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Multidose Prefilled Pouches for Pandemics

Developing Countries Vaccine Manufacturers Network: Event Seminar

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8th April 2021

A global partnership

Vision

A world where epidemics are no longer a threat to humanity

Mission

To accelerate development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks

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Our strategic objectives

Preparedness

Advance access to safe and effective vaccines against emerging infectious diseases

Response

Accelerate the research, development and use of vaccines during outbreaks

Sustainability

Create durable and equitable solutions for outbreak response capacity

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Innovation in a time of crisis for LMIC deployment

Technologies not yet licensed, may have application/s, accelerated in Covid-19 context

By Q4/2021 innovations*:

- Blow fill seal technologies
- Multi-dose bag systems

Next generation innovation:

- Micro-array patches
- Oral delivery
- Thermostable formulation

Key trade-off:

Perceived public health need and potential impact (e.g. hesitancy) vs realistic timeline and product profile

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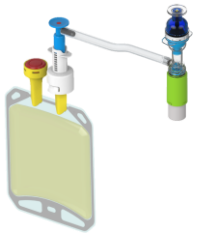
Abbreviations: LMIC, low-and-middle-income countries; *in development having good acceptance and user profile

Vaccine drug product approach to achieve billions of doses

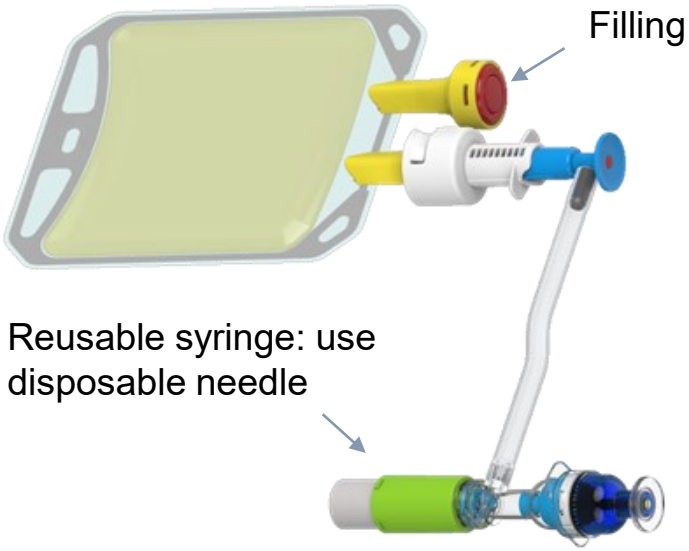
Resolution in-process | Aspects to resolve, design space

	Capacity and costs	Usability and acceptance	Access
Single-dose vial 	Insufficient capacity (vials, F/F, cold chain, …)	Standard, high quality solution	Limited F/F and cold chain capacity
Multi-dose vial (20 doses) 	Up to 2 BN doses Issues: wastage and need for syringe	Standard accepted solution, limited time of use	Global DP manufacturing network
INTACT™ 200-dose bag 	Up to 1.5 BN doses Low wastage, no need for syringe, low cold-chain footprint	Novel solution, introduced to users and regulators	Flexible and fast placement of fillers in region of choice
Blow-fill-seal 	Requires evaluation for LMICs	Requires compatibility testing, significant process development	COGS well suited for worldwide access

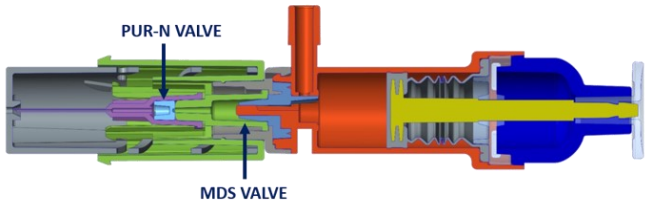
Approach to achieve BN of doses reveals gaps that drive opportunities for innovation/s

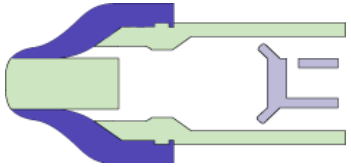
Abbreviations: BMGF, Bill & Melinda Gates Foundation; COGS, cost of goods sold; F/F, fill-finish; DP, drug product

Multi-dose pouch (INTACT™ Solutions)



1-way valve is anti-retro-contamination





One-way valve in multi-dose syringe

1. Secure disposable needle

2. Administer vaccine

3. Dispense needle

See YouTube video: Socially Distanced Vaccination

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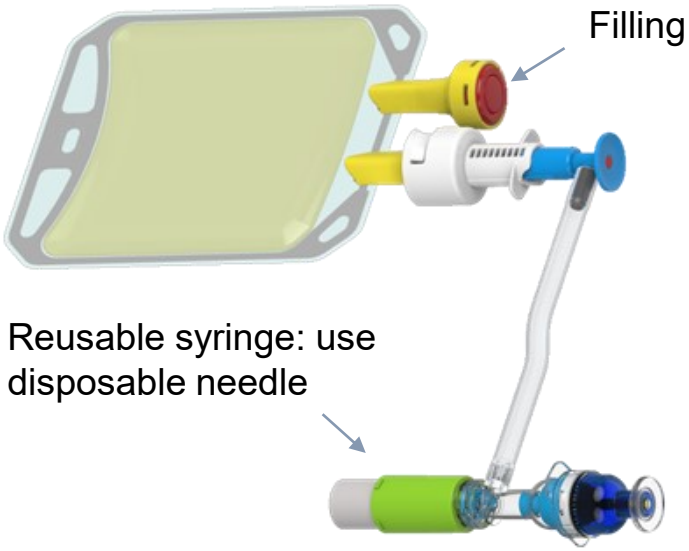
Multi-dose pouch (INTACT™ Solutions)



