CEPI

2021 Annual Progress Report

Abbreviations

ACT-A	Access to COVID-19 Tools Accelerator
AMC	Advance Market Commitment (COVAX/ GAVI)
BMGF	Bill & Melinda Gates Foundation
CfP	Call for Proposals (CEPI funding opportunity)
CEPI	Coalition for Epidemic Preparedness Innovations
CEPINET	CEPI Community Engagement Network
CMC	Chemistry, Manufacturing Controls
COGS	Cost of Goods Sold
COVAX	Vaccine Pillar of ACT-A (comprising CEPI, GAVI, WHO and UNICEF)
COVID-19	Coronavirus Diseases 2019 (due to SARS-CoV-2 virus)
DRC	Democratic Republic of Congo
EC	European Commission
EDCTP	European Development Countries Clinical Trials Partnership
EMA	European Medicines Association
EMRO	Eastern Mediterranean Region (WHO)
EUA	Emergency Use Authorisation (FDA)
EUL	Emergency Use Listing (WHO)
EID	Emerging Infectious Diseases
FDA	Federal Drug Administration (US)
GHIT	Global Health Innovative Technology Fund (Japan)
IAVI	International AIDS Vaccine Alliance
IFC	International Finance Corporation
IDM	Institute for Disease Modelling
JCG	Joint Coordination Group (CEPI)
KPI	Key Performance Indicator
LMICs	Low- and Middle-income Countries
MERS	Middle East Respiratory Syndrome
NIBSC	National Institute for Biological Standards and Control (UK)
NITAG	National Immunization Technical Advisory Group (or local equivalent)
PAHO	Pan American Health Organization
PAVM	Partnerships for African Vaccine Manufacturing
PSMB	Portfolio Strategy and Management Board (CEPI)
R&D	Research and Development
RDMIC	Research and Development and Manufacturing Committee (CEPI/ COVAX)
RVF	Rift Valley Fever
SWAT	Support Work to Advance Teams (COVAX)
TPP	Target Product Profile
TRG	Technical Review Group (CEPI/COVAX)
WHO	World Health Organization

Introduction from the CEO

2021 marks the culmination of CEPI's first business cycle (2017 through 2021). This Progress Report therefore reflects broadly on CEPI's achievements over this period and takes a deeper dive into its performance in 2021 - a year of significant challenges for CEPI and the world as the COVID-19 pandemic continued to dominate the global health landscape.

It is worth pausing to reflect on recent progress made by the scientific community, while acknowledging that CEPI's work to combat the COVID-19 pandemic has led to multiple advances in vaccines science. CEPI's achievements in response to COVID-19 have informed our bold ambitions for the CEPI 2.0 strategy, elements of which we have already started to take forward.

These achievements have only been possible through extensive partnership across the coalition. Maintaining and expanding these partnerships will be essential as we proceed into 2022 and beyond. During the past 5 years, CEPI has extended its focus from filling a critical gap in the emerging infectious diseases (EID) vaccine research and development (R&D) ecosystem to rapidly responding to a global pandemic -while keeping access at the heart of our mission. In addition, we have overseen a number of scientific "firsts" that would likely not have happened without CEPI investments and expert support. These include breakthrough designation for Valenva's single-shot Chikunguya vaccine candidate, the advancement of the first-ever Nipah and Lassa virus vaccines into Phase I clinical trials and the first ever MERS-CoV vaccine into Phase II trials, as well as three SARS-CoV2 vaccines receiving Emergency Use Licensure (EUL) and a fourth in phase III trials.

2021 also presented tremendous challenges. Despite the tools that the world has developed and despite the unprecedented effort to deploy them, the COVID-19 virus has stayed ahead of us, mutating, gaining speed, and causing wave after wave of infection. In parallel, we witnessed a terrible chasm emerge between rich and poor countries and access to these tools, especially vaccines, is still far from equitable. In response, CEPI played a leading role in establishing COVAX in 2020—with the World Health Organization (WHO) and Gavi—to get vaccines developed, distributed, and deployed to the world. As of 31 March 2022, COVAX had delivered over 1.4 billion doses to 145 countries and economies around the world.

CEPI successfully harnessed the momentum of 2021 to make great strides towards the objectives outlined in its CEPI 2.0 USD 3.5 billion pandemic plan. As we enter 2022, the formal start of CEPI's 2022-26 business cycle, we issued a call to advance the development of a library of vaccine candidates that could be used against the 25 or so viral families known to infect humans. We also co-convened the Global Pandemic Preparedness Summit with the UK Government, during which international policymakers, scientists, and representatives of industry, philanthropy and civil society were united in endorsing CEPI's ambition to have safe, effective, and globally accessible vaccines against the next pandemic threat ready in just 100 days. Over USD 1.5 billion was raised at the Summit to help kick start CEPI's ambitious plan to tackle epidemics and pandemics, potentially saving millions of lives and trillions of dollars in lost economic output.

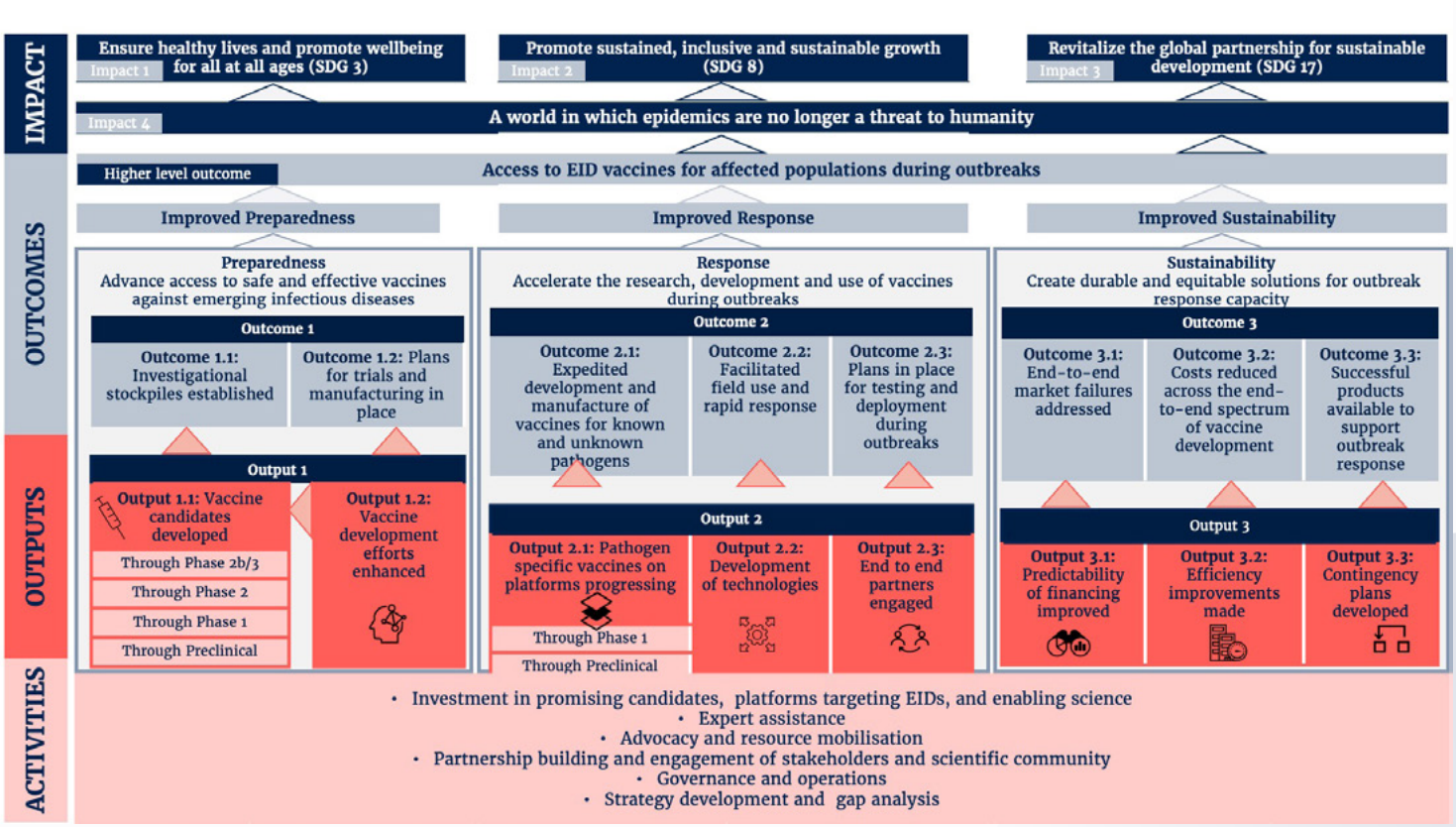
CEPI now moves forward into 2022—and our new strategy—with the agility, experience, and knowledge forged during our first five years of existence, and with more determination than ever to reduce or even eliminate the future risk of epidemics and pandemics so that our children never again face the hardship and loss we've had to endure from COVID-19.

Dr Richard Hatchett, CEO of CEPI

CEPI 1.0 Theory of Change

CEPI's mission in the past five years has been to accelerate the development of vaccines against EIDs and enable equitable access to these vaccines for affected populations during outbreaks. The three strategic objectives underpinning CEPI's first five-year business cycle (CEPI 1.0: 2017–2021) – improved preparedness, response and sustainability – were developed in support of CEPI's founding vision of a world in which epidemics are no longer a threat to humanity. Figure 1 below illustrates the theory of change for CEPI 1.0.

Figure 1: CEPI 1.0 Theory of Change



Five Years of CEPI: Highlights from 2017 to 2021

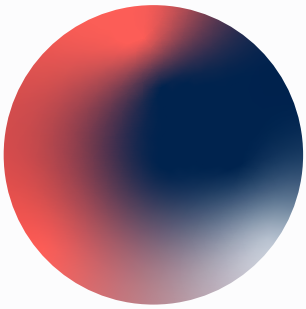
The global need for CEPI was recognised after the devastating Ebola epidemic of 2014–16 in Guinea, Liberia, and Sierra Leone, which killed more than 11,000 people and had an economic and social burden of over USD 53 billion. The world's response to this crisis fell tragically short. A vaccine that had been under development for more than a decade was not deployed until over a year into the epidemic. That vaccine was shown to be 100% effective, suggesting that much of the epidemic could have been prevented.

CEPI was launched at Davos in 2017, by the governments of Norway and India, the Bill & Melinda Gates Foundation, the Wellcome Trust, and the World Economic Forum, as the result of consensus that a coordinated, international, and intergovernmental plan was needed to develop and deploy new vaccines to protect against epidemics caused by emerging infectious diseases.

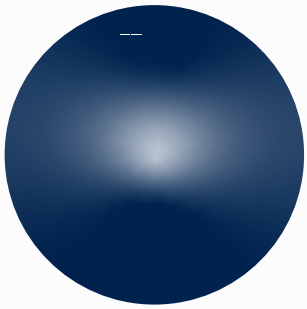
Guided by the WHO R&D Blueprint[1], CEPI prioritised a number of pathogens to accelerate vaccine development against these threats because of the potential health, social, and economic damage they might inflict on vulnerable populations, especially those living in low- and middle-income countries (LMICs).

These priority pathogens are Ebola, MERS, Nipah, Chikungunya, Lassa Fever, Rift Valley Fever and Disease X, as well as SARS-CoV-2.

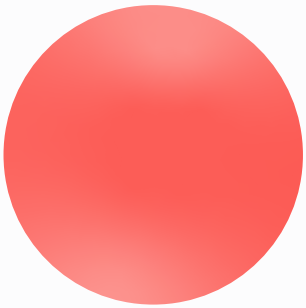
CEPI's accomplishments over its first five years include:



Priority Pathogen Research & Development & Enabling Science

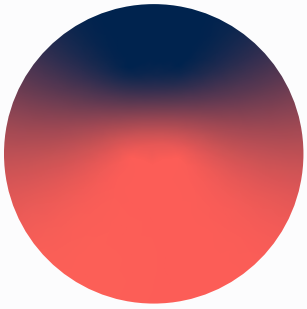


COVID-19 response



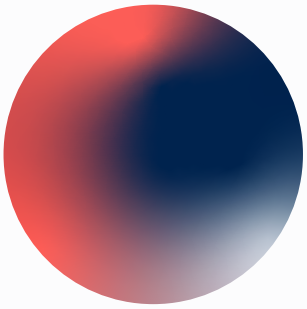
Establishment of COVAX

Support for CEPI 2.0 & the 100-Day Mission



Expanded CEPI's Reach & Influence by Growing the Coalition

[1] https://www.who.int/teams/blueprint/covid-19



Priority Pathogen Research & Development

Rapid vaccine development

CEPI has dramatically influenced the shape of the global R&D ecosystem, forging consortia where appropriate, developing new collaborations and injecting funding to jumpstart R&D when needed. CEPI is filling a critical gap in the vaccine ecosystem – working to ensure epidemics and pandemics are no longer a threat to humanity. By the end of 2021:

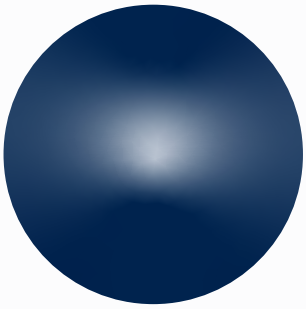
- Over 21 emerging infectious disease vaccine candidates in CEPI's portfolio were actively being advanced through clinical trials that were either CEPI- or self-funded after initial CEPI catalytic funding, including:
  - Seven COVID-19 vaccines in Phase II/III or Phase III pivotal trials (four of which have received Emergency Use Authorisation (EUA))
  - Four COVID-19 vaccines in Phase I/II;
  - Support for the completion of additional clinical trials to broaden the populations eligible for the Ebola vaccines
  - Three Chikungunya projects in Phases II and II/III;
  - Three MERS projects in Phases I and II;
  - Three Lassa projects in Phase I;
  - One Nipah project in Phase I.
- Three dedicated rapid response platforms to develop vaccines against Disease X (the threat of an unknown virus) were established, with Imperial College London, University of Queensland, and CureVac. The "Molecular Clamp" platform developed by the University of Queensland was quickly deployed against COVID-19 and advanced into Phase 1 trials, generating positive safety and immunogenicity data. While the vaccine candidate was not progressed into Phase II/III clinical trials due unsuitability for broad deployment, the platform technology shows promise against other emerging infectious disease threats.

