

Transformative Concepts for Mass Vaccination and Pandemic Response

Global Vaccine Immunization Research Forum, 2021

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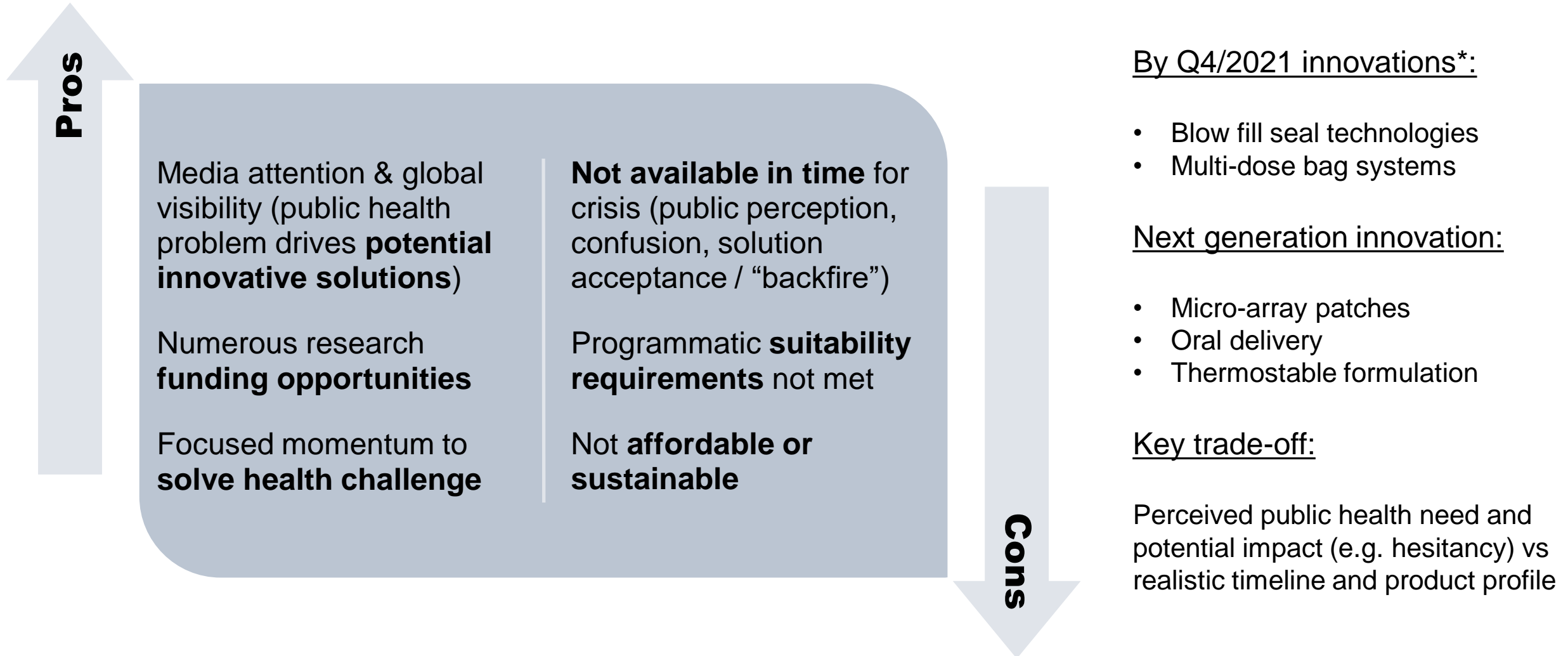
Sustainable Manufacturing Lead, CEPI (London, UK)

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Innovation in a time of crisis for LMIC deployment – Pros & Cons





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



Vaccine drug product approach to achieve billions (BN) of doses

Resolution in-process

Aspects to resolve, design space

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

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

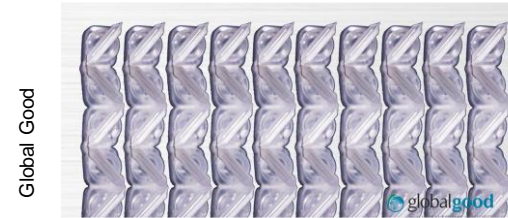
Blow-fill-seal (BFS) primary container

- BFS technology is a method of producing **liquid-filled single/multi-dose containers**: formed, filled, sealed in a continuous, automated system
- An advanced **aseptic process** for packaging numerous sterile pharmaceutical products

Single and multi-dose

- Multiple mono-dose BFS design used for GSK Rotarix™
- Global Good: low cold chain volume ampoule
- Delivered with AD/RUP needle & syringe - separate needle, design dependent

Single and multi-dose BFS containers



Ampoule (prototype)



Container with insert septum (prototypes)