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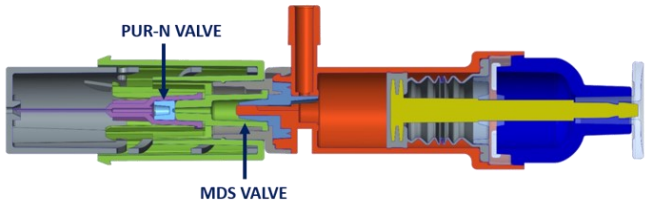

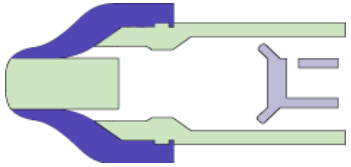

One-way valve in multi-dose syringe

INTACT™ Solutions platform

- Multidose container for mass vaccination, enables rapid administration, lower cold chain footprint per dose
- One-way valve, prevents ingress of contamination into the container as doses are dispensed
- Could significantly expand F/F capacity for C19 vaccines through use of 200-/400-dose pouches and alternative filling facilities
- Fillers can be installed flexibly at existing CMOs, low environmental requirements and high capacity

Technology status

- Advanced prototypes with COVAX engagement
- PATH HCD simulated use evaluation ongoing (Seattle, Kenya, Zambia)

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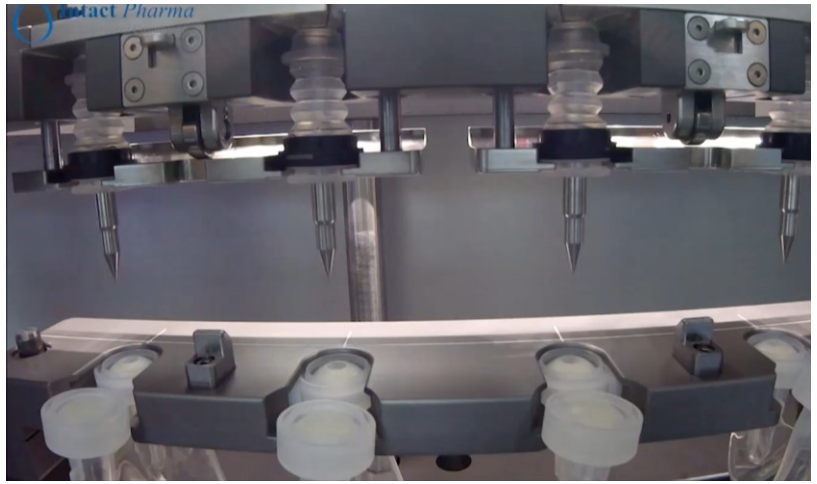
Abbreviations: HCD, human centered design; F/F, fill-finish; CMO, contract manufacturing organizations

Pause, any initial questions, handover to Renske

Why use INTACT™ multidose bag?



Speed

- Rapid filling at 4000 doses/minute
- Fast and flexible installation of filling equipment in ISO 8 / class D environment

Scale

- Creates new Drug Product capacity, no dependency on glass vial supply
- One filler can fill 1.5BN doses/year

Access

- Rapid mass vaccination with PFS-like ease of use
- Sterility and dose accuracy assured
- Cost effective with low cold chain footprint

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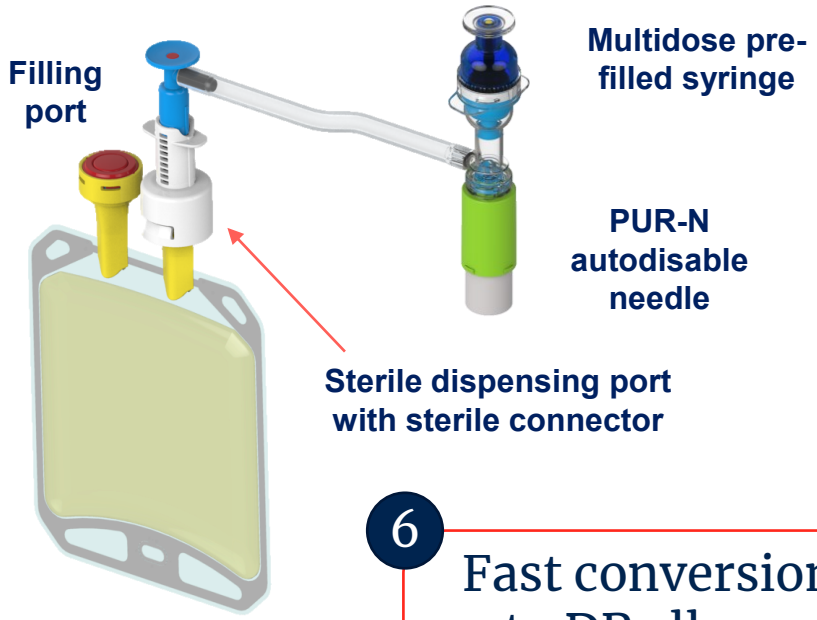
The multidose prefilled syringe for pandemics

