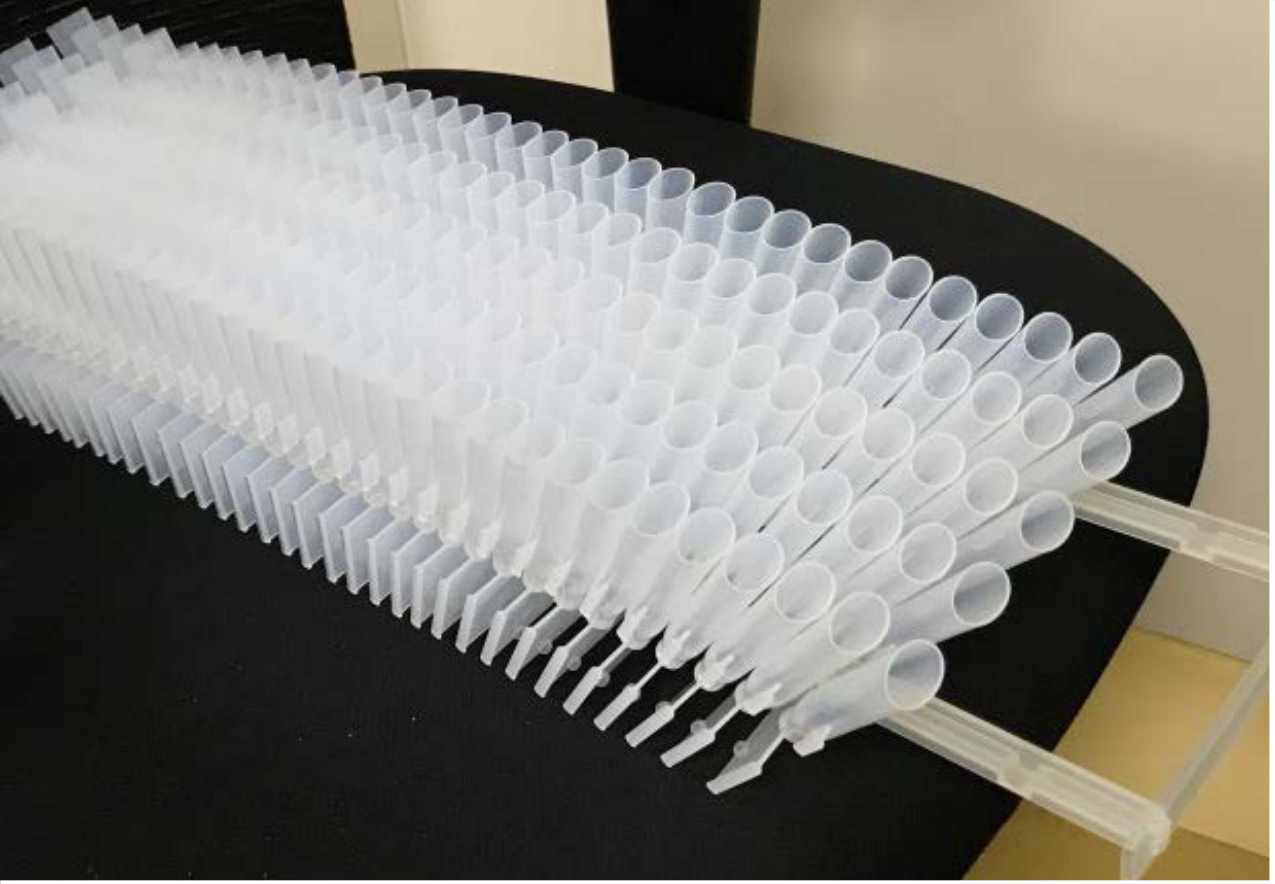


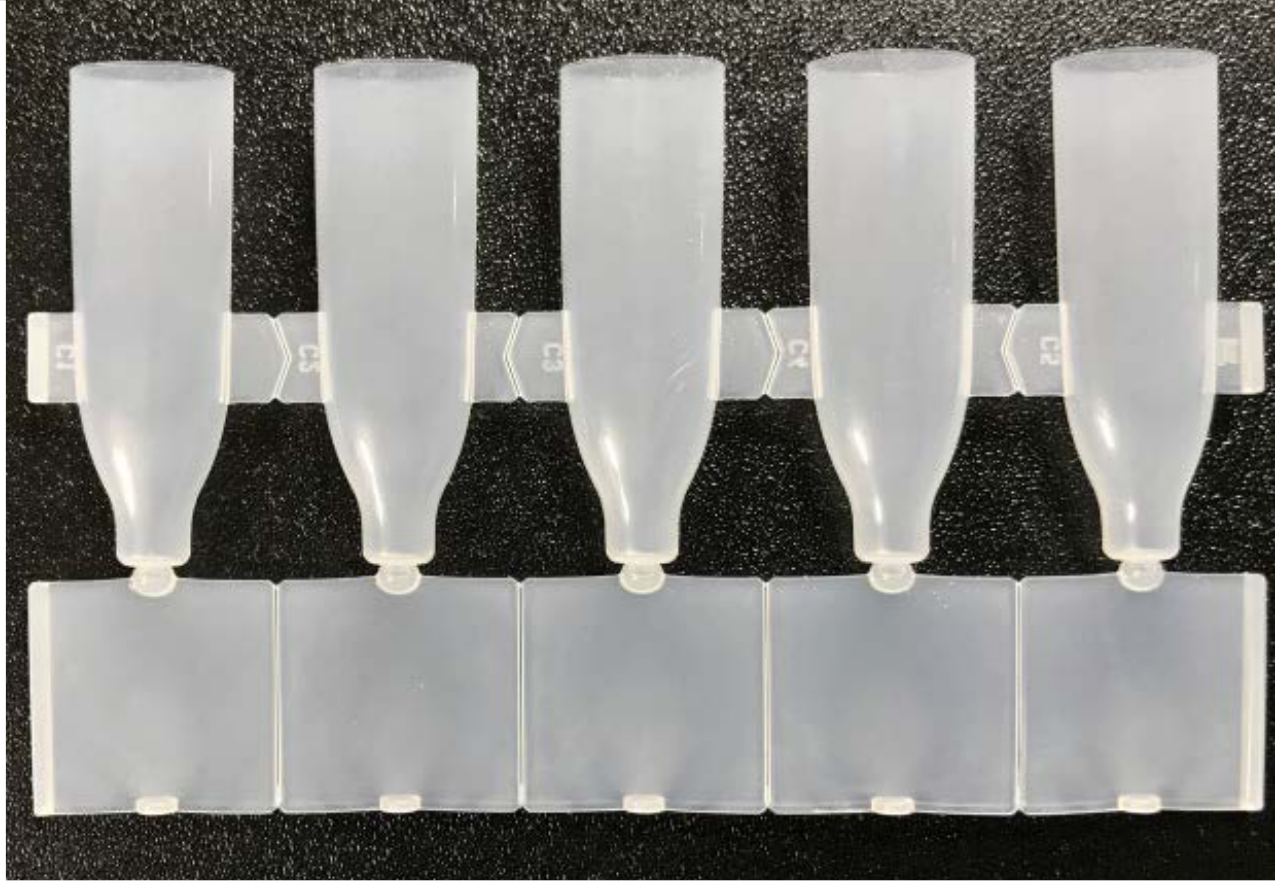
Container design-Other

- Options to engrave- Not selected by us as it would obscure the inspection of contents
- Option to reduce height by adding a separate label space, not opted by us due to a drastic rise in complexity of labeling
- Example of single tab VVM