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Single dose prefilled injector (ApiJect platform)

- Parenteral injection capability - AD feature preventing reuse expected to be developed – in line with programmatic suitability requirement
- DH&HS - \$138M USD contract (stockpile – 45M per month in SC)
- US International Development Finance Corporation - \$590M loan for BSL-2 “Gigafactory” (RTP) - 250M doses per month on ≤15 isolated lines

Single and multi-dose BFS containers



Global Good



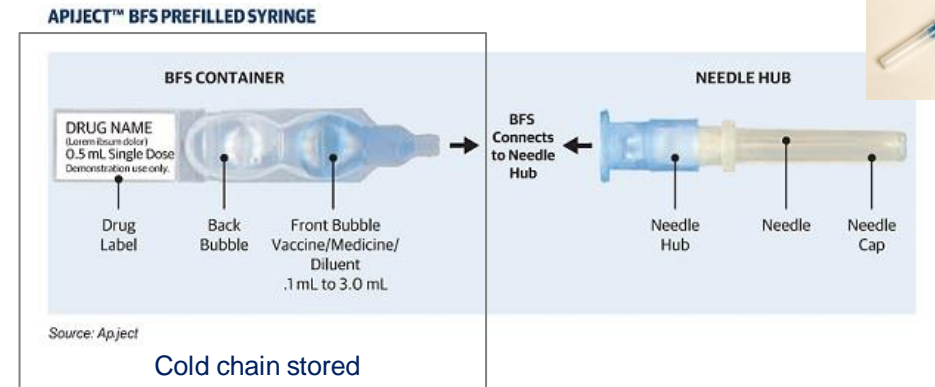
Ampoule (prototype)



Rommelag

Container with insert septum (prototypes)

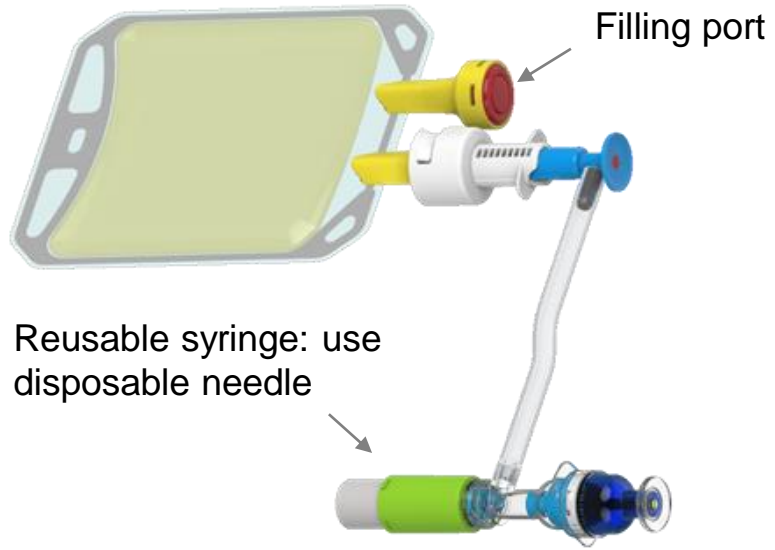
Single dose prefilled injector



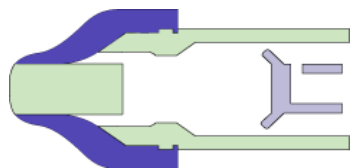
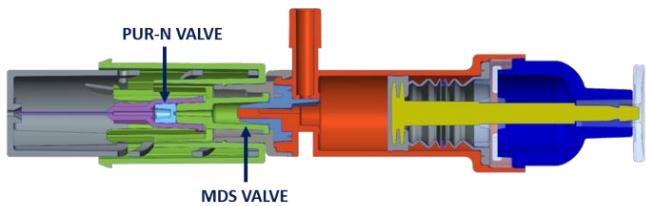
Apiject



Multi-dose pouch (INTACT™ Solutions)