1. Ease of use: PFS that refills itself, valve prevents backflow

2. Accurate dosing for every subject

3. Auto-disable and sharps-injury prevention needle guarantees injection safety for HCW and patient



4. Cold chain footprint reduced by half vs. MDV

5. Costs similar or lower than multidose vial

6. Fast conversion of DS to DP allows rapid response to outbreaks of known pathogens

7. Earlier availability of vaccine during outbreaks of novel pathogens

8. Higher sterility assurance and safety than current standard

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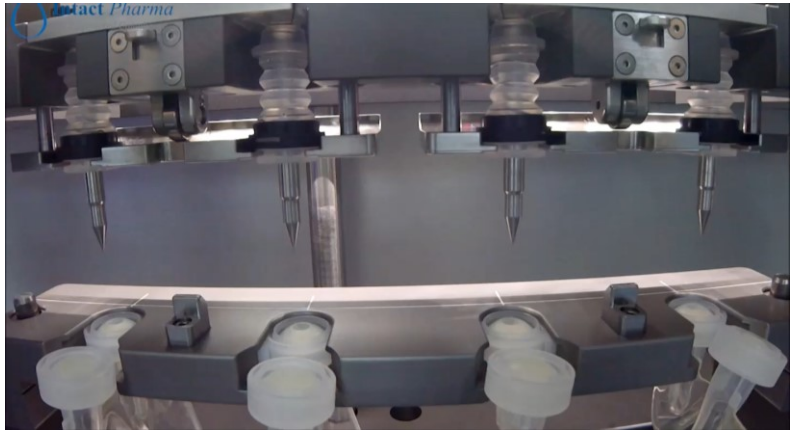
Fast and flexible filling

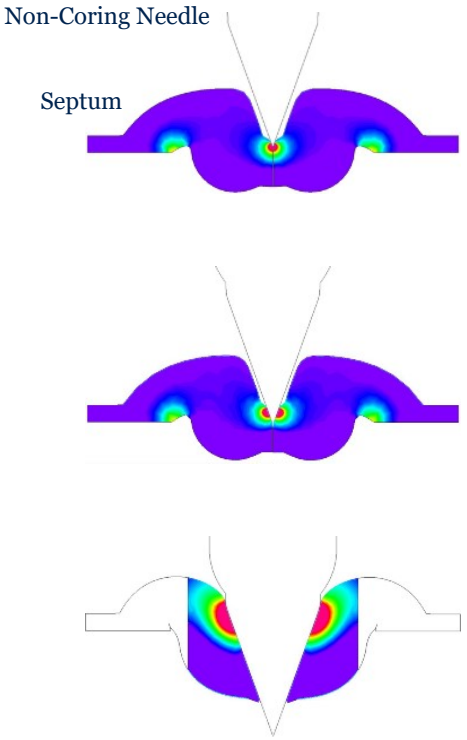
- Filler can be installed in 3 months in ISO 8 / class D environment (per US FDA/CDER recommendation) within a 10m x 6m space, multiple fill sites have expressed interest
- Filling line is modular and portable to other countries as new needs appear
- 1 Filler can fill 4000 doses/minute, 5M doses/day or 1.5BN doses/year (running at 3 shifts/day with 25 production days/month and 90% OEE)
- Filling process has been approved for sterile injectables in several US states
- Media fills passed under microbial challenge conditions of a million times more than expected, directly to the port and in aerosol form



It takes only a few seconds to fill 200 doses

Link to Filler Video

Closed system filling guarantees sterility



- Both filling needle and container are closed and sterilized by irradiation
- Septum-needle interaction wipes the contact interface and enables sterile transfer even in the harshest environment (6 log/m^3 proof)
  - FDA-CFSAN accepted in non-classified environment
  - USP 1211 new standard for aseptic processing
  - CDER recommended operations in ISO 8
- No contact with operators or external air, HEPA filter as precautionary measure
- Validation by media fills

Table IV: Intact media fills.

Closed needle / Closed vial	Background environment	Fill environment	Media	Media fill results	
				# Units tested	# Units contaminated
Various	CNC	CNC	Various	17,331	0

Table V: Intact media fills with microbially contaminated septum.