Enabling Science Programmes

- CEPI launched the Enable study to better understand the burden of the deadly Lassa fever infection, which impacts West Africa annually. Enable, the largest epidemiological study of the disease, has enrolled 23,000 participants across Nigeria, Benin, Liberia, Guinea, and Sierra Leone. Its findings will help guide the location of future vaccine trials and potential vaccination strategies.
- Together with Nipah-affected country institutes and the few Nipah survivors, CEPI participated in ground-breaking research to better understand the immune response generated following Nipah infection.
- Working alongside the UK National Institute for Biological Standards and Control (NIBSC) and other partners CEPI helped to develop antibody standards – essential tools needed to support vaccine R&D – for Lassa Fever, Nipah, Rift Valley Fever, MERS, and COVID-19. Both the COVID-19 antibody standards and MERS antibody standards have been endorsed by the WHO Expert Committee on Biological Standardization.

Centralized Lab Network

- CEPI created the world's largest centralized laboratory network – which works across multiple regions to harmonize the evaluation of COVID-19 vaccine candidates undergoing preclinical and clinical trials. This network is unique in terms of size and scale and has been used by over 30 COVID-19 vaccine developers to assess over 15,000 clinical trial samples. In November 2021, CEPI expanded this COVID-19 vaccine testing network to also assess the development of vaccines against other epidemic and pandemic diseases.



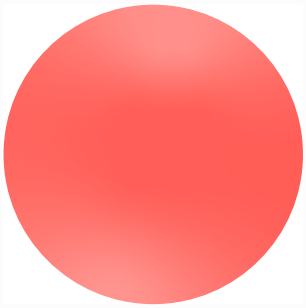
COVID-19 response

Advancing COVID-19 Vaccine Development

CEPI was one of the first actors to respond to COVID-19, convening expert scientific governance bodies and initiating investments in three COVID-19 vaccine candidates in January 2020, when there were just 581 cases of COVID-19 worldwide.

CEPI initiated the development of the world's largest and most diverse COVID-19 vaccine portfolio, built on the principles of speed, scale and access. Of 14 CEPI-funded COVID-19 vaccine candidates (including mRNA, DNA and protein vaccine technologies), six remain in active clinical development, and three CEPI-funded vaccines (Oxford-AstraZeneca, Moderna and Novavax) have received WHO Emergency Use Listing and are being used around the world, saving lives.

- Funding for seven programmes was announced, to advance broadly protective coronavirus vaccines against SARS-CoV-2 variants and potentially other Betacoronaviruses.
- A USD 140 million call was launched to support the rapid generation of additional clinical research on COVID-19 vaccines, to generate evidence on clinical vaccine effectiveness. and expand access to COVID-19 vaccines as part of the global vaccination rapid rollout. The call included funding for clinical trials in pregnant women, infants and children, and immunocompromised populations, as well as for studies on booster doses, length of vaccine efficacy, 'mix and match' strategies, and dosing intervals.
- CEPI led development of second-generation COVID-19 vaccine candidates to provide protection against emerging variants and for use in low-resource settings



Establishment of COVAX

In March 2020, CEPI circulated a concept note for a Fair Allocations of Innovations for Pandemic Relief (FAIR) system to establish a globally-equitable system for allocating COVID vaccines. CEPI, together with Gavi and WHO then created COVAX, the vaccines pillar of the Access to COVID-19 Tools Accelerator (ACT-A), to enable equitable access to COVID-19 vaccines.

- COVAX has legally-binding commitments in place to access up to 3 billion doses of CEPI-funded COVID-19 vaccines for equitable distribution which has saved millions of lives. COVAX delivered its 1 billionth dose on 15 January 2022.
- CEPI helped create the first and only international vaccine injury compensation mechanism. The No-Fault Compensation (NFC) programme offers eligible individuals in Advance Market Commitment (AMC)-eligible countries and economies a fast, fair, robust and transparent process to receive compensation for rare but serious adverse events associated with COVAX-distributed vaccines.

Support for CEPI 2.0 and the 100-Day Mission

Launched CEPI 2.0 Strategy

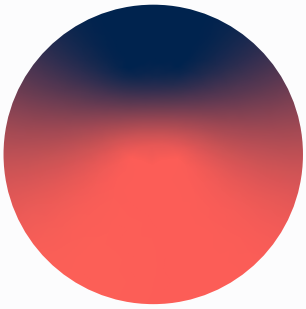
- In 2021 CEPI launched a USD 3.5 billion, 5-year plan to tackle the risk of future pandemics and epidemics with equitable access as its foundation. Building on CEPI's first five years, CEPI 2.0 aims to dramatically reduce or even eliminate the future risk of pandemics by: addressing critical R&D gaps including against the most prominent known threats and optimizing current COVID-19 vaccines, addressing variants of concern and developing next-generation COVID-19 vaccines, as well as initiating the development of broadly protective coronavirus vaccines.

Raised over USD 1.5 billion towards CEPI 2.0

- In March 2022, CEPI and the UK Government co-hosted the Global Pandemic Preparedness Summit to explore how the world should better prepare for future pandemics and to support CEPI's mission. Over USD 1.5 billion was raised in support of CEPI's next five-year pandemic plan and new stakeholders joined our global coalition.

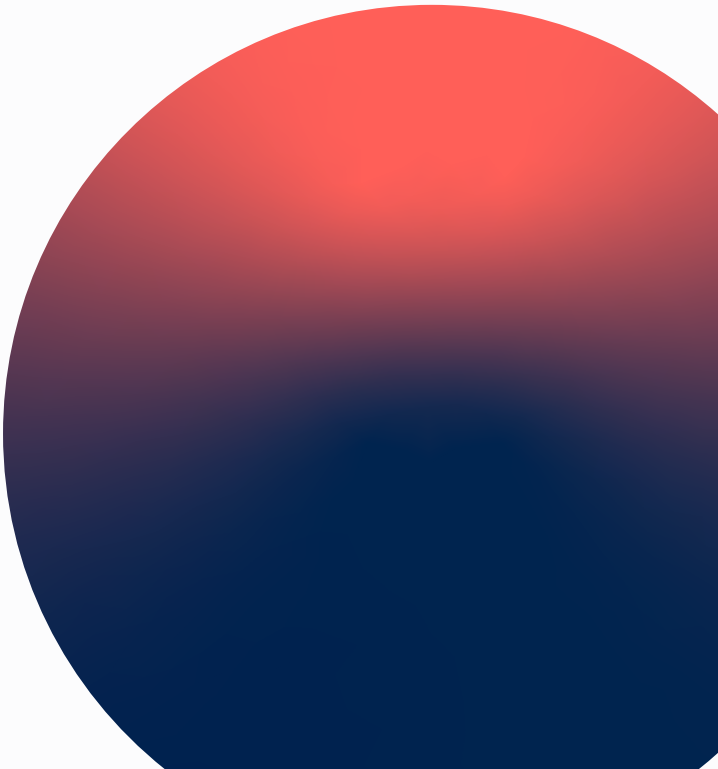
Galvanized International Support for CEPI's 100-Day Mission

- G7 and G20 leaders publicly backed CEPI's 100-day mission to have safe, effective, and globally accessible vaccines against the next pandemic threat in just 100 days.



Expanded CEPI's Reach and Influence by Growing the Coalition

- CEPI now works with over 30 donors/investors – including governments, philanthropic foundations and private sector partners.
- CEPI has forged strategic and operational relationships with major global, regional and national bodies such as the Africa Centres for Disease Control and Prevention, the Chinese Ministry of Science and Technology, the International Finance Corporation (IFC), Gavi, the Pan American Health Organisation (PAHO), the United Nations Children's Fund (UNICEF) and WHO.
- By December 2021, CEPI had signed over 70 partnership agreements with life sciences organizations around the world to establish a portfolio of vaccine candidates, rapid response technology platforms and enabling science programmes across a broad range of emerging infectious diseases, including COVID-19.
- CEPI has bolstered its in-house capacity and at the time of writing employed over 150 staff originating from 45 different countries based in Oslo, London and Washington DC, alongside a team of global expert consultants.



Looking Toward CEPI 2.0

With the 2021 launch of the CEPI 2.0 strategy and investment case, CEPI began to transition to its next five-year (2022-2026) business cycle. The mission for CEPI 2.0 is to accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats so they can be accessible to all people in need. The strategy builds on past learnings and the experience of responding to the COVID-19 pandemic and in so doing incorporates a technical evolution. This includes:

- Continuation of vaccine development of priority pathogens beyond late stage (Phase IIb/III) towards licensure for priority pathogens with a clear unmet need, where vaccines could have an impact.

- Modest investments in products beyond vaccines by initiating the development of a monoclonal antibody programme focusing on certain parameters—driving down costs and making these technologies accessible to all, with the target of two priority pathogen monoclonal antibodies ready for emergency use.

- Expanded focus on Disease X—a disease with pandemic potential caused by a pathogen currently unknown to cause human disease—by harnessing innovations in vaccine development and manufacturing. This includes investments in virus family vaccine libraries, prototypic vaccine approaches and innovations that can 'transform' manufacturing cheaper, faster and closer to an outbreak.

- Elevation of CEPI's role in connecting with other stakeholders to enable rapid countermeasure development, effective response and equitable access for those in need. This will include working with partners to articulate the configuration of a 'target ecosystem profile', investing and supporting networks of ready-to-act entities across a set of core functional areas (e.g., enabling sciences), and promoting sustainable diversified manufacturing for CEPI-funded programmes.

Given the evolution of the SARS-COV-2 virus, and the urgency to end the acute stage of the pandemic, CEPI brought forward some activities from CEPI 2.0 into 2021, including the launch of a Call for Proposals (CfP) for the development of a broadly protective vaccine for Betacoronaviruses, work on viral families and aligning stakeholders around the 100-day mission. Relevant activities are reflected in this report.

The CEPI 2.0 results framework, theory of change and key performance indicators are available on CEPI's website. The 2022 Annual Progress Report will be based on the new results framework and will track progress against the new strategic objectives Prepare, Transform and Connect and associated indicators.

Focus on 2021

The following pages highlight CEPI's 2021 progress:

Section 1: Outlines how CEPI has progressed against the three strategic objectives. It describes key activities and progress against targets as set out in the Results Framework for CEPI's core portfolio of priority pathogens, Disease X and platform technologies. It describes activities and progress against targets for CEPI's COVID-19 vaccine portfolio under each strategic objective. For each indicator, a Status Box is provided with an assessment of progress against the 2021 targets. Supplementary information is provided in a commentary box and accompanying narrative. Some indicators include targets for 2022, with an explanation of how these activities will be carried over into the next strategic period – from 2022 to 2026 – and how they will be tracked in the next progress report.

Sections 2 and 3: Provide a summary of CEPI's finances and funding sources and outline CEPI's approach to risk management

Appendices 1 through to 5 provide information on CEPI's organisational structure, human and financial resources, and key governance bodies.

1. Progress Against the Strategic Objectives

1.1. Strategic Objective 1: Preparedness

By the end of 2021, CEPI had made investments in 20 vaccines candidates against its initial priority pathogens, in three rapid response platforms to develop vaccines against Disease X, increased its COVID-19 portfolio to 15 active vaccines (3 were down selected), and invested in an array of enabling science programmes. Through targeted investments in R&D, CEPI has also overseen a number of scientific "firsts", including the first Phase III trial of a Chikungunya vaccine (started in September 2020) launched with co-primary endpoints successfully met, and the advancement of the first-ever Nipah and Lassa virus vaccines into Phase I (started February 2020 and October 2019 respectively), as well as the first ever MERS-CoV vaccine into Phase II (started August 2021.).

Throughout 2021, CEPI continued to deliver on its promise to work towards a world in which epidemics are no longer a threat to humanity, pioneering push funding mechanisms and solutions (including access commitments) to advance the development of vaccines against EIDs[2]. Funding vaccine development of priority pathogens and rapid-response vaccine platforms, and deploying an agile approach to selecting and advancing the portfolio of vaccine candidates have allowed CEPI to continue to play a central role in the global response to COVID-19, creating the world's largest portfolio of COVID-19 vaccines, three of which have received WHO EUL and are in use around the world, saving lives. CEPI in 2021 made four investments in broadly protective approaches, in response to the emergence of COVID-19 variants.

CEPI is the only public sector funder of R&D that has leveraged its investments to enable equitable access to vaccines. COVAX – the vaccines pillar of ACT-A and of which CEPI is a founding partner – has legally-binding commitments in place to access up to 3 billion doses of COVID-19 vaccines from CEPI-funded programmes for equitable distribution.

CEPI's R&D investments continue to strengthen the world's defences against COVID-19 by optimizing use of the current vaccines, addressing variants of concern, developing next-generation vaccines well-suited for low-resource settings, and developing broadly protective coronavirus vaccines.

CEPI's 2021 efforts to support improved Preparedness to advance and support equitable access to safe and effective vaccines against EIDs (including both non-COVID-19 and COVID-19) are highlighted below. Drawn from the theory of change, CEPI's 2021 activities are described under the following sections and subsections:

- Invest in promising candidates targeting EIDs to drive the development of vaccines suitable for use in LMICs where market incentives are insufficient, including:
  - Advance access to safe and effective vaccines against EIDs
  - Continued work on the Ebola vaccine
- Promote equitable access through robust clinical and manufacturing plans and contract terms to allow for trials and eventual deployment of vaccines during outbreaks[3] including:
  - Partner with at-risk countries in planning for clinical trials
  - Ensure fit-for-purpose provisions to support equitable access
- Provide expert assistance and funding, enabling science and technologies to enhance vaccine development efforts, including by accelerating vaccine development through enabling science

[2] identified in the WHO R&D Blueprint for action to prevent epidemics

[3] This description has been updated to more accurately reflect CEPI's activities in this area. In previous Annual Progress Reports, this group of activities was described under the heading "Facilitate the establishment and maintenance of the investigational stockpiles and developing robust plans to allow for trials and eventual deployment of vaccines during outbreaks."

I.I.I. Invest in promising candidates targeting EIDs to drive the development of vaccines where market incentives are insufficient

Advance access to safe and effective vaccines against emerging infectious diseases

Overall positioning and progress

By December 2021, CEPI had signed over 70 partnership agreements with life sciences organizations around the world to establish a robust portfolio of vaccine candidates, rapid response technology platforms and enabling science programmes across a broad range of emerging infectious diseases, including COVID-19. As illustrated in Figure 2 below, CEPI's R&D portfolio consisted of 20 vaccine candidates against its initial priority pathogens (six against Lassa virus, five against MERS-CoV, four against Nipah virus, three against Chikungunya, two against Rift Valley Fever), 14 vaccine candidates for COVID-19 and three rapid response platforms to deploy against unknown threats, or Disease X (including one MERS and one Lassa as pilot pathogen vaccine candidates). This also includes investments in a range of pathogen-specific and cross-cutting enabling science activities that support vaccine development as well as funding activities towards "finishing" Ebola.

By the end of 2021, over 21 EID vaccine candidates in CEPI's portfolio were actively being advanced through clinical trials that were either CEPI or self-funded, including:

- Seven COVID-19 vaccines in Phase II/III or Phase III pivotal trials (four of which have received Emergency Use Authorisation (EUA))
- Four COVID-19 vaccines in Phase I/II;
- Three Chikungunya projects in Phases II and II/III;
- Three MERS projects in Phases I and II;
- Three Lassa projects in Phase I;
- One Nipah project in Phase I.

