Enabling accelerated COVID-19 vaccine manufacturing

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Outline

• What is the Coalition for Epidemic Preparedness Innovation (CEPI) and COVAX?
• How have we prepared for Global Pandemics?
• How are we responding to COVID19?
• An approach to supply the world with vaccine for COVID19
• How to be better prepared for the next outbreak
A global coalition...forming from Ebola lessons learned

Made up of public, private, philanthropic and civil society organizations

We **identify priority threats** and **act when market forces fail** to drive needed development

We will stimulate, finance and coordinate vaccine development for emerging infectious diseases

We will build **capabilities for rapid response to unknown threats**

We will move vaccine candidates through late preclinical studies to proof of concept and safety in humans before epidemics begin

Launched in January 2017; managing ~2BN USD funding for 5 years
Our vision

A world in which epidemics are no longer a threat to humanity

Our mission

CEPI accelerates development of vaccines against emerging infectious diseases and enables equitable access to these vaccines for affected populations during outbreaks
Access to COVID-19 tools (ACT) accelerator

CEPI is pursuing a range of approaches to help overcome these challenges and increase global access to any future COVID-19 vaccine.

We are founding partners of the ACT (Access to Covid-19 Tools) accelerator, a global coalition to accelerate the development, production of and equitable access to new Covid-19 diagnostics, therapeutics and vaccines.

ACCESS TO COVID-19 TOOLS (ACT) ACCELERATOR
A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines

VACCINES (COVAX)

ACCESS TO COVID-19 TOOLS (ACT) ACCELERATOR
A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines

Key players

SOURCE: (ACT) ACCELERATOR Commitment and Call to Action 24th April 2020
**COVAX’s goals**

- To develop the largest and most diverse actively managed portfolio of vaccine candidates so that the best vaccines are made available and the world has access to the best science.
- To deliver at least 2 billion doses by end of 2021.
- To guarantee fair and equitable access to COVID-19 vaccines for every country in the world.
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
CEPI had multiple investments against priority pathogens when COVID began

<table>
<thead>
<tr>
<th>Disease</th>
<th>Investments</th>
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<tbody>
<tr>
<td>MERS</td>
<td>5 vaccine candidates</td>
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<tr>
<td>Lassa</td>
<td>6 vaccine candidates</td>
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<tr>
<td>Nipah</td>
<td>4 vaccine candidates</td>
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<td>Chikungunya</td>
<td>2 vaccine candidates</td>
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<tr>
<td>Rift Valley fever</td>
<td>2 vaccine candidates</td>
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<tr>
<td>Disease X</td>
<td>3 platform technologies</td>
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CEPI’s Rapid response platforms preparing for Disease X

CEPI will **accelerate** development by use of **vaccine technology platforms**

**Aspirational goals**
- 16 weeks from identification of pathogen to product for clinical trial
- 6 weeks from first dose to clinical benefit
- 8 weeks to manufacture 100,000 doses

**CEPI funding approach**
- Test platform versatility on three pathogens, two into phase I
- Characterize the safety and immunology profile
- Live fire exercise – for disease X

**Platforms**
- mRNA - RNA
- DNA -
- Recombinant proteins – molecular clamp
- Viral vector

CEPI
When COVID emerged, we **leveraged the rapid response platforms** and prior development partnerships to create a robust portfolio of vaccine approaches. This was supplemented by a new Call for Proposals to further broaden the portfolio.

CEPI is proactively preparing for production (at risk) of **billions of doses of vaccine in 2020 and 2021** for COVID19.

**Up to 12 programs will be approved and in clinical development in 2020.** Additional programs are added to COVAX through the BMGF and Gavi/UNICEF call for proposals.

**Formulation and Filling have a high potential to be the bottleneck** by the end of 2020. Mitigations are planned.

**The world may need 8-16 BN doses of vaccine** (2 doses per person); estimated ~65% of the global population will need to be immune by vaccination or natural infection for the outbreak to stop. (The global annual production of commercial vaccines is about 20BN doses.)