Closed needle / Closed vial	Background environment	Fill environment	(CFU/septum)	Media	Media fill results	
					# Units tested	# Units contaminated
Various	Non-classified	Non-classified	4 Log and higher	Various	1,718	0

Table VI: Intact media fills in non-classified environment

Closed needle / Closed vial	Background environment	Fill environment	Media	Media fill results	
				# Units tested	# Units contaminated
Various	Non-classified	Non-classified	Various	54,828	0

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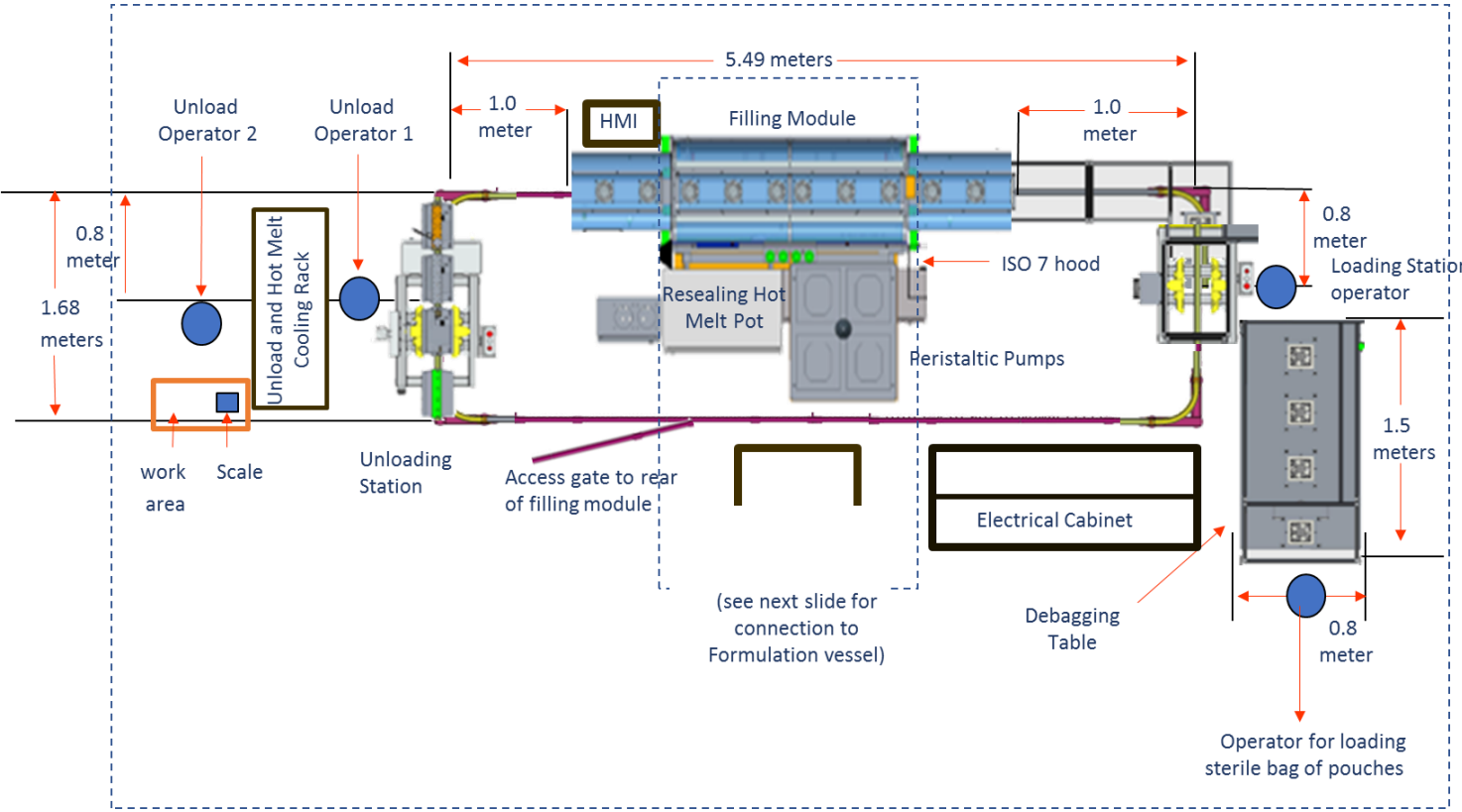
Filler requirements

Floor Plan



Used for sterile injectable manufacturing in USA

- 1 Filler can fill 1.5BN doses in a year

System Requirements:

Footprint	10 m x 6 m space
Power	Three-phase (3Ø), 480 volts, 100 ampere service
Compressed Air	External, oil-free source at a rate of 6.20 – 7.58 bar
Dosing	Peristaltic pump continuously adjustable for each single filling head and selected for multi-dose fills (100-dose or 200-dose per pouch)
Weight	Approx. 2 tons
Environment	ISO 8 room recommended
Operators	4

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Vaccine compatibility

- Vaccine drug product filled in the bags needs to retain the right quality throughout its shelf life
  - Filling process validation, storage stability, shipment, administration process
  - Focus on sterility, stability, leachables, particulate matter, dose homogeneity


