SINGLE-USE PULSE 2021

A WEBINAR SERIES EXPLORING THE BUSINESS OF SUTS

WEDNESDAY, JUNE 16

10:30-11:30 AM EDT

GLOBAL COVID-19 VACCINE SUPPLY CHAIN LANDSCAPE

MATTHEW DOWNHAM
COALITION FOR EPIDEMIC PREPAREDNESS INNOVATIONS (CEPI)

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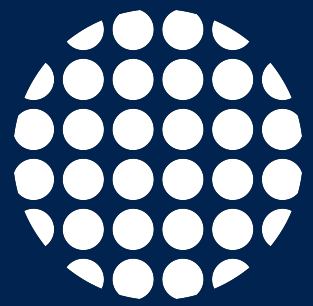
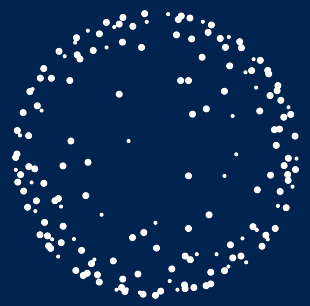
Global COVID-19 Vaccine Supply Chain Landscape

Bio-Process Systems Alliance

Matthew Downham: Sustainable Manufacturing Lead, CEPI

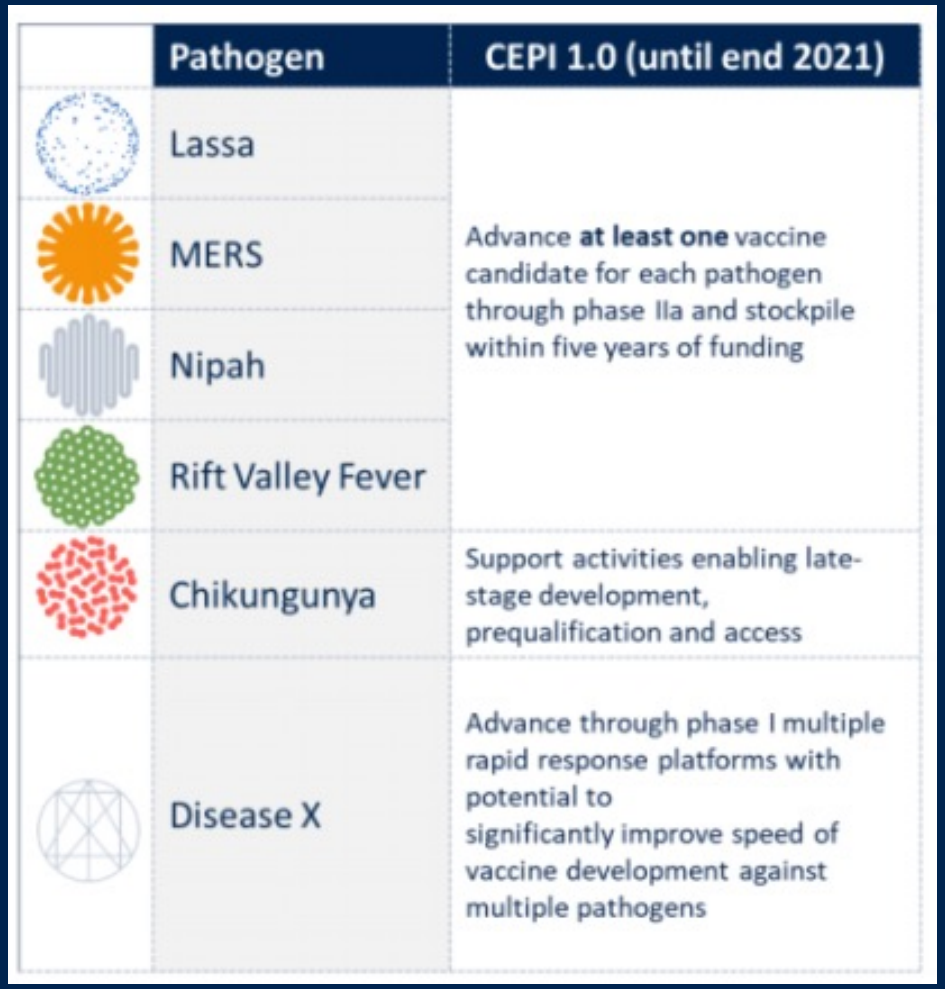
16th June 2021





Coalition for Epidemic Preparedness Innovations

- Launched in Davos in 2017
- Innovative global partnership between public, private, philanthropic, civil society organizations
- Develop vaccines to stop future epidemics
- Priority pathogens for vaccine R&D projects