Each of these vaccine candidates is designed to meet a Target Product Profile (TPP), the specific characteristics targeting a particular disease, that is designed to enable use of the vaccine in LMICs. TPPs include dosing regimen, thermal stability, presentation and cost of goods as well as other characteristics. Partners and manufacturing plans are reviewed from the perspective of supply security as well as cost and contractual mitigations, such as technology transfer as appropriate, to enable equitable access.

Details of CEPI-funded clinical studies are made available through ClinicalTrials.gov or similar, and results are submitted for publication on an open access basis within 12 months of final study report to accelerate the field in general and avoid duplicative use of public funds.

Progress per disease area

Lassa - Three vaccine candidates are in clinical development, constituting the world's first-ever Lassa vaccines to enter into mid-stage clinical development, including in West Africa. A strong enabling science programme, specifically an international reference standard for immunological assays, is n place and will allow comparisons and decisions on the development of the most promising vaccine candidates. In addition, the largest ever Lassa epidemiology study, Enable, will help determine the optimal design for late-stage clinical trials of the most promising vaccine candidates, from 2023 onwards. Despite progress, the Lassa portfolio is behind schedule vis-à-vis its initial five-year goal. Substantial delays and setbacks have occurred, largely due to COVID-19, but also because of partnership challenges and different levels of maturity of projects in the Lassa portfolio. For instance, the technical re-evaluation of one of the portfolio's leading candidates following MSD's (Merck) acquisition of CEPI's development partner, Themis, has been a significant setback in the portfolio's ability to deliver the Phase IIa target by end-2022. Moreover, CEPI's Lassa portfolio has encountered challenges with regards to manufacturing and in the preparation of full clinical development plans.

Nipah – The vaccine portfolio is an early-stage portfolio that continued to face significant delays because of COVID-19, with only one of the four vaccine candidates active in clinical development[4]. Despite the challenges, all of CEPI's vaccine candidates have now demonstrated preclinical proof of concept. CEPI approved the progression of Oxford Nipah and PHV Nipah to Phase I and conditionally endorsed the progression of University of Tokyo Nipah to Phase I. In addition, CEPI has established a strong portfolio of enabling activities that is critical to the feasibility of Nipah vaccine development, including the development of biological standards, regulatory-compliant animal models and upcoming epidemiological work to understand strain diversity.

Middle East Respiratory Syndrome (MERS) – While CEPI continued to support the progression of its MERS vaccine candidate portfolio, CEPI had to redirect some of its partners' efforts to develop vaccines against COVID-19. The MERS portfolio requires strengthening given a mix of preclinical and clinical data for projects, technical and partnership challenges, as well as a mixed performance of platforms against both MERS-CoV and COVID-19. Going forward, CEPI's development efforts for MERS will be considered also in the context of broadly-protective coronavirus approaches, which CEPI has started to fund as part of CEPI 2.0.

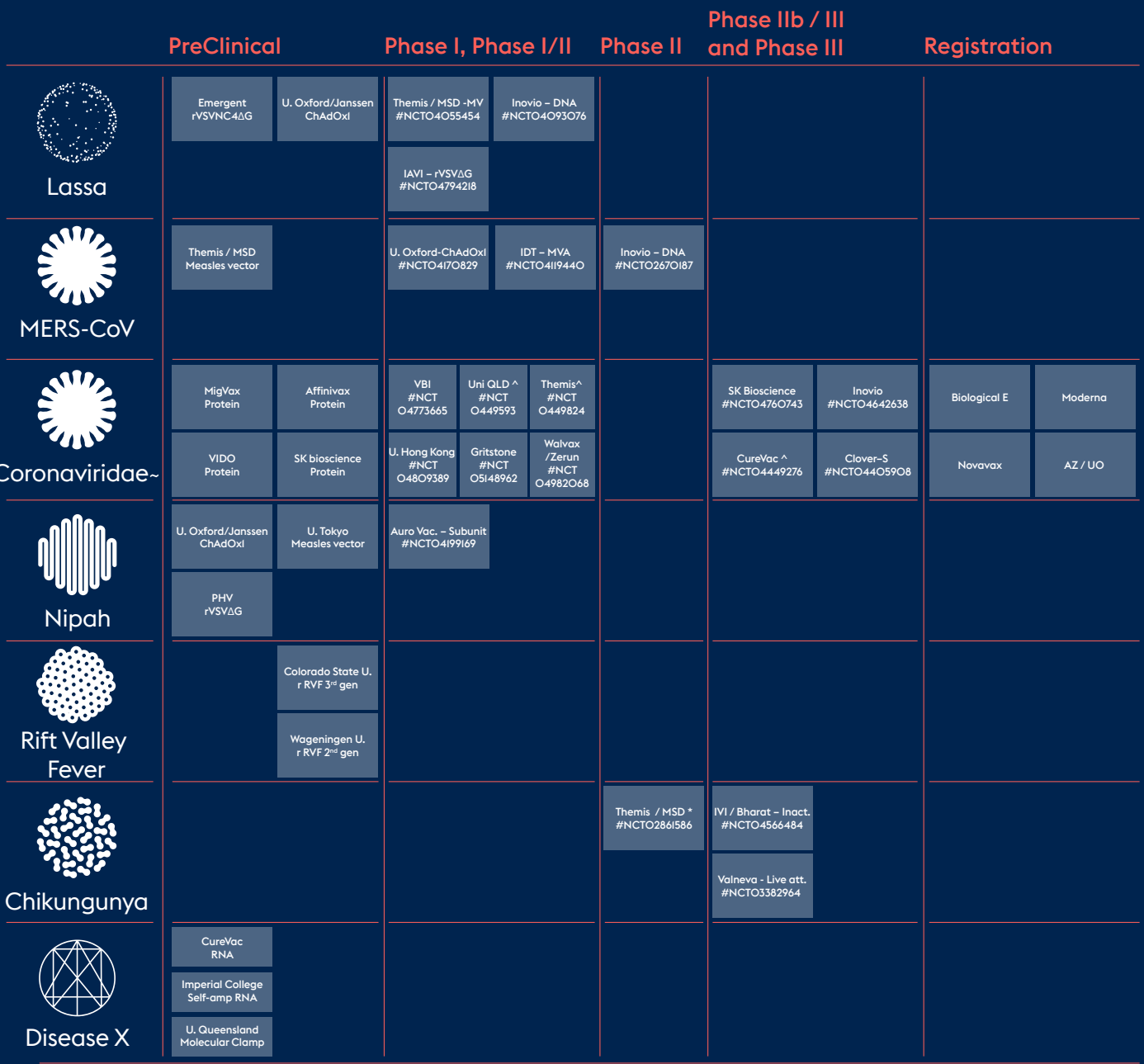
Chikungunya – 2021 has been a strong year for this vaccine portfolio, with the world's first-ever Chikungunya vaccine Phase III clinical trial (Valneva) delivering positive results, the initiation of IVI/Bharat's Phase II/III clinical trial, and with two of the portfolio candidates (Valneva, IVI/Bharat) expanding key partnerships for manufacturing, clinical development and equitable access in Brazil and India. Some delays focussed on LMIC use have been encountered, but working with partners, CEPI has been able to keep these large-scale development programmes generally on track, in the face of substantial COVID-19 disruptions over the past two years.

Rift Valley Fever (RVF) – The vaccine portfolio is relatively small (only two candidate live-attenuated vaccines). Both vaccine projects are progressing towards respective endpoints but have experienced delays due to COVID-19 and due to lack of clarity on co-funding. CEPI has approved the Larissa RVF candidate to progress into Phase I based on a technical review and is planning to expand its RVF portfolio through an upcoming CfP. CEPI has experienced an increasing volume of activities and excellent progress on the enabling sciences front, these include an antibody standard which will soon go to NIBSC, as well as an ongoing epidemiology study to help predict where outbreaks are likely to occur and to determine the feasibility of vaccine efficacy trials for RVF.

COVID-19 – Progress for the COVID-19 vaccine portfolio is captured under Section 1.2.2. CEPI's response work connected to COVID-19

[4] A second candidate (PHV) initiated clinical development in January 2022

Fig. 2 Portfolio overview – CEPI-funded vaccine candidate portfolio as of December 2021



~ Most of the COVID-19 projects are co-funded by other partners together with CEPI (R&D/procurement)
^ COVID-19 projects now terminated
* Pilot pathogen candidates of rapid response platforms have been evaluated through preclinical and phase I

Following a strategic review of its R&D portfolio in November 2021 (See section 1.3 Sustainability), CEPI identified several areas that the Coalition will need to work on to continue to deliver on its objectives:

- Regulatory requirements for several of CEPI's supported platforms;
- Manufacturing-supply chain risks and technical innovations capabilities within vaccine development partnerships;
- Enabling activities to support late-stage clinical development and licensure while remaining organisationally agile.

The portfolio review highlighted that CEPI's future plans under CEPI 2.0 will need to adapt with regard to each pathogen by positioning investments in the right areas for even greater catalytic impact:

- Platforms that allow CEPI to pivot and add pathogen targets as new threats emerge;
- Enabling activities that strengthen accelerated pathways to product development and capacity for global access;
- Deeper understanding of country plans for use, demand and prioritisation to fine tune TPPs and equitable access plans;
- Alignment with other actors across all phases of pre-approval research and post-approval purchase and distribution; and
- Skills and expertise for enabling manufacturing capabilities in LMICs.

Table 1: Summary of CEPI's vaccine candidate portfolio

Pathogen	Phase	Target 2021	Actual 2021 (+ additional successful Stage Gate Reviews)	Comment
"Core" priority pathogens	Pre-clinical	13	17	The pipeline is progressing broadly as expected but experiencing delays due to the impact of COVID-19.
	Phase I	11	8(+3)	
	Phase II	4	3	
	Phase III / Licensure	1	1	
COVID-19	Pre-clinical	NA	4	As of end-of 2021, 4 CEPI-supported candidates have achieved licensure, with 7 additional candidates in clinical development.
	Phase I/II	NA	4	
	Phase II/III	NA	3	
	Phase III / Licensure	NA	4	
Total	Pre-clinical	13	21	Pathogen projects and COVID-19 projects, CEPI is ahead of its 2021 targets.
	Phase I	11	12 (+3)	
	Phase II	4	6	
	Phase III / Licensure	1	5	

Output 1.1 – KPI 8: Number of vaccine candidates advanced for each priority disease							
Pathogen	**Phase**	**Baseline**	**Target 2021**	**Actual 2021** [5]	**Target 2022**		**Status**
Lassa	Preclinical	0	4	6	0	In CEPI 2.0 the milestone for 2022 has been adjusted to: 2 candidates in preclinical, 6 in Phase I, 4 in Phase II and 2 in Phase III.	**WILL BE TAKEN FORWARD UNDER CEPI 2.0***
	Phase I	0	3	3 (+1)	0		
	Phase II	0	2	0	3		
Nipah	Preclinical	0	4	4	0		
	Phase I	0	3	1 (+2)	0		
	Phase II	0	1	0	3		
MERS	Preclinical	4	4	5	0		
	Phase I	0	3	3 (+1)	0		
	Phase II	0	1	1	3		
Chik	Preclinical	3	0	0	0		
	Phase I	2	1	0	0		
	Phase II	0	0	2	1		
	Phase III	0	0	1	0		
	Licensure	0	1	0	0		
RVF	Preclinical	0	1	2	0		
	Phase I	2	1	0 (+1)	2		
	Phase II	0	0	0	0		

Comment: For 2021 targets per core priority pathogen, CEPI is slightly behind on progressing the portfolio in the clinical Phase (I and II). Progress per disease in 2021 includes:

Lassa:

- Start of Phase Ib study in Ghana (the first clinical trial for Lassa from CEPI's portfolio to be undertaken in an affected country (Inovio));
- Phase I first-in-human study (US). Preparation for Phase IIb under European and Developing Countries Clinical Trials Partnership (EDCTP) agreement (IAVI);
- Conditional commitment to funding progression of Oxford Lassa to Phase I.

Nipah:

- Continued funding to progress to Phase I (Oxford, PHV and University of Tokyo).

MERS:

- Commencement of Phase Ib study in Germany and the Netherlands (IDT);
- Initiation of multi-country Phase II study (Inovio);
- Successful completion of preclinical development

Chikungunya:

- Technology transfer to Brazil. Preliminary supply strategy and awarded Food and Drug Administration (FDA) breakthrough designation following FDA fast track designation and EMA PRIME designation. Announced positive Phase III data (Valneva);
- Initiated multi-country Phase II/III of its Chikungunya candidate (IVI);
- Strengthening of project plan including an additional Phase II study, and chemistry and manufacturing control (CMC) development (Themis).

Rift Valley Fever:

Project progressing towards Phase I based on a technical review (Wageningen).

***CEPI 2.0**

CEPI will continue vaccine development of priority pathogens and expand its support to late stage (Phase IIb/III) development towards licensure with a clear unmet need, where vaccines could have an impact. Future targets include development of vaccine candidates and monoclonal antibodies against priority pathogens, with at least two vaccines reaching licensure for two or more priority pathogens (including at least one WHO Prequalification), and at least two monoclonal antibodies for two priority pathogens ready to use under outbreak conditions.

[5] Some vaccine candidate projects have successfully passed the Stage Gate Review to enter the next development phase but have not yet initiated the next phase in terms of dosing study subjects. These numbers are added as (+SG) in the table above.

Continued work on vaccine against the Ebola virus

A trigger for CEPI's establishment in 2017 was to support the attainment of licensure for two or more Ebola vaccines. The Ebola virus remained a public health challenge throughout 2021:

- The 12th and 13th outbreaks in the Democratic Republic of Congo (DRC) from February to May, and from October to December resulted in 23 cases and 15 deaths.

- A second Ebola outbreak in Guinea from February to June, resulted in 23 cases and 12 deaths.

CEPI's investments in this area are guided by the following principles:

- Achieve goal of attaining licensure for two or more vaccines;

- Facilitate licensure through data collection and analysis needed by advancing scientific understanding of immune response and supporting novel approaches to authorisation and licensure;

- Support clinical trials in affected countries including in an outbreak situation (when they aim for licensure in risk groups and subpopulations, and advance or simplify the delivery of vaccines in the field through vaccine-related innovation);

- Support a general approach to sustainable manufacturing that includes Ebola vaccines;

- Not exclusively fund the deployment or delivery of vaccines.