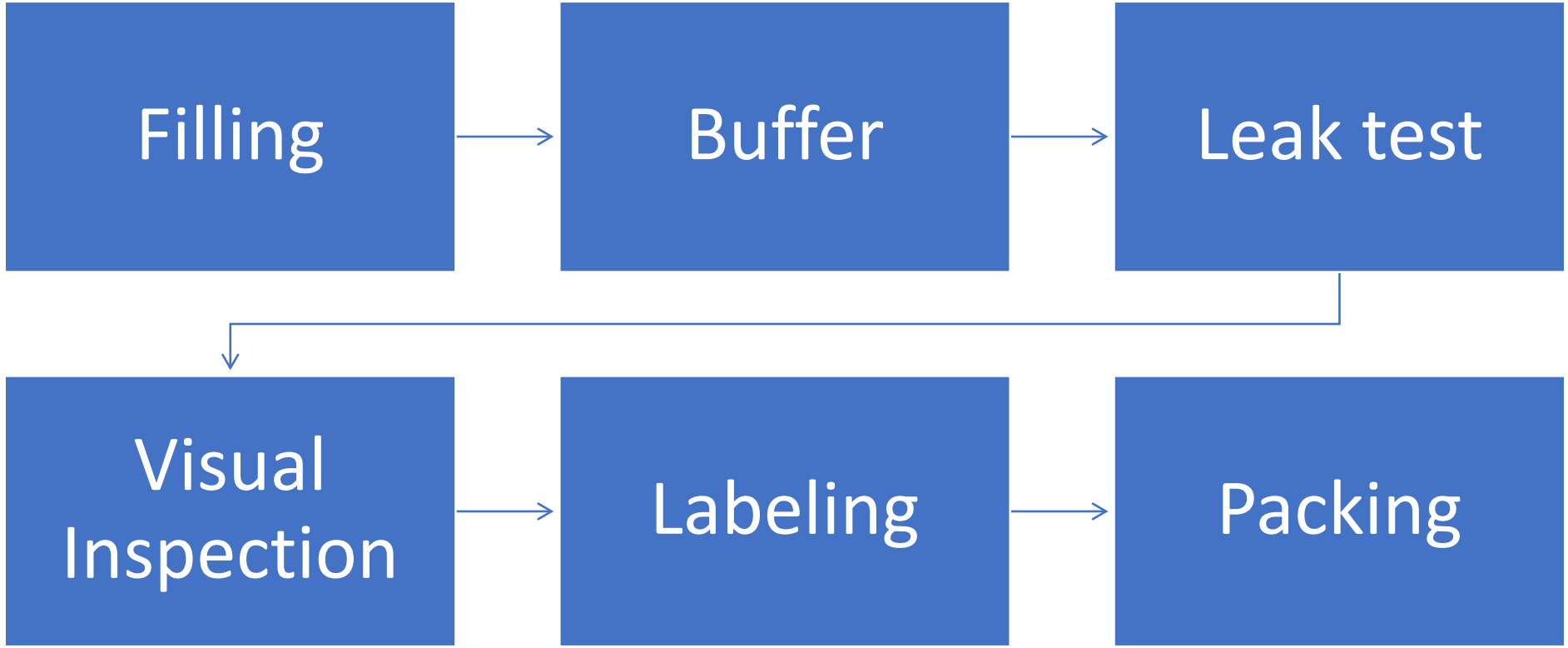
Empty containers –
Sterilized by Gamma radiation at 25 kGy, triple bagged

Design considerations – Commercial line

Going by the nature of the container – A packing line ‘On-line’ with the filler was the considered option. Most lines we saw were designed this way.

- **Buffer system:** To prevent stoppage of filler during a stop from the packing line
- **On-line leak testing:** We decided on 100% leak testing. Challenges included evaluating the impact of High voltage on virus
- **Visual inspection:** For gross particulates – Manual inspection
- **Labeling:** The tabs need both side labeling given the amount of text required by the Indian laws and VVM
- **Overwrap:** Initially included in design and later deleted as stability indicated it was not required

Elements of the commercial line



Operational Aspects – Loading empty containers

View of the Filling room

Final comparisons Volume per dose

Presentation	1 dose 'cm³/Dose'			2 dose 'cm³/Dose'		
	Below 25°C	2 to 8°C	Ambient	Below 25°C	2 to 8°C	**Ambient**
Lyophilized, 25°C, VVM250	17.6	NA	132	10.6	NA	105
Lyophilized 2 to 8°C VVM30	NA	17.6	132	NA	10.6	105
Liquid Vial 2 to 8°C VVM7	NA	17.6	105	NA	10.6	82
Liquid Ampoule 2 to 8°C VVM7	NA	20.06	NA	NA	NA	NA