	Pathogen	CEPI 1.0 (until end 2021)
	Lassa	Advance **at least one** vaccine candidate for each pathogen through phase IIa and stockpile within five years of funding
	MERS	
	Nipah	
	Rift Valley Fever	
	Chikungunya	Support activities enabling late-stage development, prequalification and access
	Disease X	Advance through phase I multiple rapid response platforms with potential to significantly improve speed of vaccine development against multiple pathogens

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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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CEPI 2.0 strategic objectives (2022-2026)

Prepare for known epidemic and pandemic threats

Develop vaccines and promising biologics against the most prominent known threats, building on COVID-19 achievements and CEPI 1.0

- End the COVID-19 pandemic
- Eliminate the risk of coronavirus pandemics
- Accelerate development of vaccines and other biologics against known high-risk pathogens

Transform the response to the next novel threat

Harness innovations in technology and systems to significantly reduce the global vulnerability to threats of novel pathogen outbreaks

- Use vaccine development innovations to give us a head-start on other novel threats
- Invest and scale critical research innovations which underpin rapid vaccine development
- Invest in innovations so vaccine manufacturing is cheaper, faster, and closer to an outbreak

Connect to enhance and expand global collaboration

Drive the development of a post- pandemic consensus and design a more robust and effective global preparedness and response architecture

- Build a strong, post-pandemic global coalition
- Push for collaboration and solutions which will enable a faster system-wide response
- Coordinate a scalable on-demand manufacturing network

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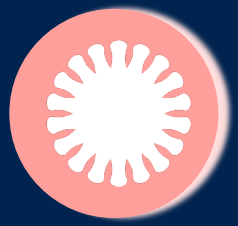
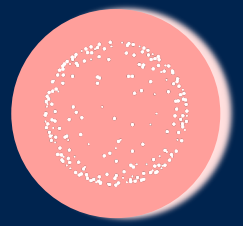
CEPI's vaccine portfolio



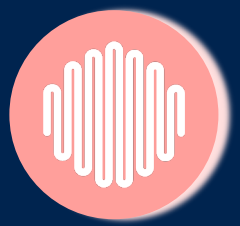
MERS

5 vaccine candidates



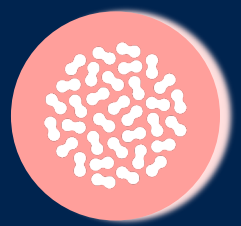
Lassa

6 vaccine candidates



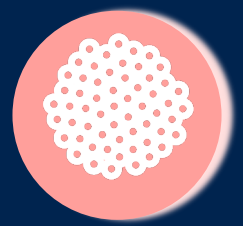
Nipah

4 vaccine candidates



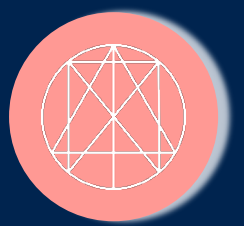
Chikungunya

3 vaccine candidates



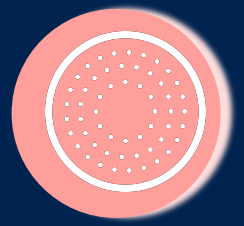
Rift Valley fever

2 vaccine candidates



COVID-19

12 vaccine candidates – 10 in active dev.