The Janssen vaccine, which is an important milestone in efforts to improve prevention and response to future Ebola outbreaks, is supported by CEPI and was granted WHO prequalification in April 2021. As part of the European Medicines Agency (EMA) post-licensing commitments for the Janssen vaccine, the company is conducting a clinical trial in pregnant women in Rwanda. The study, which aims to enrol 2,000 pregnant women to evaluate the safety and immunogenicity of the vaccine, is well underway, having enrolled more than 75% of the required volunteers.

A large effectiveness study in the DRC, also using the Janssen vaccine, closed in February 2022. Other CEPI-supported clinical trials with the Janssen vaccine include a trial in Uganda for frontline workers, (in the final safety follow-up phase for pregnant women) and two trials in the EBOVAC3 consortium in Sierra Leone, Guinea and DRC that have either completed vaccinations or are still evaluating a booster dose.

The Merck Ebola vaccine is currently being tested by Canadian Immunization Research Network / Dalhousie University in HIV+ populations in Burkina Faso and Senegal (the ACHIV study). CEPI is supporting an additional study cohort to evaluate the safety and immunogenicity of a second vaccine dose.

CEPI is also supporting clinical trials and immunological read-outs (PREVAC-UP) [6] for both the Merck and the Janssen Ebola vaccine, though delays continued to be experienced due to the COVID-19 pandemic.

[6] PREVAC-UP: The Partnership for Research on Ebola Vaccination

1.1.2. Promote equitable access through robust clinical and manufacturing plans and contract terms to allow for trials and eventual deployment of vaccines during outbreaks[7]

1.1.2.1. Partner with at-risk countries in planning for clinical trials[8]

Epidemiological studies, such as cross-sectional, case-control or prospective cohort studies, and mathematical modelling, are essential to address key issues in vaccine development. Such studies contribute to current knowledge of the burden of disease, correlates of immunity, strain circulation, vaccination effectiveness and impact, and facilitate the design and inform the location of vaccine trials. In addition, they offer an opportunity to strengthen capacity in priority pathogen-endemic countries by building on national surveillance and ongoing research – while providing a framework for enhanced laboratory diagnostics and good clinical practice for future vaccine trials.

In the context of the priority pathogens and anticipating Lassa vaccine candidates to be ready for advanced-stage clinical development, CEPI has made significant progress in the conduct of the multi-country prospective cohort study in five West African countries. Known as the Enable Lassa Research Programme, this programme is the result of many years of effort by CEPI and its country partners to address a critical knowledge gap impairing the delivery of a vaccine for Lassa fever.

In 2021, Enable achieved several important milestones including:

- Public launch of the programme and study enrolment activities in Benin, Guinea, Liberia and Sierra Leone;
- Completion of participant enrolment in all five countries, meeting cohort targets. Partners now actively follow over 23,000 volunteers across the five countries;
- Completion of the second six-month follow-up of 3,000 infection cohort participants in Nigeria;
- Facilitation of the Ebola public health response in Guinea by providing laboratory supplies (Ebola PCR kits);
- Selection of the serology ELISA kit (Zalgen) and, with the support of the coordinating and implementing partners, developed a comprehensive training and analysis suite to improve ease of analysis and data quality.
- Formalization of support to vaccine developers for the preparation and conduct of late-stage clinical trials with potential to achieve proof of concept and / or the demonstration of pivotal efficacy of novel Lassa virus vaccine candidates in Lassa endemic countries.

An anticipated outcome of investment in Enable is an enhanced capability to plan and conduct clinical trials in Lassa fever-affected countries, to inform vaccination strategies and enable equitable access.

CEPI has also undertaken activities to expand understanding of the evolutionary development of the Nipah virus in endemic countries and any associated epidemiology in humans to ensure vaccine development efforts are suitably addressing strain variation. A specific CfP was launched in November 2021 to invite research organisations or consortia to support CEPI's efforts.

[7] The description of this activity has been updated to more accurately reflect CEPI's activities in this area. In previous reports, the work in this section was described under the heading "Facilitates the establishment and maintenance of investigational stockpiles and develops robust plans to allow for trains and eventual deployment of vaccines during outbreaks".

[8] See section 1.2.3. Support the development of technologies to facilitate field use and rapid response.

An investigational vaccine can only help curb an outbreak if the vaccine can be accessed— either through clinical trials, or emergency use provisions. Developing accurate vaccine manufacturing estimates for ready reserves of clinical trial material for CEPI target pathogen strategies is therefore crucial. In 2019, CEPI released a CfP for "Epidemiology and vaccine demand curve modelling for CEPI target pathogens" to support sustainable manufacturing efforts for CEPI's priority pathogens. This information helped CEPI to better understand potential vaccine impact and paved the ground for drafting a modelling strategy to inform the methodology for priority pathogens and manufacturing strategy under CEPI 2.0. The results of the research were published in a preprint publication: "Projecting vaccine demand and impact for emerging zoonotic pathogens", (undergoing peer review, February 2022).

Furthermore, close collaboration with the Institute for Disease Modelling (IDM) group at the Bill & Melinda Gates Foundation (BMGF) resulted in the creation of a dynamic mathematical model to support COVID-19 vaccine allocation in LMICs and to assess expected impact on cases and deaths averted. The results of this collaboration were published early in 2022 in PLOS Global Health: Rural prioritization may increase the impact of COVID-19 vaccines in a representative COVAX AMC country setting due to ongoing internal migration: A modelling study. ¨

In 2019 and 2020, CEPI released a tender for a systematic literature review to inform the Chikungunya and RVF vaccine development strategies. Results of both reviews have now been published in PLOS Neglected Tropical Diseases as follows:

- "The global epidemiology of chikungunya from 1999 to 2020: A systematic literature review to inform the development and introduction of vaccines"

- "Paving the way for human vaccination against Rift Valley fever virus: A systematic literature review of RVFV epidemiology from 1999 to 2021"

Strengthening community engagement as part of vaccine development has further advanced and the CEPI Community Engagement Network (CEPINET) is now taking shape. The mission of CEPINET is to strengthen the relationship between communities and research institutions by expanding and deepening existing partnerships and forging new ones, with the goal of facilitating effective community engagement that enables vaccine research, development, and uptake against CEPI's priority pathogens. A dedicated project charter and core team have been established and the project will be officially launched in 2022.

I.I.2.2. Provisions fit for purpose to support equitable access

Equitable access is a key imperative of CEPI's work. From supporting enabling science that benefits the entire field, enabling manufacturing in multiple geographies or at lower cost, to striving for ease of delivery in low-resource settings, CEPI looks at every way possible to develop vaccines that are available, affordable and appropriate. In line with its equitable access policy, CEPI requires commitments by its partners to make appropriate products affordable and available to those who need them most, commencing with programme selection through to licensure to manufacturing. CEPI also works together with stakeholders in the value chain to pass on the value of those commitments, particularly to those responsible for negotiating final price, volume purchase and allocation agreements, as well those engaged in last-mile delivery.

With every investment, CEPI's commitment to access focusses on enabling the ultimate delivery of doses to those that need them the most through outcomes that are within CEPI's scope:

- Data available to scientific community on an open access basis
- Enabling science to expedite a broader research agenda
- Products available at an affordable price as close to cost as is sustainable and developed in line with target product profile
- Adequate availability of supply of appropriate products for lower- and middle-income countries
- Manufacturing capacity adequate to meet demand at an affordable price and where possible local to areas where the disease is most likely

To achieve these outcomes, CEPI relies on partners. It can be difficult for partners to commit to measurable access commitments early in the development process as not all characteristics of the final product and its manufacturing are known in early-stage development, or the partners may have other funding which exceeds CEPI's contribution. CEPI's influence depends on its level of investment, the stage of product development, and the presence or absence of other investors who may have their own conditions and requirements with regard to access. CEPI's approach is thus to review its access provisions with partners at pre-determined decision points on continued funding and add in, or renegotiate terms, as appropriate, before investing further.

CEPI's approach to supporting equitable access is grounded in the following activities:

1. **End-to-end coverage** – coordinating development partners, critical consumable suppliers and manufacturers to facilitate procurement and delivery;

2. **Funding and access to development tools** – providing tools and knowledge for developers all over the world to accelerate timelines and make smarter decisions;

3. **Clinical and regulatory advancement** – facilitating regulatory and clinical collaboration across products and geographies;

4. **Manufacturing and supply of doses** – providing for "scale-up" of a developer's existing capacity and "scale-out" to build local capacity and de-risk supply continuity, through expansion of vaccine production to other geographies, particularly in upper middle-income countries (UMICS) and LMICs, as well as clinical trial ready-reserves for rapid response to an outbreak even before product licensure;

5. **Pricing** – driving down costs of production through innovation, streamlining development and signing agreements with development partners for affordable pricing of vaccines;

6. **Project continuity** – retaining a public health licence for use if a partner decides not to continue with product development or is in breach of access agreements; and

7. **Access to data and materials** – requiring data sharing, public disclosure of results on an open access basis, and sharing of project materials including animal models to accelerate the field.

Table 2: Examples of CEPI actions that increase access

Affordability for end purchaser	Affordability clauses; where feasible cost or cost-plus requirements; risk sharing agreements; commercial benefits sharing agreements; investment in cost-efficient manufacturing platforms; facilitation of voluntary licensing and tech transfer
Accessibility of science and technologies developed with CEPI investment	Inclusion of tech transfer; sharing of project materials (animal models, standardized assays, biological samples, candidate vaccines; lab structures); sharing of clinical data and results in a timely manner; sharing of lab structures; open access publishing requirement; public health license
Availability in LMICs	Requirements for sales to public procurement agents; right to redirect excess capacity; investment in scale-up of manufacturing process; regulatory harmonization and support for product registration and licensing; investment in ready reserves; requirement that development partners for Phase III trials complete registration in at least one country and have a path to WHO pre-qualification; technology transfer and stand up of local manufacturing; purchase of ancillary supply
Appropriate for target populations	Research and development based on patient need informed TPPs; attention to storage conditions, methods and routes of administration; user-centred design (fewer injections, thermostability); expansion of clinical trials networks to include low-income countries

To facilitate transparency around what is included in its agreements, CEPI regularly publishes access summary reports for its core portfolio and for COVID-19 related investments.

In March 2020, CEPI circulated a concept note for a Fair Allocations of Innovations for Pandemic Relief (FAIR) system to establish a globally fair system for allocating COVID vaccines, which ultimately led to CEPI co-establishing COVAX. Since this early advocacy around equitable access of COVID-19 vaccine, CEPI has continued access-related work with its investments in COVID-19 vaccines. CEPI's focus has been on starting projects rapidly, securing first rights of refusal to doses for fair allocation, reasonable pricing, and procurement to be passed onto the COVAX Facility. CEPI continues to work to expand manufacturing capacity in multiple geographic regions to provide the greatest hedge against vaccine nationalism, which could prevent countries—without manufacturing capability or resources to purchase vaccines— from having access. The lessons learned from this global experience will be used to improve access in future. In 2021 the focus shifted to real-world evidence and the assessment of heterologous prime boost and other strategies including fractional dosing to enable maximised use of available vaccines.

Outcome I.I – KPI 5: Number of vaccine candidates in investigational stockpile[9] for outbreak situations and ready for efficacy studies and emergency use

Baseline	Target 2021	Actual 2021	Target 2022	Status
0	0	0	At least 4 candidates (total) for at least 2 priority diseases (Lassa, MERS, Nipah, Rift Valley Fever)	**WILL BE TAKEN FORWARD IN CEPI 2.0***

Comment:
While the 2021 target for the number of vaccine candidates under investigation is zero, the overall portfolio progress relative to achieving four candidates as a ready reserve of clinical trial material in 2022 is significantly delayed. For Lassa and Nipah Phase II studies the lead candidates are expected to start in 2022, while one MERS project (Inovio) has initiated Phase II so far. Delays can be attributable to:

- The COVID-19 pandemic;
- Time required to establish vaccine candidate portfolios;
- Technical challenges (including candidate construct, CMC);
- Partnership challenges.

CEPI continued to actively monitor and mitigate throughout 2021.

***CEPI 2.0**
Project development plans are being reviewed to reflect a planned strategic re-positioning of the portfolio towards mid/ late-stage development and licensure. This will include post-licensure strategies and continuity management and engaging with other downstream partners. CEPI will further its ambition for priority pathogens from a ready reserve of clinical trial material and readiness for efficacy studies/emergency use to late stage (Phase IIb/III) development towards licensure.

[9] As part of CEPI's 2.0 strategy, the targets for the priority pathogens have been amended to work towards licensure (replacing "investigational stockpile" target as an outcome indicator)

Outcome 1.2 – KPI 6: Percentage of vaccine Partnership Agreements that have manufacturing plans in place to enable vaccine production in response to an outbreak
Subject to completion of Phase I and transitioning to Phase II

Baseline	Target 2021	Actual 2021	Status
N/A	100%	100%	ON TRACK

Comment:
In the "core" portfolio, CEPI's vaccine candidates against Chikungunya are the most advanced along the product development pathway. All three Chikungunya vaccine programmes (IVI/ Bharat Biotech consortium, Themis (now part of MSD) and for a single dose vaccine with Valneva) contain provisions to enable equitable access. By way of example the agreement (entered into in 2019) with Valneva to enable equitable access to a Chikungunya vaccine for LMICs in an end-to-end approach included the following elements:

- TPP focused on LMICs including a plan for WHO prequalification and presentation in a low COGS manner (high-income country (HIC) product is pre-filled syringes, LMIC product is not);
- Free virtual stockpile available before and after marketing approval of 200,000 doses. This stockpile is replenishable once used at CEPI's option and at cost;
- Commitment to supply LMICs in event of an outbreak;
- Technology transfer underway to Butantan in Brazil;
- Commitment to increase manufacturing capacity in the event of an outbreak. (nine months to increase capacity);
- Commitment to equitable pricing principles.

Outcome 1.2 – KPI 7: Percentage of vaccine development partners agreeing to terms that are fully consistent with CEPIs Equitable Access Policy and implementation guidance

Baseline	Target 2021	Actual 2021	Status
0%	100%	100% (non-COVID)	ON TRACK

Comment:
All core portfolio vaccine development partners have agreed to terms fully consistent with CEPI's Equitable Access Policy and implementation guidance. Each agreement contains contract terms to enable equitable access to the resulting vaccine for LMICs in an end-to-end approach:

- TPP focussed on LMICs including WHO prequalification and low COGs;
- The right for CEPI to call for a clinical trial ready reserve of vaccine candidate at or after Phase II;
- Provision for more/amended research and development in the event of an outbreak
- Commitment to supply LMICs in event of an outbreak;
- Equitable pricing principles;
- Planning for supply security including where appropriate by requiring technology transfer at Phase II;
- Open access publication requirements to enable the field as a whole.

Each of these agreements is designed to evolve as more is known about both the disease and the vaccine candidate with the aim of enabling equitable access that works in practice for LMICs. For vaccine candidates in advanced development, CEPI 2.0 strategic objectives include a component connecting other stakeholders with the aim of creating pathways for smooth transitions to procurement and ultimately last mile activities.