CEPI incentivizes development and manufacturing by accepting a significant financial risk to develop multiple platforms and invest in manufacturing before clinical proof of concept is available.
A diverse R&D portfolio has been built

- COVAX has built a portfolio of 9 candidate vaccines, with others in due diligence / negotiation, to support 3-5 licensed products. The approaches include recombinant proteins (with lipid-based adjuvants), DNA with electroporation, mRNA with lipid nano particle adjuvant, and viral vectors. Considering additional viral vectors and inactivated vaccines.
COVID19 Manufacturing in Fast Forward

Typical Vaccine Development Process & Timing (4-7 years on average)

COVID19 Vaccine Development (12-18 months)

We are funding up to 12 programs but expect only 2-3 to reach licensure

No time for new facilities, must find existing capacity

The risks we take are financial, not human safety risk; all regulations are followed to protect human subjects

CEPI incentivizes development and manufacturing by accepting a significant financial risk to invest in manufacturing before clinical proof of concept is available. Otherwise, doses for vaccination campaigns would be delayed and outbreak prolonged.
Building Capacity at Risk – Multiple products

Partners produce early doses to support clinical studies.

Processes scaled up to industrial scale before advanced clinical trial begin.

Each product is scaled-out in different countries to expand capacity.

Bulk vaccine is stockpiled in anticipation of dose level definition.

Some projects will fail during clinical development.

Those facilities may be repurposed for successful products.

2-3 successful programs with productive processes should support 2-4BN doses by the end of 2021.
Drug Substance Considerations

- Scale-up at risk (before clinical proof of concept)
- Scale-out at risk (how many sites?)
  - Nationalism (risk of blocked export); distributed supply
- Process yield (mg/L) not known until June - August
- Final dose not known until July – Dec (some even later); final dose is key to understanding productivity and cost of goods sold.
- **The impact of the dose and yield information can change predicted outcome by >10-fold.** We have assumed low yield and middle dose in our model assumptions, but vary over clinical testing range. Higher yield and lower dose will increase total supply available.

- **CEPI has executed a global capacity survey and has found enough open capacity for >10BN doses of vaccine**

CEPI has financed >$1.4BN for vaccine development and scale-out at risk. Must execute a high-risk path to ensure doses are available as early as possible. (Financial risk taking, but not risking quality or safety.)

Planning with many unknown variables requires extensive modeling of outcomes to understand the universe of solutions that are possible and likely.
Manufacturing capacity mapping
Available capacity

Volume Summary per Region (exclude RNA)

- India
- Europe
- North America
- Rest of Asia / Oceania
- South America
- China
- Africa

Currently Open Capacity

Volume Summary (RNA)

Europe
Belgium
Portugal
North America
USA

Drug Substance Volume Estimate by Country (Exclude RNA)

Summary:
- Analysis is based on liters or grams of production
- Number of doses will depend on actual dose proven in clinical trials
- Substantial DS capacity (L) is available with concentration in certain countries/regions
- Survey does not represent global capacity – only the capacity of respondents.
Drug Product Considerations

- Drug Substance Availability starting in June at earliest
- Dose will not be known until ~September 2020. Cannot start to fill without confirming dose/formulation.

- We have surveyed the global sterile capacity and found sufficient capacity for >4BN doses of vaccine (assuming 20-dose vials).

- We have found a global medical glass shortage which will constrain vaccine supply in 2021
  CEPI has invested in 5 new glass vial manufacturing lines to support 2BN doses of vaccine vials.

- For upside capacity, we are considering alternative drug product images including blow-fill-seal, plastic vials, and a 200-dose bag. These approaches are being studied with user groups in multiple markets.