Disease X

3 platform technologies

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Vaccine's pillar of the Access to COVID-19 Tools (ACT) Accelerator coordinating the COVAX Facility, a global risk-sharing mechanism for pooled procurement and equitable distribution of COVID-19 vaccines (founded Q1/2020)

The COVID-19 pandemic…

Over 3.7 million lives now lost

Expected to cost the global economy **USD 28 trillion by 2025**

Destroyed the livelihoods of hundreds of millions, fractured societies, and broken the very essence of ‘normal life’

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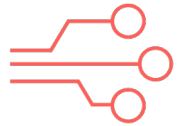
Today* - 10 CEPI-supported COVID-19 vaccines

	DNA / mRNA			Viral vector		Protein				
COVID-19	**Inovio**	**Moderna**	**CureVac**	**University of Hong Kong**	**AstraZeneca / Univ. Oxford**	**Novavax**	**Clover BioPharma**	**Biological E**	**SK Bio**	**VBI Vaccines**
Location	USA	USA	Germany	China	UK	USA	China	India	South Korea	USA/ Canada
Platform	DNA	mRNA	mRNA	Viral Vector	Viral Vector	Protein	Protein	Protein	Protein	eVirus Like Particle
Antigen / Adjuvant	Full-length S protein	Full-length S protein	Full-length S protein	Receptor Binding Domain (RBD)	Full-length S protein	Full-length S protein / saponin-based Matrix-M	Full-length S protein / CPG1018	Monomer RBD / CpG-alum	Recombinant RBD / Alum, AS03 or CpG+Alum	Full-length S protein (B.1.351 strain) / Alum
Current phase	Phase II/III	Phase III ongoing. WHO EUL granted	Phase II/III	Phase I	Phase III ongoing. WHO EUL granted	Phase III	Phase II/III	Phase I/II	Phase I/II	Preclinical

Speed



Scale

Access

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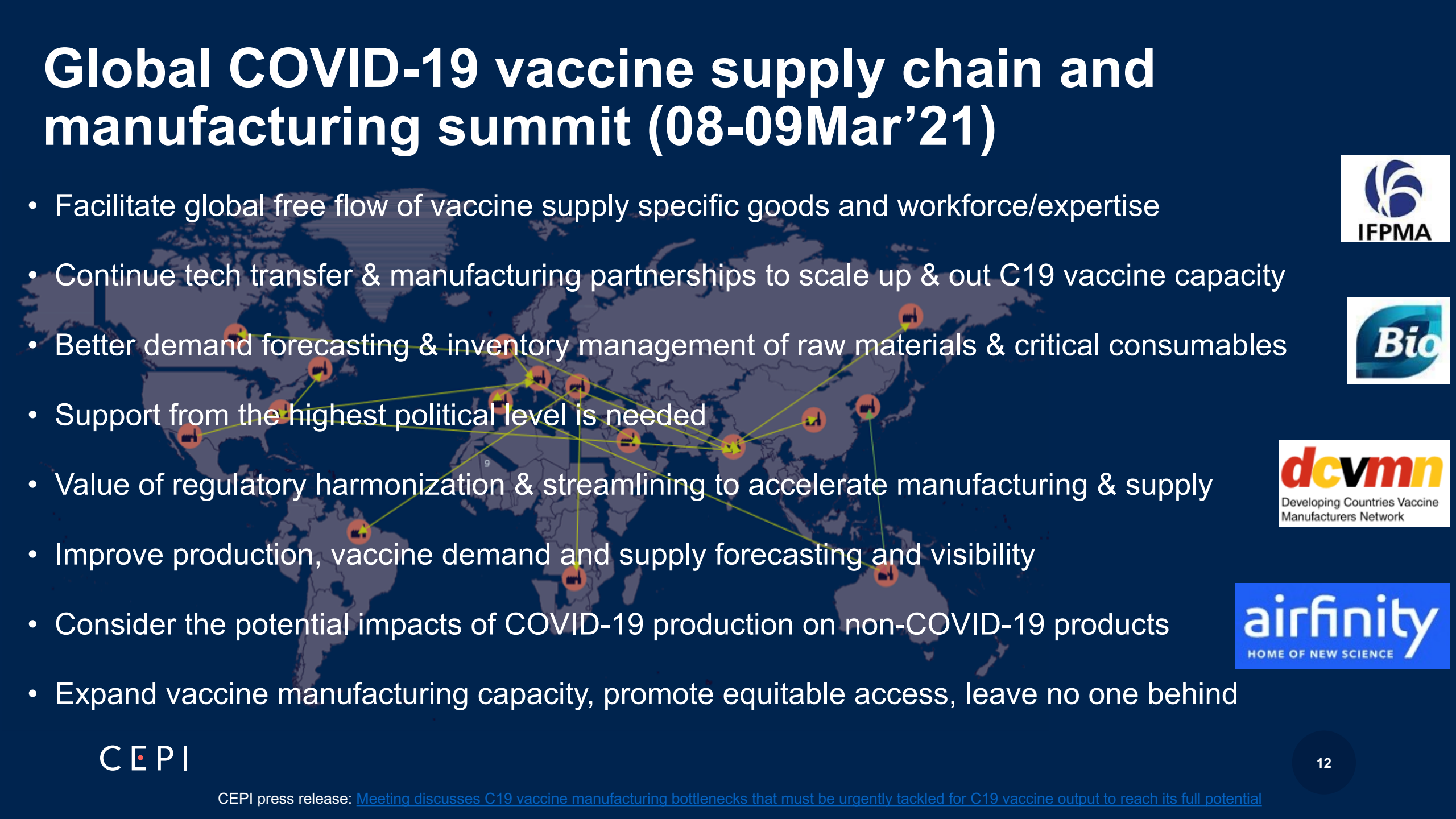
*Current as of 14th May 2021