Outcome 1. 2 – KPI COVID-19: Percentage of vaccine development partners agreeing to terms that are fully consistent with CEPI's Equitable Access Policy and implementation guidance			
Baseline	**Target 2021**	**Actual 2021**	**Status**
0	100%	95%	**ON TRACK**

Comment:

All COVID portfolio vaccine development partners have agreed to terms fully consistent with CEPI's Equitable Access Policy and implementation guidance for the type of funding received. Where a partner was unable to commit to CEPI's implementation guidance for other types of funding, no such additional funding was granted. Similarly on the rare occasion where there was a disagreement over terms or a delay in meeting commitments, CEPI used the escalation and dispute resolution procedures available to it.

For COVID agreements that continued to full funding, essential components of access included:

- TPP focussed on LMICs including WHO EUL and low COGS;
- Commitment to scale-up production and in many cases to scale-out production through technology transfer to different geographic regions;
- A first right of refusal for the COVAX Facility over a specified proportion of production commensurate with CEPI's investment;
- Provision for continuity in the case of both development and manufacture;
- Equitable pricing principles[10] and in later agreements, pricing formulae;
- Open access publication requirements to enable the field as a whole.

CEPI has worked with Gavi and UNICEF to implement advance purchase agreements for the COVAX Facility to access up to 3 billion doses of vaccine which have had R&D funding from CEPI.

[10] That is, affordable for countries of all GNP levels but sustainable to manufacturer. For more information see CEPI's equitable access policy

1.1.3. Provide expert assistance and fund enabling science and technologies to enhance vaccine development efforts

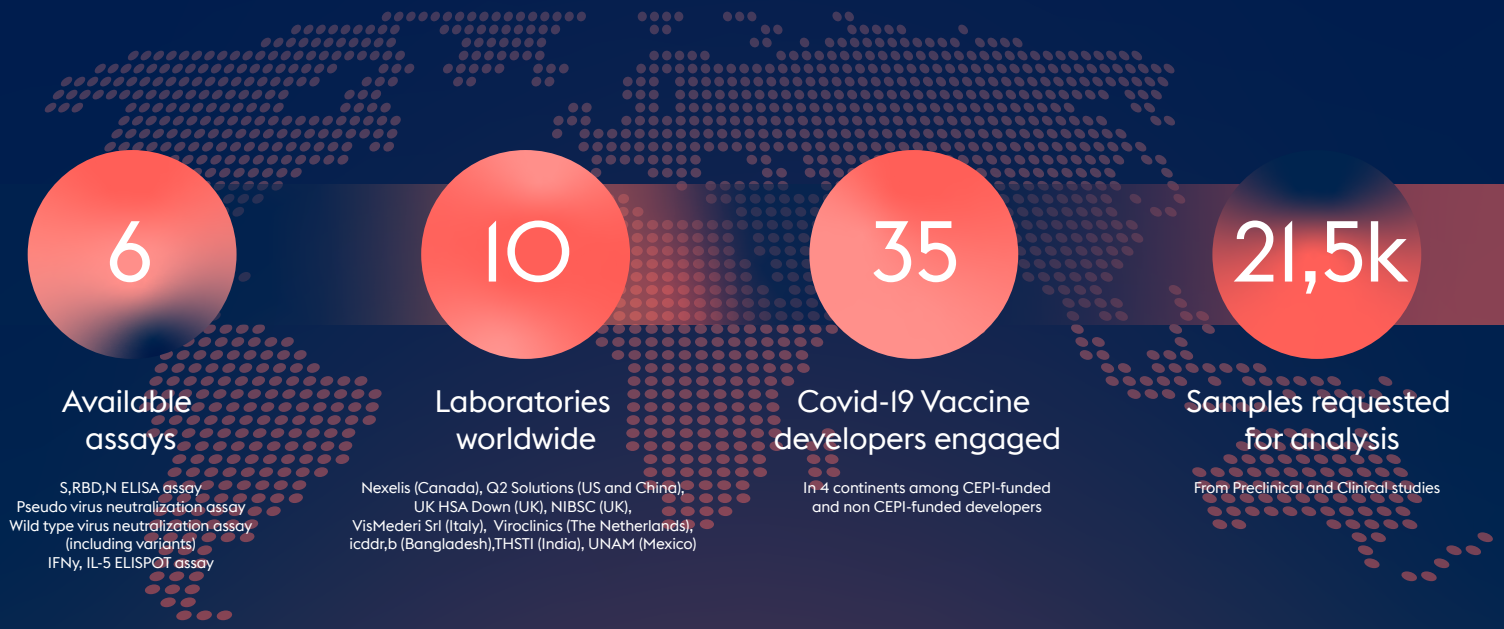
Accelerate vaccine development through enabling science

CEPI's enabling science programmes have progressed significantly in 2021. Highlights include:

- Lassa epidemiology study Enable was implemented in Nigeria, Guinea, Benin, Liberia, and Sierra Leone and the recruitment target of 23,000 subjects across five countries was met.
- The Lassa International antibody standard was approved by WHO Expert Committee on Biological Standardization (WHO ECBS) and CEPI awardees had access to common Lassa immunoassays.
- Field evaluations of Lassa serology assays were conducted.
- MERS common antigens were produced and made available to CEPI awardees, which in addition to the approved MERS International Standard contributes to the standardization of assays across developers.
- The development of a Rift Valley Fever antibody standard and serum panels were launched with partners in Uganda, Kenya and the UK, aiming at the establishment of an International Standard by the end of 2022.
- Development of Nipah standards has progressed with serum collection started in Malaysia and plans are well developed for activities in Bangladesh.
- The development of Nipah animal models suitable for regulatory approval have been planned and initiated.
- A specific call for the characterization of Nipah strain worldwide was executed.
- Marburg serum collection has begun in collaboration with African, US and UK partners.
- Systematic literature reviews for Rift Valley Fever and Chikungunya were conducted, leading to two peer-reviewed publications.

Global laboratory networks that were established in 2020, such as the *Centralized Laboratory Network* and the *Preclinical Model Network*, were further expanded in 2021. New networks established for SARS-CoV-2 will be useful for the core portfolio in the future, including for Systems Immunology and Predictive Modelling.

Figure 3: CEPI Centralized Laboratory Network achievements as of November 2021



Other critical activities maintained in 2021 include Task Forces for Lassa, Nipah, MERS and Rift Valley Fever, as well as regular interactions with members of the Standards and Assays Working Group reporting to the Joint Coordination Group. CEPI's service provider, the Safety Platform for Emergency Vaccines Project of the Task Force for Global Health, continues to be available to developers to enhance their regulatory strategy and submissions to licensing agencies, and to obtain an overall safety database for clinical trials.

Output I.2 – KPI 9: Number of available biological standards and validated assays (including standard operating procedures) for evaluation of vaccine candidates against CEPI's priority pathogens

Baseline	Target 2021	Actual 2021	Target 2022	Status
0	No specific target for 2021	8 completed and 2 in progress: 3 antibody standards completed (MERS, Lassa, SARS-CoV-2), 2 antibody standards in progress (RVF, Nipah); 2 common antigens/assays available (MERS, Lassa); 3 validated assays available through CEPI Centralized Lab Network (SARS-CoV-2)	• Necessary Biological Standards for evaluation of immune responses against 2022 for Rift Valley Fever will be developed • At least one validated assay for each of Lassa fever, Nipah, MERS and Rift Valley Fever will be used for evaluation and comparative measurements of the CEPI supported vaccine projects	**ON TRACK***

Comment:
Despite challenges due to COVID-19, CEPI has achieved its goal to provide harmonization across developers with the timely establishment of standards and common assays. Specifically, this included the establishment of the first antibody standards for Lassa and SARS-CoV-2 as well as making a MERS antigen available for vaccine developers. Development of standards for Rift Valley Fever and Nipah were initiated in 2021 and are well underway, expected to be completed within 2022. Key partnerships and laboratory networks such as the *Centralized Laboratory Network*, the *Preclinical Model network*, *Systems Immunology Network* and *Predictive Modelling Network* have laid the ground for further progress in this area for the coming five years.

***CEPI 2.0**
Under 2.0 CEPI will expand its reach and increase funding to transform outbreak preparedness and response through scaling enabling sciences to accelerate vaccine development and deployment. Activities started during CEPI 1.0 will be carried forward and expanded to include standards, preclinical models, assays, diagnostics, computational modelling of the impact of virus evolution, translational immunology, correlates of protection, sentinel safety surveillance and epidemiological models and studies of CEPI priority pathogens and for the virus family approach.

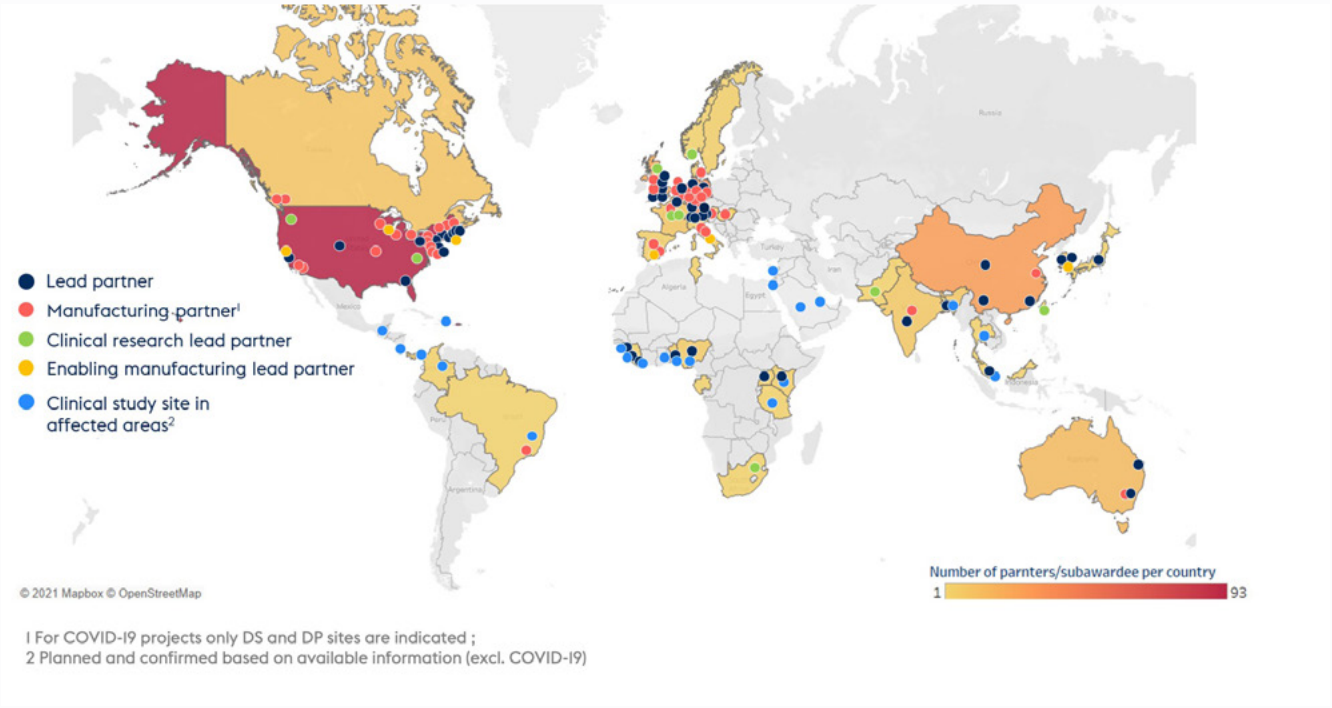
Output 1.2 – KPI 10: Percentage of vaccine candidates in clinical development (e.g. being tested in humans), with relevant engagement from regional and/or national authorities—including regulators—in at-risk countries			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	Target for each of the diseases in every stage: 100 percent	100%	**ON TRACK**

Comment:
Despite the impact of COVID-19, all vaccine candidates that are in the clinical development phase have clinical studies in at-risk countries.

Output 1.2 – KPI COVID-19: Percentage of vaccine candidates in clinical development (e.g. being tested in humans), with relevant engagement from regional and/or national authorities in relevant geographies—including regulators			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	100%	100%	**ON TRACK**

Comment:
All vaccine candidates that are in the clinical development phase have clinical studies in at-risk countries.

Figure 4: Map overview of CEPI's >70 partnerships with life sciences organisations



1.2. Strategic Objective 2: Response

Accelerate the research, development and use of vaccines during outbreaks

CEPI prioritizes Disease X for early cross-cutting research based on the knowledge that the next international epidemic or pandemic could be caused by a pathogen currently unknown to cause human disease. An effective response to an unknown pathogen requires development of the necessary tools before a potential outbreak to expedite vaccine development. This is because the use of innovative technologies can increase uptake and delivery of a vaccine and help to contain an outbreak as quickly as possible, thereby minimising the risk of an epidemic becoming a pandemic. To support these aims, CEPI:

- Invests in vaccine platforms and innovative supportive technologies to speed the development and manufacture of safe and effective vaccines;
- Engages in a dedicated programme of response activities connected to the COVID-19 pandemic (since early 2020);
- Supports the development of technologies to facilitate field use and rapid response;
- Engages end-to-end partners to plan for the testing, manufacturing, stockpiling and deployment of vaccines during outbreaks.

1.2.1. Invest in platforms to speed the development and manufacture of vaccines

''Vaccine platform technologies'' refers to a system that uses the same basic vaccine components as a backbone, which can be adapted or built upon for use against different pathogens by inserting new genetic information or protein constructs. Prior to the COVID-19 pandemic, CEPI had supported the development of new and innovative platform technologies that have the potential to radically accelerate the development and manufacture of vaccines to rapidly respond to future outbreaks of emerging infectious diseases and unknown pathogens, known as Disease X.

CEPI's Disease X portfolio comprised three rapid response platform technologies which have broad application potential with each platform being tested through Phase 1 for three diseases. In addition, these platforms have the potential for additional vaccines being produced against: influenza (2); rabies (2); MERS (1); Marburg (1); Lassa (1); Respiratory Syncytial Virus (1); yellow fever (1)[11]. Furthermore, CEPI is investing in current and novel mRNA platforms and enabling technologies for the development of vaccines against known and potentially emerging pathogens. The investment in mRNA platforms will be the primary platform on which to develop vaccine libraries for each virus family to meet the 100-day mission for a safe and effective vaccine against Disease X – a key component of CEPI 2.0 strategy.

In 2020 and 2021, CEPI leveraged these innovative vaccine approaches as well as technology platforms employed for the development of core pathogen vaccines to advance COVID-19 vaccine development. All three of CEPI's rapid response platform technologies funded through CfP2[12] as well as three platform technologies funded through CfP1[13] and CfP3[14] underpinning CEPI's core portfolio, were pivoted toward COVID-19 vaccine development. Having the contractual agreements already in place allowed CEPI to rapidly switch focus to COVID-19 vaccine development early in 2020.