1-way valve is anti-retro-contamination



One-way valve in multi-dose syringe



1. Secure disposable needle



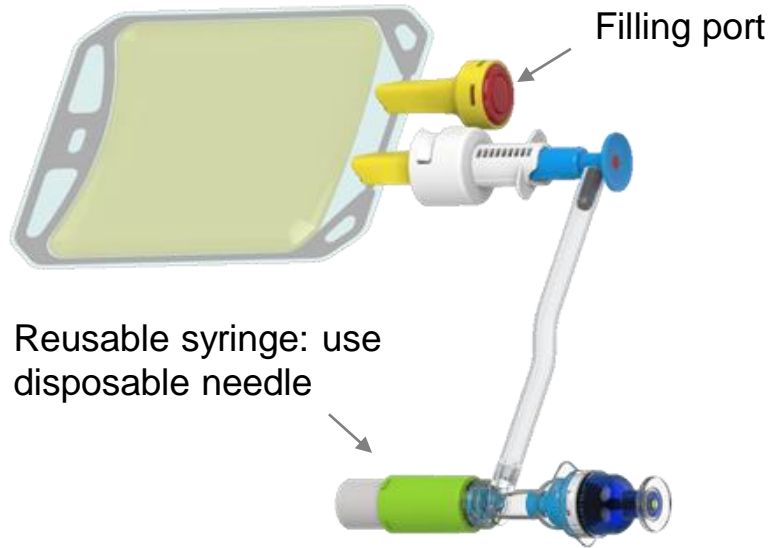
2. Administer vaccine



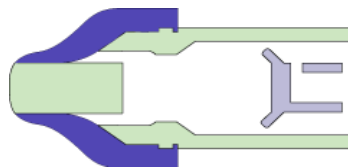
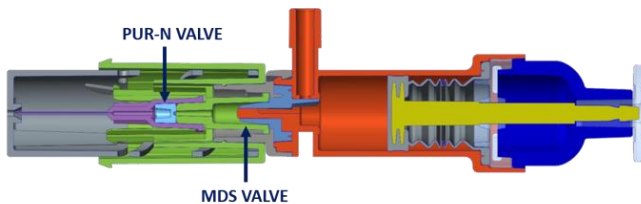
3. Dispense needle

See YouTube video: [Socially Distanced Vaccination](#)

Multi-dose pouch (INTACT™ Solutions)



1-way valve is anti-retro-contamination



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

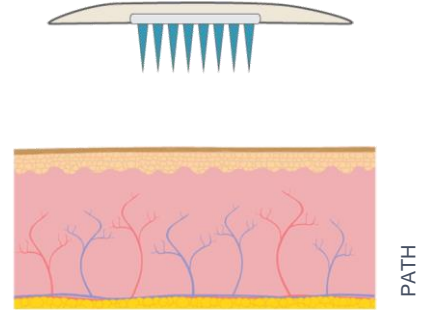
Technology status

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

Micro-array patches (MAP)

First vaccine-MAP could be licensed in 5 years

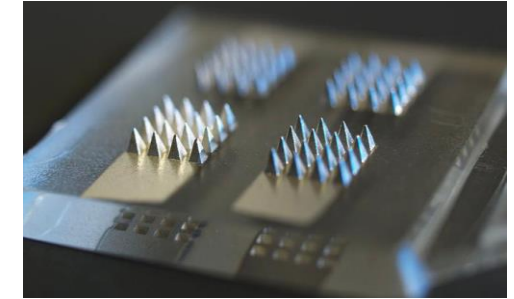
- MAPs consist of hundreds of tiny projections that penetrate the top dermal layer delivering vaccines or drugs into the skin
 - Several Ph.1 studies completed for influenza vaccines (Georgia Tech, Vaxxas, CosMED, Zosano Pharma)
 - Phase 1 MR clinical trials to be initiated in 2021 (Vaxxas, Micron)
- Some platforms require an applicator for delivery
- Wear times range from seconds to hours to release API, depending on design
- [PATH Center of Excellence for MAP Technology](#)
- [VIPS](#) (Gavi, WHO, UNICEF led collaboration with PATH and BMGF) top tier prioritized technology
 - Action plan in development (5 yr strategy finalized, multiple funders engaged)



Micro-array patches (MAP) – next generation

Technology status (COVID-19 vaccine):

- [Swansea University IMPACT](#)
 - Coated microneedle array/smart device (skin biomarker monitoring)
- UPMC: dissolvable array/subunit vaccine ([PittCoVacc](#))
- Vaxess - dissolvable, MIMIX™ Smart Release patch, pre-fusion spike protein
 - [Single dose, self applied, room temperature stable](#)
 - [Combined COVID-19 and QIV \(Medigen Vaccine Biologics Corp\)](#)
- [Verndari VaxiPatch™](#) (coated array), SARS-CoV-2 recombinant spike receptor binding domain protein
- UCONN: dissolvable array, additive, micro-mold fill/finish process, spike protein (BARDA funded)



Swansea University



UPMC



BARDA

Oral delivery

- GI tract mucosal delivery – oral, stomach, small intestine
- Capsule and tablet based, pain free, self administration
- Live-attenuated and inactivated vaccines for enteric disease
- Oral subunit, DNA and mRNA vaccines in development

Technology status (COVID-19 vaccine)