Global COVID-19 vaccine supply chain and manufacturing summit (08-09Mar'21)

- Facilitate global free flow of vaccine supply specific goods and workforce/expertise
- Continue tech transfer & manufacturing partnerships to scale up & out C19 vaccine capacity
- Better demand forecasting & inventory management of raw materials & critical consumables
- Support from the highest political level is needed
- Value of regulatory harmonization & streamlining to accelerate manufacturing & supply
- Improve production, vaccine demand and supply forecasting and visibility
- Consider the potential impacts of COVID-19 production on non-COVID-19 products
- Expand vaccine manufacturing capacity, promote equitable access, leave no one behind



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CEPI press release: Meeting discusses C19 vaccine manufacturing bottlenecks that must be urgently tackled for C19 vaccine output to reach its full potential

Rapid global vaccine manufacturing scale-up

COVID-19 vaccine producers by continent, with stage 3 and late stage products

Europe

- AstraZeneca
- BioNTech/Pfizer
- Gamaleya Research Institute
- J&J
- Moderna
- Novavax

North America

- AstraZeneca
- BioNTech/Pfizer
- J&J
- Moderna
- Novavax

South and Central America

- AstraZeneca
- CanSino
- Gamaleya Research Institute
- SinoVac

Asia

- AstraZeneca
- Beijing/Sinopharm
- Bharat/ICMR/NIV
- Cansino
- Chumakov Federal Scientific Center
- Gamaleya Research Institute
- J&J
- Novavax
- Serum Institute of India
- Sinovac
- VECTOR

Australia

- AstraZeneca

Africa

- J&J

+ around **15 companies with earlier stage** products and **>150 partnerships** with C(D)MOs

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Potential shortages impact vaccine value chain

*Not used in high volumes in other COVID-19 vaccines or other biologics in general, often used in gene therapy
In bold - input with potential/current supply challenges highlighted by majority of interview partners