[11] The pilot pathogen projects that were part of the original rapid response platform projects have been put on hold during the COVID-19 pandemic and their future development is under review.

[12] CfP2 was the call for vaccine platform technologies

[13] CfP1 was the call for vaccine candidate development against MERS, Nipah and/or Lassa viruses

[14] CfP3 was the call for vaccine candidate development against Rift Valley fever and Chikungunya viruses

Standardized platform systems allow the same basic components to be used as a backbone for producing vaccines against different pathogens. Given some of these innovative platforms have resulted in the successful and rapid development of safe and effective COVID-19 vaccines, there is a good chance that they can also be used to quickly develop vaccines against another known, and unknown, infectious diseases. Looking to the future, the world needs to expand the breadth of focus and investment beyond coronaviruses extending into all 25 virus families.

In 2021 CEPI began to focus its efforts on whole virus families – including the development of a Betacoronavirus vaccine[15]. This work will continue under the CEPI 2.0 strategy over the next 5-year period. Through the CfP "*Broadening protection against SARS-CoV-2 and new broadly protective Betacoronavirus candidate vaccines*" a number of candidates were identified as interesting and novel, with potential to feed into the CEPI 2.0 strategy. Three applicants were in early development, and it was decided to award seed funding to establish preclinical Proof of Concept for the technology, and support parts of the CMC process:

- One orally administered vaccine tablet to induce broad protective immunity against SARS-CoV-2 (MigVax);
- One novel technology platform vaccine based on the innovative Multiple Antigen Presenting System (MAPSTM) technology platform. This represents a new technology in CEPI's portfolio, easily adaptable for other indications than SARS-CoV-2. (Affinivax);
- One novel technology platform vaccine and one with particularly novel immunogen design, each allowing for different variants of concern (VIDO).

Outcome 2.1 – KPI 11: Number of vaccine platform technologies that can be rapidly adapted to develop vaccines against unknown pathogens for use in humans

Baseline	Target 2021	Actual 2021	Target 2022	Status
0	No specific target for 2021, but for 2022	0	2 or greater, including at least one novel (innovative) platform, i.e., that has no prototyped licensed vaccine	**WILL BE TAKEN FORWARD IN CEPI 2.0***

Comment:
All rapid response technology platform projects initiated prior to the COVID-19 pandemic continue to experience delays due to their engagement in the COVID-19 response. At the same time, engagement in the COVID-19 response has accelerated the clinical validation of their rapid response potential. Learnings to inform future work in these areas include:

- Pilot pathogen projects on hold. CEPI support reduced at CureVac's request;
- Pilot pathogen projects on hold while reworking construct for COVID-19 variants (Queensland);
- Pilot pathogen projects put on hold pending the outcome of RNA transcript work following results from COVID-19 clinical study (Imperial College).

***CEPI 2.0**
This target has been adapted in CEPI 2.0 and will focus on developing prototypic vaccines for existing vaccine-preventable diseases (with prevalence in LMICs) using rapid response vaccine platforms. The work will also be a critical enabler of CEPI's 100-day aspiration. CEPI's target for the next 5-year period is two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations. To support this work, CEPI launched a new funding opportunity for the development of RNA vaccine platform technologies and vaccine library development against emerging and select endemic infectious diseases in January 2022. The three current platform projects as well as incoming projects of the RNA funding opportunity will be an essential part of CEPI 2.0 and the 100-day aspiration.

[15] The Broadly Protective Betacoronavirus Candidate (BPBC)call was opened on 1 April 2021.

Output 2.1 – KPI 14: Number of vaccine candidates progressing through preclinical and Phase I using CEPI funded platform technologies				
Baseline	**Target 2021**	**Actual 2021**	**Target 2022**	**Status**
0	No specific target for 2021, but 2022	- 9 COVID-19 candidates progressed through preclinical, 7 started & 4 successfully completed Phase I - Additionally, CEPI-funded rapid response platforms had progressed before pivoting to COVID-19: 3 completed preclinical, 1 successfully finished Phase I	8 products through preclinical and 6 products progressed through Phase I NB: *Work on the pilot pathogen projects is on hold pending review of future direction of collaboration with partners as part of Disease X strategy.*	**ON TRACK***

Comment:

See also KPI 11. CEPI-funded vaccine developers, including vaccine candidate and rapid response platform developers have developed COVID-19 vaccine candidates using platform technology, also funded by CEPI. With all CEPI-funded rapid response platforms under review, work on the following pilot pathogen projects is also on hold.

- Yellow Fever: active preclinical, Rabies: completed Phase I, Lassa: active preclinical; COVID-19: completed Phase III); CEPI support reduced at CureVac's request;
- Influenza: completed preclinical; COVID-19: completed Phase I; COVID-19 variant: active preclinical (Queensland);
- Marburg: preclinical complete; Influenza: preclinical on hold; Rabies: preclinical on hold; COVID-19: Phase I complete (Imperial).

***CEPI 2.0**

Going forward the focus is on developing prototypic vaccines for existing vaccine-preventable diseases (with prevalence in LMICs) using rapid response vaccine platforms. This work will also be a critical enabler of CEPI's 100-day aspiration. CEPI's target for the next five-year period is two licensed vaccines against viable targets for LMICs using prototype and/or platform innovations.

1.2.2. CEPI's response work connected to COVID-19

CEPI's progress under the strategic objective Response is relayed in the following sections and focuses particularly on the investment in CEPI's COVID-19 portfolio during 2020-2021. CEPI has invested in a diverse portfolio of COVID-19 vaccine platform technologies and large-scale manufacturing capabilities with the aim to develop at least three safe and effective vaccines which can be distributed and deployed to the world through COVAX.

By end of 2021 CEPI had signed 18 partnership agreements to support COVID-19 vaccine candidate development and manufacturing programmes. In addition, CEPI redirected funds from the Imperial College Disease X/platform project to support Imperial College's COVID-19 vaccine development efforts, signed a further 23 partnering agreements for cross-cutting enabling sciences activities that support vaccine development, and signed 10 partnership agreements to support complementary clinical and fractional dosing trials to expand access to and use of COVID-19 vaccines. The size and complexity of these R&D investments has been large and given the novelty of the virus and the need to respond at pandemic speed, many investment decisions were taken with a higher tolerance for risk than under traditional circumstances.

In Q3 2021, CEPI conducted an exercise in conjunction with Amanda Glassman from the Centre for Global Health Development to assess learnings from investments made by the COVAX Research and Development and Manufacturing Investment Committee (RDMIC) and identify how future global health security preparedness could be strengthened. A summary of the key findings was published on the Centre for Global Health Development website.

Notable achievements related to CEPI's COVID-19 vaccine R&D portfolio in 2021 include:

- Accelerated advancement of COVID-19 vaccines through pivotal trials for EUA: Throughout 2020 and 2021, CEPI and its COVAX partners managed to support the unprecedented, accelerated development of nine Wave-1[16] COVID-19 vaccines through the clinic.
- Optimisation of COVID-19 vaccines to maximise global access potential: A Wave-2[17] portfolio of translational candidates has been established with investment from CEPI and the Bill and Melinda Gates Foundation. By the end of 2021, five partnerships for Wave-2 candidate vaccines with the potential to deliver optimised vaccine profiles had been signed. All five projects have progressed into the clinic with one in Phase III, one in Phase I/II and three in Phase I trials.
- Additional new developers targeting broadly protective vaccine candidates: As the pandemic continues to evolve with the emergence of new variants, CEPI has partnered with vaccine developers on four broadly protective SARS-CoV-2 candidates (three seed-funding grants, one full award). In addition, CEPI launched a CfP for broadly protective Betacoronavirus vaccines.
- Launch of two CfPs targeting complementary clinical trials and fractional dosing: In 2021 CEPI extended funding for clinical trials with the aim of
  i. rapidly expanding access to and confidence in COVID-19 vaccines and
  ii. generating data on fractional doses of COVID-19 vaccines given as additional doses in primed populations.

As of the end of 2021, CEPI had signed 10 partnership agreements to fulfil these knowledge gaps (eight for complementary clinical trials and two for fractional dosing trials). In addition, CEPI signed a framework agreement with PATH to provide support to fractional dosing projects.

- Establishment of a Technology Transfer Oversight group as a sub-group of the Technical Review Group (TRG) tasked with providing expert technology transfer oversight and input to de-risk technology transfers for current portfolio candidates.

[16] For example, vaccine candidates anticipated to deliver doses to COVAX by December 2021

[17] For example, high volumes, cost advantages, improved thermostability, new strain variants

A number of these activities initiated the gradual transition of CEPI's COVID-19 response work into core programmes, which will continue into 2022 under CEPI 2.0. This reflects a global shift toward viewing SARS-COV-2 as an endemic pathogen in the long term and coronaviruses more broadly as a perennial pandemic threat. It also reflects a shift in CEPI's strategic approach under CEPI 2.0, in which epidemic "response" will be fully integrated into the organisation's core work to prepare, transform, and connect.

Despite CEPI's successes, not all portfolio targets have been met, due to a combination of national restrictions to global access of approved vaccines, technical failures of some vaccine candidates and delays in manufacturing and regulatory submissions of other leading vaccine candidates. Three areas have been identified that contributed to either failures or delays:

- First, the pursuit of speed led to suboptimal dosing regimens and shed light on areas where some platforms could improve in the future.
- Second, CMC and technology transfers for large scale manufacturing have been a challenge with first-generation COVID-19 vaccines. In the absence of in-house manufacturing capabilities or of sufficient technical expertise, most of CEPI's smaller awardees suffered from process scale-up and / or scale-out difficulties, (the latter where process development and tech transfers were attempted simultaneously).
- Third, supply chain issues have added to the delays, mainly in the form of access to raw materials and equipment for vaccine production. As several COVID-19 vaccines have now been licensed and variants continue to remain a threat, regulators may interpret more stringently the non-inferiority data of those vaccine candidates still under development, contributing to further delays in WHO Emergency Use Listing (EUL) and delivery of vaccine doses to COVAX.

Taking steps to counter vaccine hesitancy through no-fault compensation

In February 2021, COVAX entered into an agreement with Chubb Limited (NYSE:CB) through ESIS Inc., a Chubb Company for the administration of a no-fault compensation programme covering individuals who experience adverse serious events associated with COVAX distributed vaccines. This programme currently runs up to June 2022 with a possibility of a period extension. CEPI will work towards **similar programmes for future situations in LMICs** as part of the Connect Pillar in CEPI 2.0.

Based on the confidence in the safety of vaccines distributed through the COVAX facility, the programme provides a **vaccine injury compensation mechanism that is robust, transparent, simple, free and independent for individuals in LMICs.** Key Aspects are outlined below:

- A no fault compensation scheme serves to **counter vaccine hesitancy by allaying safety concerns** among populations;
- **Available in 92 LMICs and economies** eligible for support through the COVAX advanced market commitment facility;
- **Improves equitable access to supply**, especially for countries without their own compensation programme by de-risking manufacturers where there are concerns over indemnity and liability; hence an **incentive to supply LMICS**;
- No-fault compensation provides **justification for manufacturers in waiving indemnity and liability for humanitarian agencies involved in the distribution and administration of COVAX distributed vaccines.**

Outcome 1.1 and output 1.1. – KPI COVID-19: Number of COVID-19 vaccine candidates advancing through Phase I, Phase II/III, and authorized for distribution

Baseline	Target 2021	Actual 2021	Status
0	• Progress 10 vaccine candidates through primary analysis of Phase I end Q1/2021 • Progress 2 candidates into Phase II/III by end 2020, one candidate primary readout by end 2020 and 3 additional with primary readouts by Q3/2021 (based on primary endpoint analysis of pivotal trial) • Licensed/emergency use - up to 4 by end 2021	• 8 vaccines through primary analysis of Phase I by end of Q1 (Moderna, Inovio, Novavax, AZ/Uni Oxford, CureVac, Clover, Biological E and SK Bioscience), plus an additional candidate by end 2021 (Hong Kong) • 7 candidates progressed into Phase II/III or Phase III; 5 by end of 2020 (Moderna, Inovio, Novavax, AZ/University Oxford, CureVac), plus an additional 2 candidates that progressed by end 2021 (Clover and SK Bio) • 5 candidates have published primary endpoint analysis of pivotal trial (AZ/Uni Oxford, Moderna, Novavax, CureVac and Clover) • 3 candidates have received authorization for emergency use by WHO. 2 in 2020 (Moderna, AZ/Uni Oxford) and 1 in 2021 (Novavax). Bio E received authorisation in India	**ON TRACK**

Comment:

CEPI has one of the largest clinical portfolios of COVID-19 vaccines, as seen in figure 5 below. While the target to progress 10 candidates through the end of Phase I was not met, the portfolio has otherwise exceeded the targets for 2021 resulting in a total of 3 licensed COVID-19 vaccines available for global use.

Figure 5: CEPI supported COVID vaccines as of January 2022

	DNA / mRNA				Viral vector			VLP	Protein					
Covid-19	Inovio	Moderna	CureVac	Gritstone	Merck/ Themis	Univ of Hong Kong	AstraZeneca/ Univ. Oxford	VBI Vaccines	Univ of Queensland	Novavax	Clover	Zerun/Walvax	Biological E	SK Bioscience
Location	USA	USA	Germany	USA	USA	Hong Kong	UK	US/ Canada	Australia	USA	China	China	India	South Korea
Platform	DNA	mRNA	mRNA	mRNA	Viral Vector	Viral Vector	Viral Vector	eVLP	Protein	Protein	Protein	Protein	Protein	Protein
Product	First generation	First generation	First generation	Second generation	First generation	First generation	First generation	Second generation	First generation	First generation	First generation	Second generation	First generation	Second generation
Antigen/Adjuvant	Full-length S protein	Full-length S protein	Full-length S protein	Full-length S protein	Full-length S protein	Receptor Binding Domain	Full-length S protein	Full-length S protein / Alum	Full-length S protein	Full-length S protein / Matrix-M	Full-length S protein/ CpG-alum	Recombinant S protein / CpG-alum	Monomer RBD / CpG-alum	Recombinant RBD / ASO3
Current Phase	Phase II/III	Phase III	Discontinued	Phase I	Discontinued	Phase I	Phase III	Phase I	Discontinued	Phase III	Phase II/III	Phase I	Phase II/III	Phase III

WHO EUL granted | Under development, active CEPI funding | Under development, CEPI-funding discontinued | Development discontinued

Outcome 1.2 – KPI COVID-19: Plans for manufacture of up to 100 million doses for emergency use by end 2020, and up to 2 billion doses by end 2021

Baseline	Target 2021	Actual 2021	Status
N/A	• 100% of partnership agreements have manufacturing plans in place • Aim to manufacture up to 2 billion doses by end 2021	• 95% • COVAX delivered over 900 million vaccine doses in 2021.	**ON TRACK**

Comment:

COVAX delivered over 900 million vaccine doses in 2021, coming close to the target allocation of 950 million doses to LMICs through the COVAX Facility's advanced market commitment mechanism. Of that total, 41% of doses delivered were from CEPI funded developers (AstraZeneca and Moderna). At the end of 2021, the COVAX Facility had signed advanced purchase agreements with four CEPI funded developers (AZ, Clover, Novavax, Moderna) as well as Serum Institute of India for access to two CEPI funded vaccines (AZ and Novavax) .