- [Esperovax EGRESS RD](#) (BARDA funding)
 - mRNA (spike protein) oral eVLP delivery technology
 - Pill based approach – yeast engineered lipid particles containing mRNA
- [Vaxart VAAST™ oral vaccine platform](#)
 - Phase I clinical development stage
 - Temperature stable Ad5 vector delivery via tablet (antigen + adjuvant)
- [Symvivo's bacTRL™ Gene Therapy Platform](#)
 - Phase I clinical trial stage



PATH



Esperovax

mRNA Vaccine thermostability

- Some current mRNA formulations require ultra cold storage to maintain stability ($\leq -70^{\circ}\text{C}$) – needs resolving
- Lyophilized / dry powder formulations in development; potential for improved thermostability and supply chains
- Innovations to ensure mRNA vaccine stability of crucial importance to ensure applicability of vaccines to LMIC settings



UPS



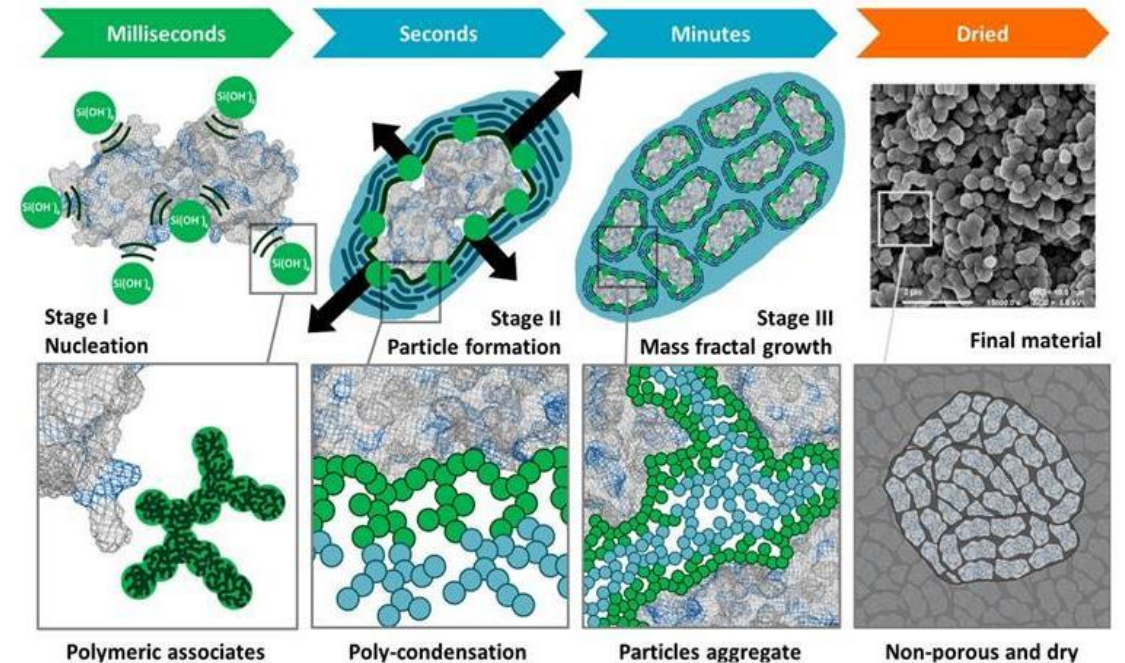
FED EX

Innovations in vaccine thermostability

Technology status (COVID-19 vaccines)

- Centre for Sustainable & Circular Technologies
 - Universities of Bath + Newcastle)
 - Ensilication process – encase protein e.g. tetanus toxoid vaccine – RT
- [Ziccum](#) – air drying Laminar-Pace technology
- Imperial College London – ionic liquid, preventing aggregation
 - Stable (RT, 50 days) self-amplifying RNA vaccine
- [Stablepharma](#) – StablevaX™ trehalose
 - Liquid vaccine loaded into a sponge - placed in syringe hub and dried

Representation of tetanus toxoid ensilication process



<https://www.nature.com/articles/s41598-020-65876-3>



Stablepharma

Conclusion

- Covid-19 pandemic has presented an unparalleled opportunity to accelerate innovative technologies
- The pandemic has also:
 - Increased the visibility of global public health inequity
 - Geo-economy differences in health system infrastructure
- Elevated the considerations to develop and deliver a truly 'global' Covid-19 vaccine:
 - Trade off in 'first past the post' vs time to develop sustainable and deployable vaccines
 - Country readiness and acceptability
- Immediate, rapid response technologies versus novel innovations on a longer lead time (possibly more applicable to next generation vaccines and presentations)
- Covid-19 has demonstrated that deployment challenges, under the compressed timelines of a pandemic, drive technology innovation to facilitate rapid, mass, public health vaccination campaigns

Thank you...



Global Vaccine and Immunization Research Forum