Drug substance manufacturing | Widely used in biologics manufacturing

Platform	2021 announced supply billion doses	Upstream process	Downstream process	Fill and Finish	Distribution/Storage
Viral Vector	 ~5	▪ **Bioreactor bags** ▪ **Single-use assemblies (including filters, tubing)** ▪ **Cell culture media** ▪ Transfection reagents* ▪ Plasmids*	▪ **Single-use assemblies** ▪ **Filters** (ultrafilters, tangential flow filtration) ▪ Chromatography monolith* & consumables (eluants, buffers, resins)	▪ **Vials** ▪ Caps/Stoppers ▪ Specific excipients (e.g. carbohydrates)	
Protein Subunits	 ~3	▪ **Bioreactor bags** ▪ **Single-use assemblies** ▪ **Cell culture media**	▪ **Single-use assemblies** ▪ **Filters** (ultrafilters, tangential flow filtration) ▪ Chromatography consumables (eluants, buffers, resins)	▪ **Vials** ▪ Caps/Stoppers ▪ Excipients ▪ Adjuvants	
RNA	 ~3	▪ **Bioreactor bags** ▪ **Single-use assemblies** ▪ Plasmid DNA template ▪ Nucleotides/amidites ▪ Reaction enzymes ▪ 5'-Cap	▪ **Single-use assemblies** ▪ **Filters** (ultrafilters, tangential flow filtration) ▪ Chromatography consumables (eluants, buffers, resins)	▪ **Vials** ▪ Caps/Stoppers ▪ **Lipid nanoparticles** ▪ Microfluidic mixing systems	▪ Dry ice ▪ Frozen storage
Inactivated (bioreactor based)	 ~3	▪ **Bioreactor bags** ▪ **Single-use assemblies** ▪ **Cell culture media** ▪ Transfection reagents* ▪ Plasmids*	▪ **Single-use assemblies** ▪ **Filters** (ultrafilters, tangential flow filtration) ▪ Chromatography monolith* & consumables (eluants, buffers, resins)	▪ **Vials** ▪ Adjuvants ▪ Caps/Stoppers ▪ Specific excipients (e.g. carbohydrates)	

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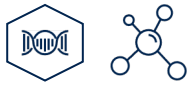
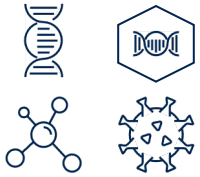
Interdependencies impacts many health products

Platform	Production capacity	Requirements to meet supply targets	Potential capacity expansion opportunities	
mRNA 	▪ Novel technology ▪ (Almost) exclusively for C-19 Vx production	▪ Rapid scale-up; most produced platform thus far ▪ Sufficient capacity online to meet 2021 announced supply targets	▪ Requires building of new capacity or potentially process/equipment effectiveness improvements ▪ No potential for repurposing	
Protein subunit/ viral vector 	▪ Uses bioreactors that are needed for other biologics &/or vaccines	▪ Can draw on installed manufacture base ▪ Meeting 2021 announced supply targets, requires <1-5% of existing capacity	▪ Further repurposing possible ▪ Risk for supply chains of other health products likely limited, given existing installed base and expected excess capacity available	
Inactivated virus 	▪ Uses different technologies, e.g. bioreactors, chicken embryos… ▪ Similar production to many common Vx, e.g. influenza	▪ High fungibility with other bioreactor-based inactivated vaccines ▪ Low fungibility with other types of capacity due to viral containment needs	▪ Repurposing of additional capacity difficult due to viral containment requirements to handle live virus	
Fill-Finish 	▪ Same capacity as for other vaccines and biologicals (that come in vials)	▪ Expected global announced supply targets of >10BN vials according to industry observers ▪ Likely need of <2.8BN vials capacity for C19 Vx (2021)	▪ Repurposing/expansion potential lacking sufficient data ▪ Potential risk of competition of capacity with other health products (e.g. vaccines, biologics)	

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Highly specific to C19 Vx; no competition with other health products

Not specific to C19, but limited risk of competition with other health products

Not specific to C19, potential risk of competition with other health products

Emerging input material challenges identified

1. **Limited data to forecast (input material) supply and manufacturing needs:**
   - Accurate forecasting of projected input material needs, impacts demand volumes
   - Short input material lead times across the supply chain - limited by visibility of their demand, prioritisation, supply allocations
2. **Increased safety stocks**
   - Indications of uncertainty-induced increased safety stocking
   - Negative consequences beyond COVID-19 vaccine availability e.g. increased write-offs, impacts on production of other health products requiring the same inputs
3. **Increased trade and regulatory barriers**
   - Concerns over expansion of trade and regulatory barriers requiring multi-agency responses to mitigate disruption to input material supply chains and manufacture of vaccines / biologicals

Key Priorities Identified

Public-private sector collaboration
Forecasting of potential needs and their communication
Visibility of input material and demand needs
Plan and anticipate potential capacity constraints