Photo: Adrian Brooks / Gavi


Photo: Francis Ato Brown / World Bank

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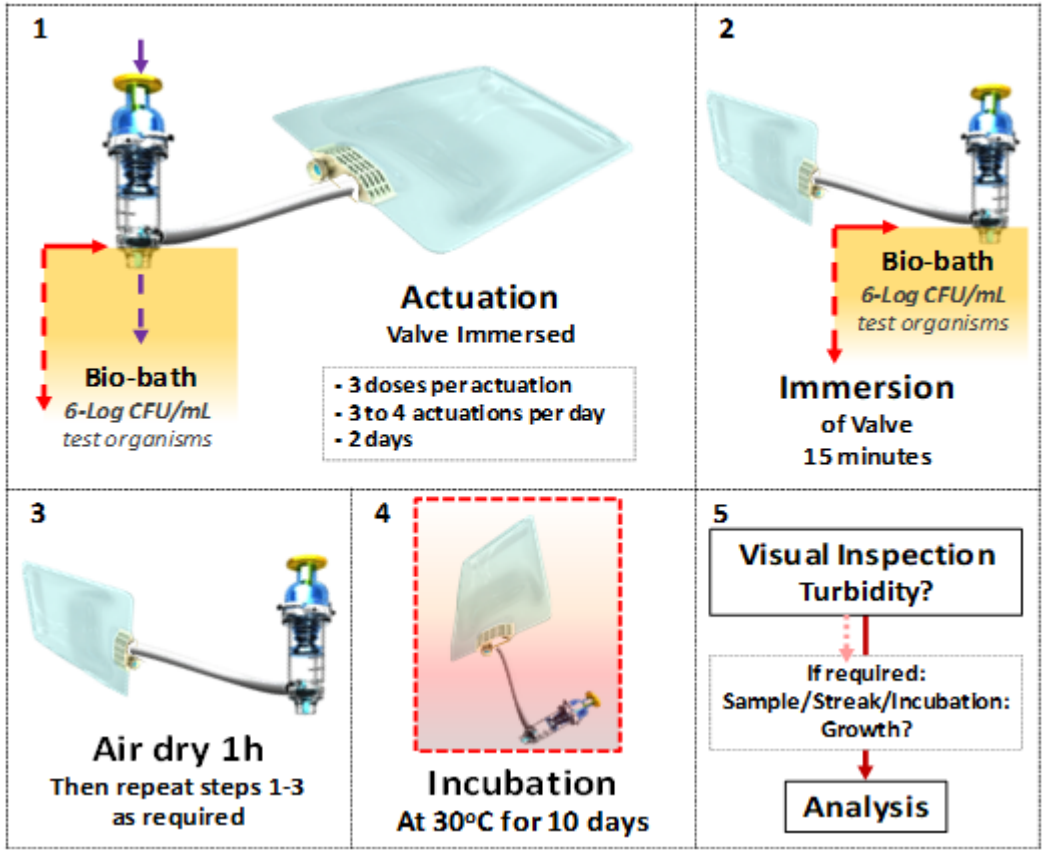
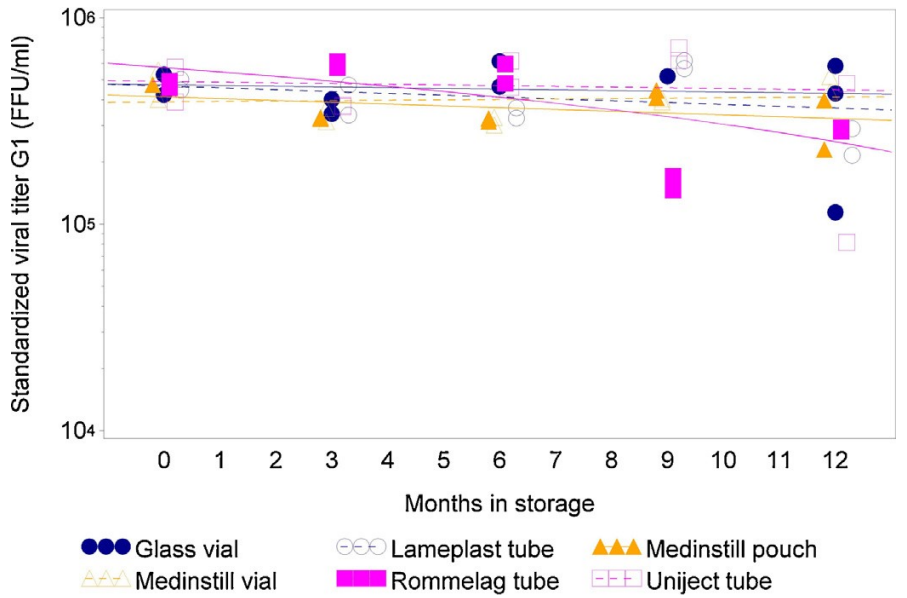
One-way valve ensures sterility

- One-way anti-retro-contamination valve keeps bag and syringe sterile, as shown by microbial challenge studies
  - Dosing while submerged in biobath (6-Log CFU/mL)
  - Microbial immersion before/after dosing (6-Log CFU/mL)
  - Dispensing 200 doses from bag with luer lock valve in environment with 3-Log CFU/m³ aerosol challenge
  - 100% sterile bags in all cases (> 75 bags and > 5000 actuations tested in total)



From vial to bag

- Bridging between vaccine Drug Product in vials to DP in bags can be done analytically
- In-use stability study required, focusing on:
  - Longer time of administration of all 200 doses, stability and sterility need to be ensured
  - Worst-case conditions in the field to be considered
  - Dose homogeneity to be confirmed, also for suspension products
- Promising preliminary data:
  - Compatibility with various vaccine products
  - Sterility even after 5 years of dispensing
  - Dose accuracy from 1st to 200th dose with <10% variability