COVAX's objective to deliver two billion vaccine doses by end of 2021 was not fully within CEPI's control and was impacted by restricted supply from manufacturers, national export restrictions (notably impacting AZ doses produced by Serum Institute of India), recipient countries' absorption capacity, and the COVAX Facility's lack of early access to financing for APAs and a resulting reliance on donated doses. The two billion dose target consisted of 950 million doses to LMICs through the COVAX Facility's AMC mechanism with the remaining 1050 million doses reserved for self-financing countries and humanitarian buffer, neither of which generated any significant demand.

Despite the well-publicised challenges and delays in manufacturing due to the technical difficulties involved with large scale manufacture of a new product in record time, in September 2021 COVAX co-leads, CEPI, GAVI, WHO and UNICEF, published a joint statement on supply forecast for 2021 and early 2022. In the new forecast, COVAX was expected to have access to 1.425 billion doses of vaccine in 2021 as the most likely scenario, and in the absence of urgent action by producers and high-coverage countries to prioritize COVAX. This figure was reduced slightly in the December forecast to 1.380 billion due to delays in development and regulatory timelines. By end of 2021 COVAX allocated ~1.6 billion doses. The key COVAX milestone of two billion doses released for delivery is expected to be reached in the first quarter of 2022.

CEPI has supported its awardees throughout, providing proactive support for manufacturing and regulatory issues. For example, CEPI secured key manufacturing supplies (e.g., adjuvant and glass vials), spearheaded the COVAX Manufacturing Task Force and the COVAX Market Place, and supported awardees with the Tech Transfer oversight group. Without that support, the delays may have been far greater.

Outcome 2.2 – KPI COVID-19: Number of CEPI-funded vaccine candidates accepted for (rolling) regulatory review

Baseline	Target 2021	Actual 2021	Status
0	Rolling review/ Regulatory consultation on advanced stage development started for at least 2 vaccine candidates Q4/2020; for 4 more vaccine candidates Q2/2021	2 in 2020 (AstraZeneca and Moderna); 4 in 2021 (Novavax, Bio E, Clover and CureVac)	**ON TRACK**

Comment:

Three CEPI-funded candidates progressed through rolling regulatory review: Four received authorization for emergency use by national regulatory agencies (AZ and Moderna at end of 2020 and Novavax and Bio E in 2021). Three of these were also granted WHO Emergency Use Listing (EUL) in 2021 (AZ, Moderna and Novavax). The rolling regulatory review also commenced for two (Clover and CureVac). One subsequently withdrew (CureVac).

Output 1.2 – KPI COVID-19: Number of CEPI-funded validated enabling science programmes available to accelerate preclinical development and evaluation of vaccine candidates against COVID-19

Baseline	Target 2021	Actual 2021	Status
0	1 international antibody standard by end Q1/2021	6 CEPI-funded programmes available and 1 more in development: • Standard development:1 international antibody standard available; VOC-specific panels in development • CEPI Centralized Lab Network: 10 labs, 3 assays validated, VOC assays included • Preclinical Model Network: 8 partners • Agility: 13 variants assessed • Systems Immunology: 2 partners • 8 complementary clinical trial projects • 2 fractional dosing trials • Predictive modelling request for proposals completed in 2021 and due diligence ongoing	**ON TRACK**

Comment:

CEPI has achieved its goal to support international antibody standard development. Additionally, the establishment of key partnerships and laboratory networks such as the *Centralized Laboratory Network, the Preclinical Model Network, Systems Immunology Network and Predictive Modelling Network* has laid the ground for further progress in the coming 5 years under CEPI 2.0.

Through COVAX Support Work to Advance Teams (SWAT) for clinical development and operations as well as enabling science, partners from industry, non-governmental organisations and key R&D stakeholders had the opportunity to identify and address critical questions relevant for accelerating COVID-19 vaccine development and evaluation through 23 public workshops held in 2021.

I.2.3. Support the development of technologies to facilitate field use and rapid response

In 2021, to support the deployment and expand access of COVID-19 vaccines, CEPI has invested in mix-and-match clinical trials covering a wide range of vaccine combinations for heterologous prime boosts, heterologous boosters and fractional dosing. Trials are geographically dispersed in countries across Africa, Asia, Europe, South America and Oceania and are contributing to sustainable clinical trial capacity building for future preparedness. See Figure 6 COVID Clinical trials.

Since 2020, CEPI has supported the evaluation of a novel technology for filling, transporting, and delivering vaccines particularly suitable for use in low-resource settings. The MedInstill/INTACT Solutions multi-dose pouches have been shown to be safe and effective for use as a vaccine container and compatible with multiple vaccine products. Compared to glass vials the pouches are lighter and smaller, so they reduce the cost and footprint of the cold chain. Administering the vaccine from the pouches is quick and easy, providing a rapid and low-cost solution for mass vaccination campaigns during outbreaks and pandemics. This technology has been selected by Institut Pasteur de Dakar (IPD), Senegal, to accelerate the scale-up of their vaccine production capabilities and facilitate the rapid delivery of vaccines in Africa. In January 2022, CEPI and the IPD announced signing a Memorandum of Understanding (MOU) to formalise the partnership between the two organisations to advance IPD's MADIBA project, a regional manufacturing hub for COVID-19 and other vaccines in Dakar, Senegal.

Moving into the next strategic period CEPI will continue to focus on the development of innovative technologies to improve global access to vaccines e.g through supporting technologies to improve thermostability for any type of vaccine so that complex-cold chain requirements can be reduced including launching appropriate CfPs.

Additionally, TechTalks, an informal meeting platform between vaccine developers, innovative manufacturing platform developers, and clinical development organisations continued through 2021. The CEPI TechTalk team shared information about open CfPs, and their objectives and scope to a total of 39 participants that subsequently submitted proposals for "Broadening protection against SARS-COV-2 and new broadly protective Betacoronavirus candidate vaccines" (CfP4). Other TechTalks focused on manufacturing capacity and innovations, as well as vaccine delivery devices. The number of requests for scheduling TechTalks increased substantially during 2021; to support transparency, CEPI will outline the mechanism for requesting a TechTalk on its website.

Figure 6: Clinical Trial Strengthening Sites

- Ongoing work by COVAX (through CEPI) to enhance sites' capabilities and capacity to perform clinical interventional trials in eight countries. Three of which are African countries
- To fund : personnel; training; facilities alterations and renovations; equipment and supplies- clinical, laboratory, pharmacy; surveillance
- Location of sites: Burkina Faso, Columbia, Costa Rica, Haiti, Honduras, Kenya, Niger

Output 2.2 – KPI 15: Regular analysis of available technologies and the gaps that currently exist		
Baseline	**Target 2021**	**Status**
N/A	Regular analysis on basis of identified need	**ON TRACK**

Comment:
CEPI conducted a regular analysis of available technologies and needs-based gaps. This analysis was undertaken with cross-functional collaboration and included interaction with product developers, regional/global partners including via desk-based monitoring and landscape analyses. The outputs of these activities have been utilised as a part of CEPI's portfolio management, in particular during portfolio monitoring and when seeking new investment opportunities. Key achievements in 2021:

- 87 TechTalks with product developers took place;
- Co-convened a global summit (March 2021) to discuss COVID-19 vaccine manufacturing bottlenecks that need to be urgently tackled for COVID-19 vaccine output to reach its full potential (see the link to report below);
- Regional manufacturing workshops conducted in Eastern Mediterranean (included four North African countries) September 2021 and the Americas /the Caribbean (October 2021), followed by workshops for South East Asia/Western Pacific (February 2022). These workshops leveraged the CEPI 2021 vaccine manufacturing landscaping survey data (see section 1.2.4) that was also shared with Partnerships for African Vaccine Manufacturing (PAVM) and supported the creation of the African - Framework For Action (published March 2022); follow up workshops are planned.
- Together with COVAX Manufacturing Taskforce partners (WHO, UNICEF, Gavi, IFPMA, Bio, DCVMN), CEPI launched the COVAX Marketplace to match buyers and sellers of critical manufacturing supplies and speed-up global access to COVID-19 vaccines through COVAX; see COVAX Marketplace website for details, here;
- Desk-based monitoring and landscape analysis for CEPI priority (Lassa, MERS, Nipah, Chikungunya, Rift Valley Fever and SARS-CoV-2) and other WHO R&D Blueprint diseases (Marburg, Zika) pathogens;
- Specific landscape analysis also conducted for mRNA, broadly protective Betacoronavirus, manufacturing capacity and capability landscapes, bilateral COVID-19 vaccine deals, and utilised as the basis for further investment considerations.

Relevant publications and reports:

- Towards Vaccinating The World: Landscape of Current COVID-19 Supply Chain and Manufacturing Capacity, Potential Challenges, Initial Responses, and Possible "Solution Space" - a Discussion Document
- Survey launched by CEPI to track multinational vaccine manufacturing capacity for use in future epidemics and pandemics and data at Vaccine production efforts across key regions mapped in first-of-its-kind study to prepare for future pandemics
- Status report on COVID-19 vaccines development. Current Infectious Disease Reports
- Medical countermeasures against henipaviruses: a review and public health perspective
- Globally resilient supply chains for seasonal and pandemic influenza vaccines NASEM report
- COVID-19 impact on supplies of infant and adolescent vaccines: risks, mitigations, and prospects

1.2.4. Engage end-to-end partners to plan for the testing and deployment of vaccines during outbreaks

COVAX 2021 highlights

COVID-19 has reshaped the global health ecosystem and affected the way CEPI engages with end-to-end partners. Through ACT-A, organisations with related but separate missions are collaborating towards the common goals of accelerating development, production, and equitable access to COVID-19 tests, treatments, and vaccines. Through the vaccine pillar (COVAX), CEPI, alongside Gavi, WHO and UNICEF has offered an 'end-to-end' solution to the challenge of vaccine development, manufacture, and supply. Some of the achievements have already been captured under section 1.2.2. CEPI's response work connected to COVID-19. Below is a comprehensive set of end to end key achievements in 2021:

- R&D investments totalling USD 1,8B in COVID-19 vaccine development and enabling sciences.
- Invested in the development of 14 COVID-19 vaccine candidates, four of which target variants including an expanded partnership with Gritstone Bio to evaluate an Omicron candidate.
- In addition, CEPI invested in vaccine development for four 'variant-proof' or broadly protective SARS-CoV-2 vaccine candidates.
- Delivery of over 900 million vaccine doses in 2021, the vast majority to AMC eligible countries and economies – 41% of doses coming from CEPI funded developers (Moderna and AstraZeneca).
- Novavax became the third CEPI-funded vaccine candidate to receive WHO EUL in December 2021, a prerequisite for distribution by COVAX.
- Funded expansion of the CEPI Centralized Lab network to 10 geographically distributed laboratories for harmonized assessment of vaccine immunology.
- Supported a consortium of partners in the Agility project for early assessment of impact of emerging SARS-CoV-2 variants of interest and concern.
- Funded eight partnerships for clinical research studies to expand access to vaccines and evaluate full and fractional doses as additional doses; with a focus on LMIC and vaccines supplied in-country.
- Established cross-organisation SWAT groups with industry to address key challenges to vaccine development in the evolving pandemic.
- CEPI co-led with WHO, a regulatory advisory group (RAG) composed of regulatory authorities representing all regions globally to discuss and share perspectives on emerging challenges towards emergency use of licensure of vaccines.
- Redesigned the COVAX allocation framework, moving from the supply driven Phase I to a demand driven Phase II, to enable COVAX to better meet the equitable access goals by accounting for non-COVAX supply and country coverage and calibrate towards country vaccination plans.
- COVAX, together with key ecosystem partners - Bill and Melinda Gates Foundation, International Federation of Pharmaceutical Manufacturers and Associations, Biotechnology Innovation Organization and Developing Countries Vaccine Manufactures Network - founded the COVAX Manufacturing Task Force (MFTF) in 2021 to identify and resolve vaccine manufacturing challenges and bottlenecks impeding equitable access to COVID-19 vaccines and other human health products.
- For improved visibility and to facilitate the transaction of critical, single-use consumables for COVID-19 vaccine manufacture, CEPI has played a leading role in launching and running the COVAX Marketplace and CEPI is frequently matchmaking consumable suppliers with vaccine manufacturers and/or fill-finish organisations that urgently need them to produce vaccines for fair and equitable distribution to COVAX.
- Together with WHO and Gavi, extended the no-fault compensation plan for LMICS enabling procurement of newer vaccines and providing some reassurance for recipients of the vaccines (see figure xx).

I.2.4.I. Facilitating alignment and coordination

CEPI engages with partners that are relevant to its mission. This includes work on vaccine development, both those developing the vaccines and upstream and downstream partners. The range of partners extends from CEPI's grant awardee partners, to academic and public health institutions, governments, philanthropic, industry, civil society, and others. Of the myriad of end-to-end activities CEPI carried out in 2021, some of the most notable are outlined below.

Strengthened global, regional and country collaboration

Global:

- Civil Society Organisations (CSOs): With COVAX partners and civil society, CEPI has co-hosted nine COVAX-CSO public dialogue meetings, and workshops; the "CEPI meet CSOs" interactive event in May 2021 gathered ~60 global representatives.
- Parliamentary: Through collaboration with the global UNITE parliamentary network, CEPI has worked to enhance parliamentary awareness of CEPI's mission in a roundtable in Latin America, which led to collaboration with the Global Public Health Convention and discussion on "ending infectious diseases as a global health threat" at the UNITE global Summit.