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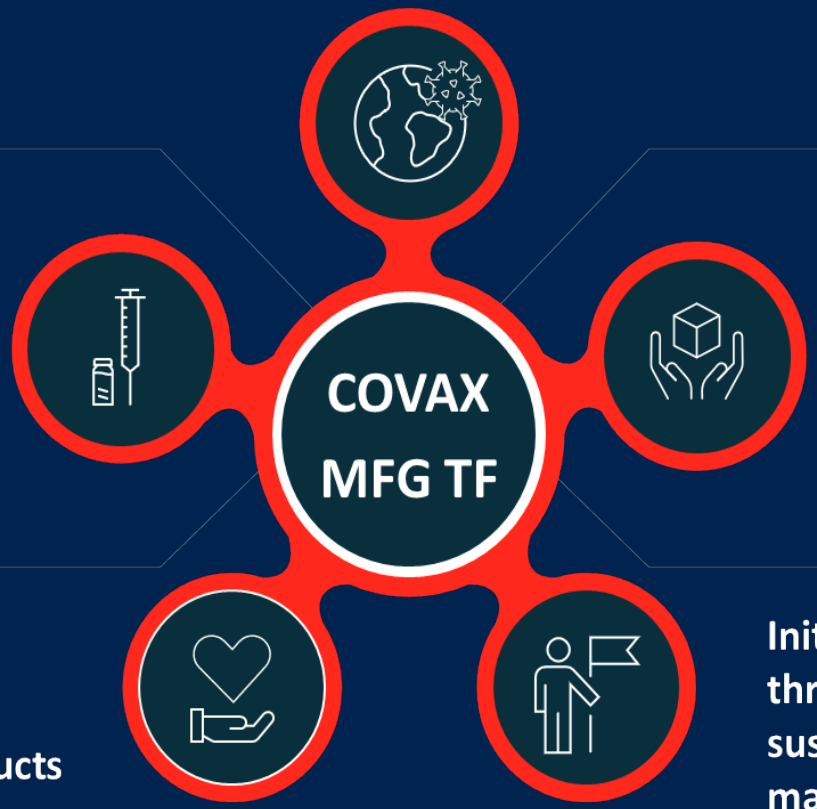
COVAX supply chain & manufacturing task force

Support COVAX mission to end acute phase of the pandemic by end 2021



Optimize the number of Vx doses manufactured in the short term

Prioritize doses for COVAX with a special emphasis on AMC92 to ensure greater equity

Mitigate unintended impact on other vaccines and health products

Initiate regional health security through establishment of sustainable regional long-term manufacturing of vaccines

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COVAX SC & MfG TF: short term objectives

- Facilitating the **establishment of global trade processes for free movement** of materials, components, reagents, and skilled workforce required for vaccine manufacture
  - Resolving the impact of import–export authorisations or bans and other cross-border trade-restrictions
- Creating a **voluntary partnership to improve visibility** of the supply of manufacturing inputs
- Identifying and **voluntary matchmaking of fill/finish capacity** between manufacturers across multiple regions
- Utilising global vaccine capacity to **support vaccine development partners** and **facilitate voluntary technology transfers** between partnering manufacturers

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https://cepi.net/news_cepi/covax-manufacturing-task-force/

COVAX SC & MfG TF: mid-long term objectives

- **Establish or upgrade vaccine manufacturing facilities**, particularly in LMICs leveraging appropriate mechanisms and business processes
- **Stimulate public-sector and private-sector investments** in vaccine manufacturing innovations to accelerate pandemic response and production of routine vaccines
- Identify **policy needs and build regulatory capabilities** to improve manufacturing capacity in LMICs in compliance with global norms and standards
- Coordinate development of **sustainable and resilient regional supply chains** across a global manufacturing ecosystem
- Defining ways to **upskill and enlarge the vaccine manufacturing workforce** in key areas (e.g. CMC)

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https://cepi.net/news_cepi/covax-manufacturing-task-force/