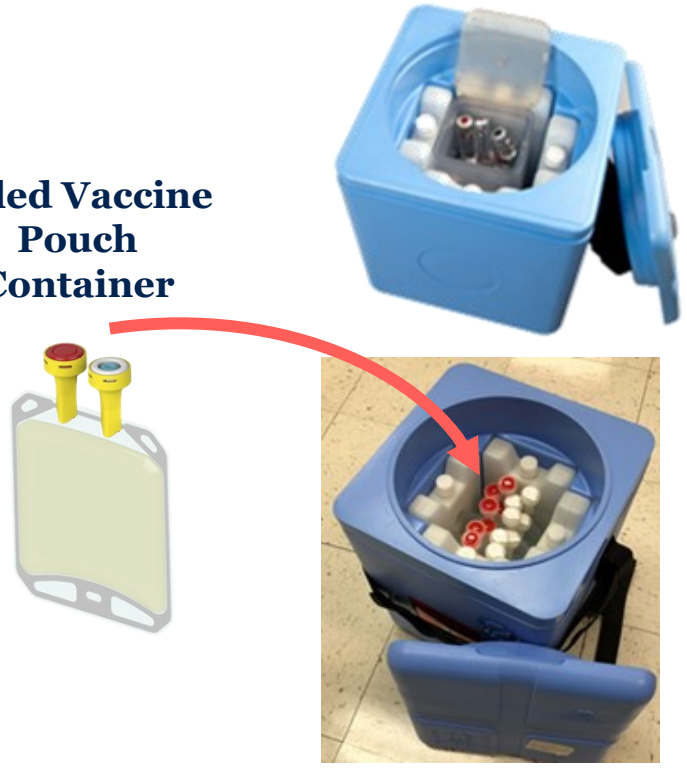


Lal, Manjari, et al. "Stability of live attenuated rotavirus vaccine with selected preservatives and primary containers." Vaccine 34.22 (2016): 2483-2489.

Low cold chain footprint

- In comparison to glass vials, these vaccine containers are lighter and smaller to store, meaning more doses can be transported at any one time while also saving on economic and environmental costs

WHO-approved vaccine carrier for protection from light and heat during transport



Presentation	Cold chain volume (cm^3/dose)*
1-dose vial	15.2
5-dose vial	4.6
1-dose BFS	~4
10-dose vial	3.3
20-dose vial	2.1
200-dose pouch	**1.4**
400-dose pouch	**1.0**

*Glass vial averages from current WHO prequalified vaccines. Source: PATH Study, 2020

Protection from light and heat during use

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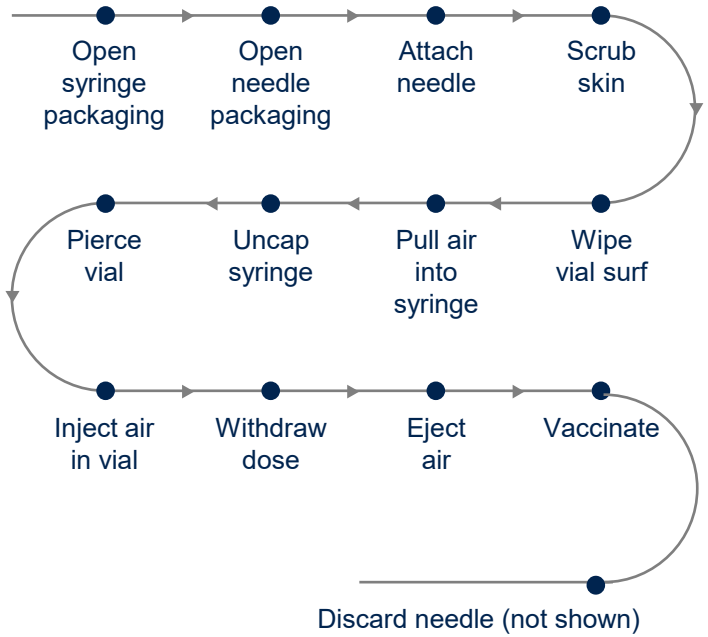
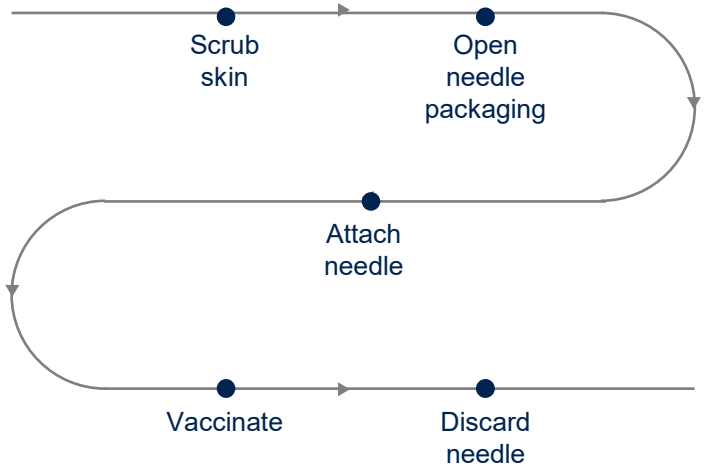
Glass Vial compared to INTACT™ Pre-Filled Syringe