CEPI procured vials and identified and reserved capacity with formulation and filling contract manufacturers at risk and provided this capacity to developers to enable a more impactful response. This work allowed developers to focus on clinical and process development.
Sustainable Manufacturing – Key Questions

Approved Projects:
mRNA/LNP (2)
DNA/Electroporation
Recombinant Protein (CHO)/Adjuvant (2)
Recombinant Protein (insect cell)/Adjuvant
Adenovirus (2)
rMeasles

• Which product(s) will advance?
• Which platforms are most productive?
• What is the maximum capacity?
• Scale-up or scale-out
• Establish capacity in multiple countries (borders closed?)
• When can capacity be productive?
• What are the limits of various supply elements?
  • LNP
  • Adjuvant

Drug Product Considerations?
• Multi-dose dose vial?
• Frozen (-60°C?)
• Alternative images?
COVID-19 Vaccine Manufacturing

Our approach

Objectives

• Maintain a good handle on **likely dose volumes and rollout potential** as R&D portfolio composition and maturity evolves

• Model different supply scenarios to inform R&D and manufacturing investment decisions, with the **objective to deliver 2 billion vaccine doses by end of 2021**

• Maintain a good handle on optimal supply chains to ensure doses of vaccine can be made available quickly, once proven safe and effective

• **Model network of different supply chains to inform delivery / allocation strategy and decision making**

• Monitor COVID-19 epidemiological forecasts

• Model different dose demand scenarios to inform dose volume targets and manufacturing capacity requirements

• **Map out capabilities**, capacities and interest in responding to the pandemic

• **Assess potential bottlenecks** in the vaccine manufacturing and work out what global capacity might be available to produce billions of doses of vaccine

• **Scale-up / scale-out at risk; fungibility of capacity**

• Establish capacity in multiple countries/regions: Active Ingredient; LNP; Adjuvant

• Focus on most productive/cost effective platforms for greatest leverage

• **Generic DP Network** to support all in portfolio

• Secure **capacity and critical components**/materials/equipment

• Prepare cold chain

Modeling was key to understanding risk, fungibility, accumulation of costs prior to proof of concept, and optimizing the investment in R&D and manufacturing. De-risking supply through a portfolio approach was key for investor management as well.
A Monte Carlo simulation model projects **attrition-adjusted portfolio delivery and dose volumes** within a specified confidence range. Modelling approach is based on available data, assumptions and expert views of project PoS and timelines, manufacturing site productivity, availability and schedules. **POS and Manufacturing estimates applied** at the portfolio level to forecast likely dose volumes for use by COVAX. Simulation repeated with any material change in PoS and/or manufacturing data (~every 2-3 weeks).

A Probabilistic Network model identifies supply chains to optimally support local supply to regions and export to certain regions. Modelling approach is based on available data from the Monte Carlo model. Connections and logistical modalities between DS sites, DP sites, other suppliers (e.g. adjuvants, devices) and regulatory authorities applied to forecast optimal delivery and help reduce supply chain complexity.
Managing from a risk-adjusted portfolio allowed problem solving and risk-taking to be manageable and helped to align the “ecosystem” to prepare for the doses that will be produced. This is not a problem a single company or regulator can solve.

- DS located in HIC and UMIC
- DP distributed in HIC/UMIC/LMIC
- May launch with limited supply chains per region with more added over time as options are approved
- Focused supply chains favors regulatory approvals
- Flexibility added over time with cross-licensing products/facilities/networks
- Managing the complexity will be an extreme challenge as noted, not just due to the network shown, but by non-COVAX suppliers and demand as well.
Conclusions

• Managing a unified, portfolio-approach provides a higher overall probability of success for billions of doses to be available for the world.

• Compilation of accurate global capacity information and leverage multiple modeling tools inform the optimal DS/DP solutions and allow assessment of scale-up risk, fungibility, accumulated financial risks, and optimizing the impact of investments to serve the maximum number of vaccine doses.

• Modeling and capacity collection allowed identification and resolution of many supply chain risks to optimize output from R&D to mass immunization.

Lessons Learned:

• Opportunities for a broader global approach exist by joining efforts of multiple government and non-government response programs.

• We were fortunate to find material capacity to respond to this pandemic. We expect there will be capacity building for future outbreaks that will not rely on luck, but careful planning – warm-ready manufacturing capacity and rapid response platforms are needed.

• Lessons from COVID are not yet complete. Regulatory harmonization and supply planning to all populations will inform what else is needed to further improve our response in the future.