Address challenges through four workstreams

Workstream	Aspiration		Convener
1 **Improve input supply availability** CEPI: N. Lurie & M. Downham	Launch **marketplace for critical input supplies** Facilitate global **free flow of critical supplies** for vaccine manufacturing Expand mid-term available input supply capacity	**Short-term COVID impact** *(1-6 months)*	CEPI
2 **Maximize mid-term manufacturing capacity** CEPI: N. Lurie & M. Downham Gavi: D. Maugeais & H. Kettler	Create consolidated **overview of manufacturing capacities** **Maximize** mid-term **expansion of manufacturing capacities**, e.g. by **Fill & Finish** matchmaking, **regulatory**, **funding**, **workforce** interventions	**Mid-term COVID impact** *(Until end of 2022)*	CEPI Gavi The Vaccine Alliance
3 **Long-Term Sustainable Manufacturing** WHO: M. Friede & R. Long	**Expand capabilities of existing manufacturers in LMICs**: grow existing capabilities and strengthen the know-how of existing manufacturers **Establish sustainable capacity** in regions with no significant capacity	**Long-term COVID-19 and beyond impact**	World Health Organization
0 **Shared fact base / Task Force Coordination Office** CEPI: M. Downham / Gavi: D. Maugeais / WHO: M. Friede, T. Cernuschi, R. Long / UNICEF: P. Kalpaxis / BMGF: D. Robinson	Create aligned **supply outlook** Conduct supply and manufacturing **ecosystem mapping** Maintain an integrated view of **enabling resources** for the Taskforce and its activities and **long term financing needs** (TBD) Set up the **Taskforce Coordination Office**	**Enabling baseline of information**	CEPI Gavi The Vaccine Alliance World Health Organization unicef Bill & Melinda Gates foundation

Input Supply Marketplace - concept

To address immediate needs we have developed a exchange concept

CEPI will organize a exchange intended to match existing supplies with current needs

1. WHO Global Vaccine Market Report 2019, 2020

Facilitate manufacturing of COVID-19 Vx doses

Current situation & challenge

Vaccine manufacturers and suppliers of key inputs **are scaling** up with an announced cumulative supply target of up to 14 billion doses by the end of 2021 – at least **three times the pre-COVID19 annual global supply** for all vaccines.[1]

Shortages in most critical input supplies have been identified by COVID-19 Vx manufacturers as a rate limiting step

Objectives

The COVAX Manufacturing Taskforce has developed a **exchange concept** to improve utilization of these scarce supplies by

- **Providing suppliers with** a broad **platform to (re-)allocate materials** and capacity slots becoming available through further scaling or sudden shifts in demand
- **Mobilizing idle stock** from vaccines and candidates that fail prior to gaining regulatory approval – as well as from those that might scale down their production in the future
- **Mobilizing potential surplus stock from** manufacturers with **non-Vx activities**

Goals

To facilitate production of COVID-19 Vx doses, promoting equitable access to vaccines in the context of COVAX

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Input Supply Marketplace - cycle

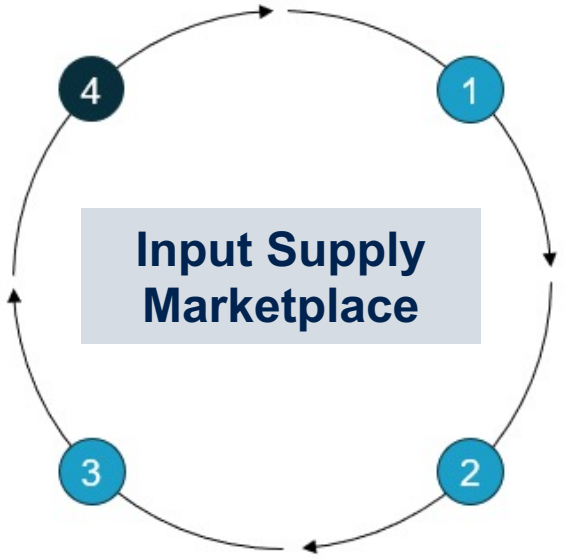
Hosted by CEPI Bilateral interaction

Transaction

- Pairs of potential provider and receiver negotiate and settle terms of transactions entirely outside platform
- Pair notifies Matchmaking Facilitator upon successful closure

Collect data

- Manufacturers/suppliers with excess supplies share data with Data Facilitator
- Vaccine manufacturers share data regarding input supply gaps with Data Facilitator