Glass Vial: ~60 sec



INTACT™ Multi-Dose Pre-filled Syringe and AD/SIP Needle: ~12 sec



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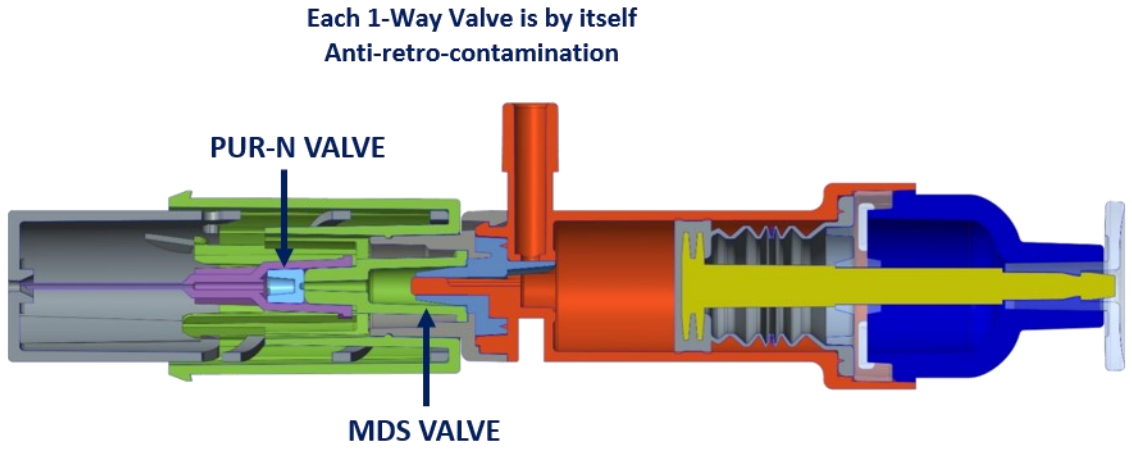
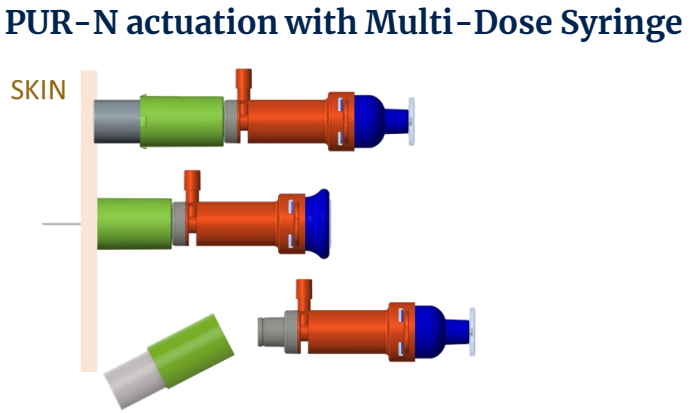
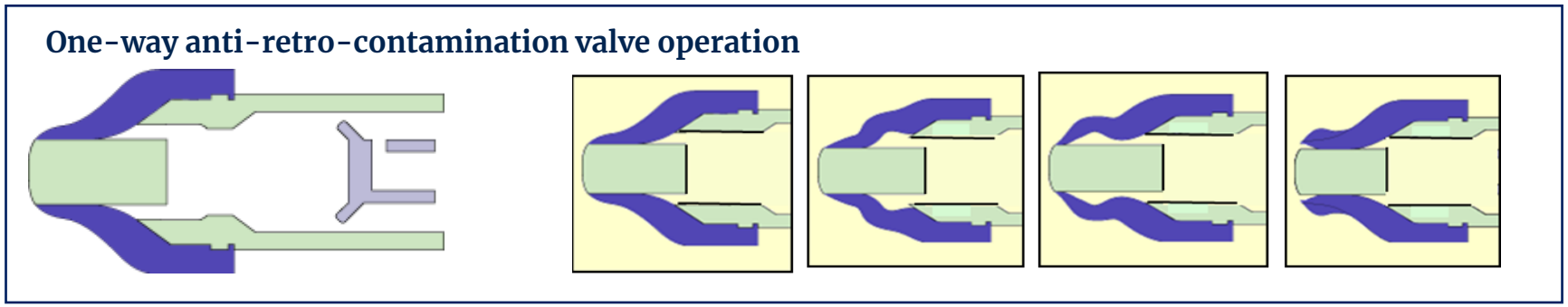
Valve in bag/syringe and needle prevent backflow

- One-way anti-retro-contamination valve in tip of multidose syringe keeps bag and syringe contents sterile
- PUR-N valve prevents backflow from the patient into the needle
- Even if needle without valve is used, worst-case flagellated germs take > 20 min to migrate through needle



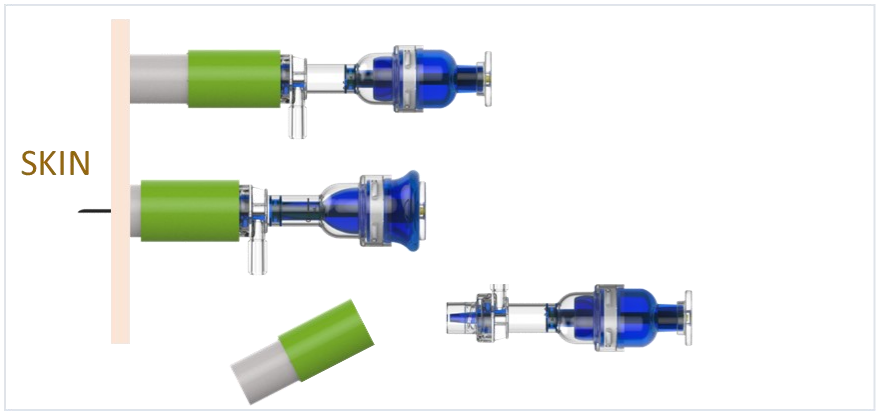




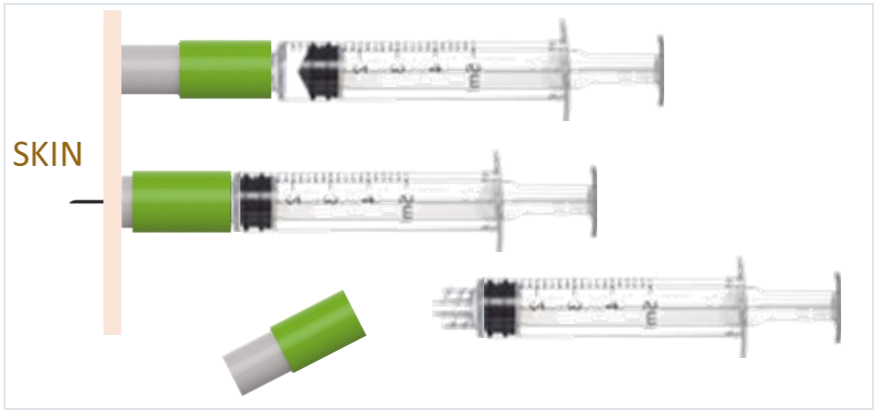
Plastic Un-Reusable Needle (PUR-N) for IM

- Autodisable, reuse prevention and sharps injury protection
- Needle not visible, reducing fear (e.g. for children)
- Can be used with MDS pouch or with any luer lock syringe
- Enables use of INTACT multi-dose syringe bag in LMIC setting
- Principle shown with ID needle, IM version in development

Multi-Dose Syringe



Any Luer Lock Syringe (RUP Preferable)



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Some stakeholder and user feedback

It would increase availability and access – *UNICEF*

Innovative device, good training will be required – *PATH Senegal*

Healthcare workers will like this new tool, best suited for campaign use – *PATH Senegal*

Stability of the vaccine needs to be ensured, temperature and light, VVM is key - *MSF*

Excited about this new presentation, it has potential for other vaccines as well - *MSF*

Autodisable syringe/needle might be required in some areas - WHO

Obvious advantages for mass vaccination, logistics, transport, cold chain - *MSF*

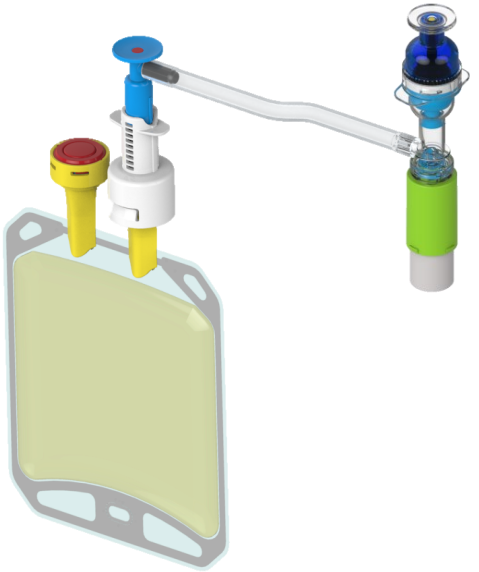
Lightweight, flexible, good for fast mass vaccination, can address vaccine shortages, easier to carry/transport – *PATH India*

Regulatory feedback

- Technology presented to COVAX Regulatory Advisory Group (RAG) in January 2021
  - Regulators from around the world including FDA, EMA and WHO
- Support for dosing from non-preserved multidose container for > 6h, with the right data package:
  - Vaccine Drug Product stability throughout dispensing of 200 doses
  - Sterility and viral safety assured by data, statistical considerations and risk assessments
- Bridging between vials and bags may be done analytically:
  - In-use stability studies covering first to last dose, under worst-case conditions
  - Dose homogeneity, aggregation and particulate matter should be evaluated
- Final DP of vaccine in bags would be considered a combination product
- Filling process has been approved for sterile injectables in several US states

Turning vaccines into vaccinations

- Billions of doses of safe and effective vaccines are needed to end current and future pandemics
- INTACT™ multidose prefilled syringe for pandemics can deliver these vaccines
  - Fast and flexible scaleup of Drug Product capacity
  - Cost-effective DP presentation with low cold-chain footprint
  - Rapid mass vaccination with prefilled syringe-like ease of use
- Several partners are currently developing their vaccines in this presentation
  - To be deployed from end 2021
  - For COVID-19 and other vaccines
- Get involved: https://cepi.net/get_involved/cfps/ or contact Renske.Hesselink@cepi.net



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