Identify matches

- Matchmaking Facilitator pairs[1] matching offers & requests and shares contact details among potential pairings

Set up the Exchange

- Data Facilitator consolidates all offers and requests
- Data Facilitator validates input and connects with participants in case of questions

1. Prioritization due to pre-defined rules may apply in cases where several manufacturers are interested in same open position

Input Supply Marketplace – launch June 2021

"Minimum viable pilot (MVP)"/prototype has been outlined for input supply exchange:

1 Partners

~20 potential partners for launch identified and interviewed:

- COVAX Vx manufacturers
- Suppliers of key materials
- Leading pharmaCos without COVID-19 Vx production

2 Supplies

6 categories of critical supplies detailed to focus the platform on:

- **Bioreactor bags**
- **Cell culture media**
- **Single-use assemblies**
- **Filters**
- **Lipids**
- **Vials**

3 Data

Dataset for posting offers and requests on the platform identified

Concept for anonymization of respective parties on the exchange detailed

4 Technology

MVP exchange system conceptualized, using standard, off-the-shelf software for launch

To be implemented over next 1-2 weeks

5 Legal

Legal draft for exchange agreement currently under development

To be shared with prospective partners for alignment on terms and signature upon joining exchange

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Shared information allows item identification & request, but not their origin

HIGHLY ILLUSTRATIVE – NO ACTUAL DATA

Key data identifying item for exchange

Example for potential exchange view

Type of submission	Product Category	Critical SKU	Supplier	Supplier part number	Unit	Size of Gap	Size of Surplus	Geogra-phy	Available stock / production capacity	Exact match / substitute possible	Required / available by
Request	Cell Culture Media	**MANIFOLD PURIF. IRR. SH3B6411.01**	Thermofisher	SH3B6411.01	,000 litre	5	-	EU	-	Exact match	immediately
Request	Filters	**Filling assembly MIL0005L1376748**	MERCK MILLIPORE SIGMA	MIL0005L1376748	Units	100	-	US	-	Exact match	immediately
Request	Single-use assemblies	**BOTTLE, PETG, SQUARE, MEDIA, 250ML**	Thermofisher	2019-0250	Pc.	10,000	-	Asia Pacific	-	Exact match	immediately
Offer	Excipients	**Dextrose Anhydrous 90.7 Kg Primary**	Avantor	1920-09, 1920-07	Packs	n/a	40	US	Stock	Exact match	Q3 2021
Offer	Filters	**KIT FILLING LINE A-BCMA MIL0005L1801624**	MERCK MILLIPORE SIGMA	MIL0005L1801624	Units	n/a	20	EU	Production capacity	Exact match	Oct-Nov 2021

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Minimum viable pilot launch preparations

For the pilot phase, we will stand up a simple, but safe environment for the exchange

MVP to be hosted by CEPI on **Standard file sharing/hosting platform** (e.g. sharepoint, sharefile, box)

MVP exchange to consist of a simple excel **spreadsheet – read-only for partners**, editing rights to data facilitator & matchmaking facilitator only

Each **partner** has a **dedicated input folder** to upload their original offers, requests and responses to offers and requests as excel spreadsheet - reading rights for data facilitator & matchmaking facilitator

Data facilitator and matchmaking facilitator only **access and compile data on systems within secured network**

- Anonymize and synchronize between partner inputs and exchange overview
- Conduct matchmaking between offers and requests

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Requirements for Change

- Partnership and collaboration are key to success
- End-to-end transformation from single use/raw material supply to vaccine provision
- Remove barriers and build the supply chain oversight/forecasting for the future
  - Requiring data – to model forecast supplies
- A system that can flex when epidemic/pandemic surge demands occur and yet have, a business-as-usual application
- Reduce and mitigate risk to improve efficiencies

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A WEBINAR SERIES EXPLORING THE BUSINESS OF SUTS

THURSDAY, JULY 15

10:30-11:30 AM EDT

FLEXIBLE WALL MANUFACTURING SYSTEMS: IMPROVING THE ENVIRONMENTAL FOOTPRINT

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