Regional:

- In an MOU signed with the African Union in April 2021, CEPI actively supported the PAVM towards improving the vaccine R&D and manufacturing value chain in Africa. This included participation in advisory groups, consultancy support for the Regulatory Strengthening, Technology & Intellectual Property and R&D Hubs, and Talent Development workstreams and contribution to the Framework for Action, endorsed by the African Union in February 2022. Specifically:
  - CEPI provided a secondee to the Africa CDC working within the PAVM secretariat, and is applying its work on regional manufacturing capacity to identify and help address challenges relevant to PAVM's objectives.
  - Exploratory roundtable meetings with BIOVAC and AVMI, based in the Republic of South Africa, to plan joint work in the vaccine landscaping and manufacturing space.
- Active dialogue with the European Commission (EC) to drive synergies and complementarity with the EU Health Emergency Preparedness and Response Authority (HERA) for a globally coordinated approach to epidemic and pandemic preparedness and response. This included co-hosting a technical roundtable followed by discussions with many parts of the Commission on synergistic activities.
- Signed a MOU with International Finance Cooperation to strengthen vaccine manufacturing capacity in LMICs, inform decision making around investment and supply vaccine expertise. The first phase of the partnership established the governance and Joint Action Plan with a focus on African countries – Republic of South Africa, Rwanda, and Senegal.
- CEPI joined the Development Financing Institutions Working Group to advise development banks and governments (Team EU, IFC, EIB) on their strategic vaccine manufacturing investment planning for Africa. CEPI is considering broader strategic engagement with regional development banks and is in the process of signing an MOU with the Asian Development Bank.
- Based on CEPI's manufacturing survey, CEPI co-hosted regional multistakeholder roundtables together with WHO regional offices in the Eastern Mediterranean and the Americas. Moreover, CEPI co-hosted a Nordic roundtable with the Finnish Ministry on behalf of the Nordic Council.

National:

- Together with government agencies from investors' countries, co-hosted 12 technical roundtables[18] to:
  - Drive national awareness and support for CEPI's activities and CEPI2.0;
  - Understand national priorities, capacities, capabilities and needs, as relevant to CEPI's future plans;
  - Explore CEPI's complementary role CEPI by identifying priority areas where CEPI can serve as a collaborator and connector to amplify domestic investments, forge regional synergies and promote global coordination;
  - Foster bilateral relationship and awareness between CEPI and key national stakeholders;
  - Inform the political workshops on whole-of-government approach and CEPI replenishment.
- Formalized strategic partnerships within individual countries, e.g. MOU with Institut Pasteur de Dakar in Senegal to advance COVID-19 vaccine manufacturing in Africa, MOU with Kenya, MOU with the Chinese Ministry of Science and Technology (MOST) and late stage discussions with Rwanda.
- CEPI and Global Health Innovative Technology have complementary mandates and have shared approaches on the assessment of CfPs, held discussions on platforms and technologies of common interest and equitable access commitment, and initiated cooperation to enhance R&D capabilities in vaccine and therapeutic development within Japan, and enhance Japan's participation in the global effort to address epidemic/pandemic preparedness.
- CEPI conducted two roundtables to explore partnership opportunities with the Republic of South Africa based BIOVAC and Africa Vaccine Manufacturing Initiative (AVMI).
- CEPI commenced discussions on a revised MOU with Indian Council of Medical Research (ICMR), India.

Informing key global ecosystem discussions

The need for a more effective, robust and coordinated global preparedness architecture is widely recognised, and countries and regions are now seeking to strengthen their domestic and regional preparedness and response capabilities. CEPI played a key role in informing G7 Pandemic Preparedness Partnership (G7 PPP) and G20 High Level Independent Panel (G20 HLIP) discussions in 2021, resulting in the 100-day aspiration for vaccine development being adopted by G7 and G20, and alignment on key elements of the future target ecosystem.

Joint Coordination Group (JCG)

Due to the regular engagement of most JCG members through COVAX and ACT-A and the overwhelming focus of these partners on COVID-19 response in 2021, CEPI held one JCG meeting in February 2021 to discuss CEPI 2.0 strategy and the necessary ecosystem changes. Many of the lessons learned by COVAX will apply to the future JCG and CEPI plans to revise the group's Terms of Reference in 2022 to take into account the evolution of the ecosystem and future need for a multi-partner coordination forum.

[18] Roundtables were held in Australia, Canada, Ethiopia, Germany, Italy, Japan, Kingdom of Saudi Arabia, Korea, Mexico, New Zealand, Norway, United Kingdom.

Outcome 2.3 – KPI 12: Percent of vaccine development partners with necessary agreements in place for vaccines to be deployed and tested during an outbreak or as preventive vaccine (as relevant)			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	100%	100%	**ON TRACK**

Comment:

All of the projects funded by CEPI involving the core portfolio or COVID-19 have as a critical equitable access obligation that vaccines be deployed as necessary and appropriate, as part of a clinical trial during an outbreak and/or as a preventive vaccine allowed by regulatory authorities. Specifics depend on the stage of development.

The Chikungunya and COVID portfolios are the most advanced. For the COVID-19 portfolio, agreements are in place with the COVAX Facility as outlined in Outcome 2.3 – KPI COVID-19. For the Chikungunya portfolio, the most advanced candidate has arrangements for CEPI to access a virtual ready reserve of 200,000 doses free of charge both before and after licensure, and a commitment to increase manufacturing output within 9 months. Further discussions with stakeholders in 2022, including the JCG, will seek alignment on paths to emergency response for affected countries and promote preparedness for these scenarios. For other priority pathogens where the portfolios are earlier stage, product developers may have an obligation to respond to CEPI's request to increase manufacturing , but this may be outlined in less detail given the early stage of development.

Outcome 2.3 – KPI 13: Percentage of vaccine development partners with plans in place for equitable access fully consistent with CEPI's Equitable Access Policy			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	100% of projects which have passed Stage Gate Review for progression from Phase I to Phase II trials.	On track (100%), all of the projects funded by CEPI involving the "core portfolio" and COVID-19 vaccines include equitable access requirements as an element in the terms and conditions of the award agreement or as a separate equitable access agreement between CEPI and the awardee.	**ON TRACK**

Comment:

Equitable access plans are designed to become more specific throughout the life of the project as more is known about both the programme and in most cases, the disease itself. The following dashboard (Table 3) gives an indication of items that are included in equitable access plans as applicable. Plans enable a faster response through preparedness; seek to promote affordability through a focus on a lower cost of goods; ensure accessibility through appropriate scale and location of manufacture; and ensure a product profile suitable for use in LMICs.

Most new agreements in 2021 focussed on COVID-19 and were for the development of a new vaccine. For those projects developers provided a right of first refusal to the COVAX Facility for early doses commensurate with the value of CEPI funding at an affordable price. Where an investigator-led trial was funded, equitable access plans focussed on prompt and open access to data and results. The impact of that data could be significant given the study designs focussed on maximising the use of existing vaccines including for potentially vulnerable sub-populations.

Table 3: CEPI Equitable Access Dashboard

Price	• Agreement on pricing principles based on LMICs affordability • Price negotiated based on LMICs affordability and business sustainability (e.g. COGs +%, no. of years for investment breakeven) • Agreement on the pricing details for public disclosure
Clinical development	• Regulatory submission strategy defined to ensure product licensure/commercialization in endemic countries • Support for 'Enabling Sciences' • Identified commercial partner & manufacturing sites
Intellectual property	• Agreement on Public Health Licence inclusion • IP rights discussed and agreed in line with the asset's specificities • Agreement to work on additional candidate on the platform/IP
Shared risk/benefit	• Financial benefits/refunds/supply after certain milestones • Share of awardee's commercial revenues from non-outbreaks • Manufacturing at-risk being initiated
Data sharing and transparency	• Open access to data, results and publications arising from CEPI funding • Clinical trial data and results publicly disclosed as per CEPI's clinical trial policy • Project materials sharing/project data publicly available in form of animal models, biological samples & disease assay
Availability and supply	• Tech-transfer to LMICs plan in place • Access to raw materials/adjuvants to ensure manufacturing sustainability • Provision to cover outbreak period and clarity on location/ownership/management of stock-pile • Ensure a resilient supply chain for logistics, storage and administration of vaccines • Commercialization and launch plan for LMICs shared and discussed • No. of doses secured/population at risk • Appropriate supply chain in place for affected territories - e.g. storage, packaging

Outcome 2.3 – KPI COVID-19: Percentage of CEPI-funded vaccine development partners with plans in place for equitable access fully consistent with CEPI's Equitable Access Policy and transitioned to the COVID-19 Global Access Facility (COVAX), as appropriate			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	100% consistent and those deemed appropriate, 100% transitioned to COVAX	Of the original 10 COVID funding agreements, 90% have equitable access plans in place consistent with CEPI's Equitable Access Policy. Of those original 10, 4 have been transitioned to the COVAX Facility, and 3 have received WHO EUL The Wave-2 portfolio all have equitable access plans in place consistent with CEPI's Equitable Access Policy including rights of first refusal for the COVAX Facility.	**ON TRACK**

Comment:
CEPI's portfolio of COVID vaccine candidates was built on investments in candidates that could be suitable for LMICs and tied to equitable access provisions. Early, small investments required commitment to CEPI's Equitable Access Policy and a path to further investment on more specific terms.
Larger investments required a commitment to provide capacity and, therefore, doses to a 'global allocation body' (now the COVAX Facility) commensurate with investment.
CEPI provided no-fault loans to select manufacturers in order to accelerate the time by which doses would be available for the COVAX Facility. To date, three billion doses of CEPI-funded vaccines have been secured for COVAX and 41% of doses delivered by COVAX have benefited from CEPI funding.
Typically, vaccine development has a 10% chance of success, 40% of CEPI's original COVID portfolio have secured advance purchase agreements from the COVAX Facility to date and 30% have received WHO EUL.
In addition to funding the development of vaccines, CEPI has also funded clinical studies of use in sub-populations such as immunocompromised individuals, heterologous series of vaccination and will soon fund studies into fractional dosing after both natural and vaccination priming. These data will then be available to inform NITAGs recommendations and therefore the access plans focus on making that data available to those who would benefit from it.

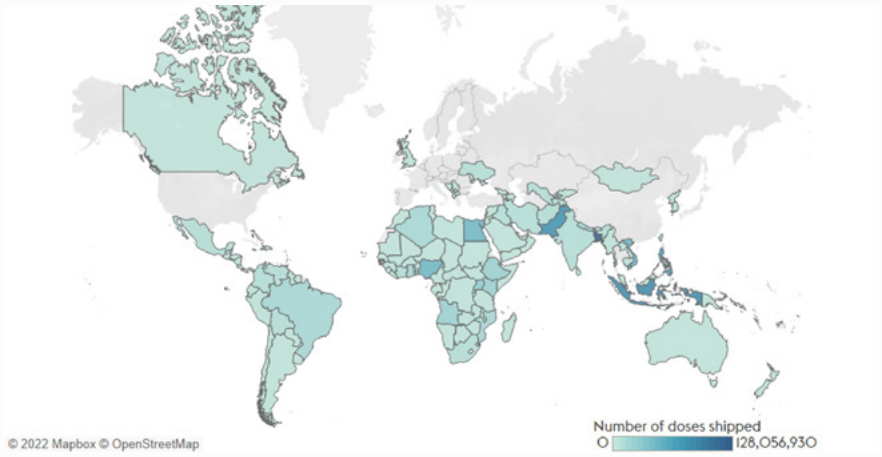
To date, three billion doses of CEPI-funded vaccines have been secured for COVAX and 41% of doses delivered by COVAX have benefited from CEPI funding (see figure 7).

Figure 7: COVID-19 doses shipped by COVAX with significant contribution from CEPI R&D portfolio

COVAX has so far shipped over 1.4 Billion COVID-19 vaccine doses to 144 participants

Approximately half of the doses are from CEPI R&D funded candidates*

The majority of these doses (~88%) have been distributed to AMC participants**



*Include Moderna (150m), AZ (241m), SII manufactured doses (49m), part of that are donated (242m)
**https://www.gavi.org/gavi-covax-amc

1.3. Strategic Objective 3: Sustainability

Create durable and equitable solutions for outbreak response capacity

While preparedness and response are key priorities for an organisation working on emerging infectious diseases, sustainability is critical to ensure that the systems, capacities and products CEPI helps to develop stand the test of time. CEPI has developed an organisational structure to ensure that investments made are robust enough to tackle the unpredictable nature of epidemics, and that they help drive systemic changes in vaccine R&D for EIDs through innovation and alignment with priorities of other organisations. To ensure that CEPI's approach is sustainable, CEPI:

1. Improves the predictability of financing to address end-to-end market failures;
2. Drives efficiencies to reduce costs across the end-to-end spectrum of vaccine development;
3. Develops contingency plans to reduce risk so that successful products are available to support outbreak response.

Progress under Sustainability is summarised under these three areas as described below.

1.3.1. Improve the predictability of financing to address end-to-end market failures

Strengthen resource mobilisation efforts

CEPI's progressive response to the COVID-19 pandemic, and co-convening role in COVAX, the Vaccine Pillar of ACT-A, has continued to amplify the critical and unique role CEPI is able to play in the global health ecosystem in fostering political support from new and existing investors, thereby paving the path to sustainable funding.[19]

In March[20] 2020 CEPI launched a USD 2 billion Investment Case to enable CEPI to develop vaccines against the COVID-19 virus. In February 2021 CEPI launched a revised COVID-19 Investment Case of USD 1 billion for 2021[21] for its work under ACT-A to combat critical challenges related to COVID-19 variants and to invest in manufacturing capacity that will secure supply of vaccines for the world. CEPI was able to expand its funding base, mobilising close to USD 1.5 billion from pledges and contributions secured in 2021 . This included portions earmarked to COVID-19 response from existing and new investors.

To date, CEPI has secured financial support from the following 34 public sector investors and philanthropic foundations: Australia, Austria, Belgium, the Bill & Melinda Gates Foundation, Canada, Denmark, the European Commission, Ethiopia, Finland, Germany, Greece, Hungary, Iceland, Indonesia, Italy, Japan, Kuwait, Lithuania, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Portugal, Romania, Saudi Arabia, Serbia, Singapore, Switzerland, Republic of Korea, United Kingdom, USAID, and Wellcome.[22]

In addition to securing financial support from the public sector, CEPI was also able to secure support from private sector entities as well as contributions from the public via the UN Foundation's COVID-19 Solidarity Response Fund in 2021.

[19] For the period 2017 – 2021, CEPI raised in total USD 2.6B from pledges and contributions secured, of which USD 402M was raised in 2021.

[20] https://cepi.net/news_cepi/2-billion-required-to-develop-a-vaccine-against-the-covid-19-virus-2/

[21] USD 264M was raised for COVID and USD 88M for Core in 2021

[22] More information on investors to CEPI in 2021 can be found in Appendix 2

To raise the investments needed to deliver against its CEPI 2.0 ambition of reducing the time from pathogen characterisation to availability of clinical data for emergency use of vaccines or other promising biologics for a future pandemic to 100 days, CEPI implemented a replenishment mechanism as the main pillar of its resource mobilisation strategy, primarily for raising funds from within the public sector. CEPI kicked off the replenishment campaign in spring 2021 by launching its USD 3.5 billion investment case, derived from CEPI's 2022-2026 strategy, and the UK government was secured in April 2021 as official host of CEPI's replenishment. An intensive 12-month campaign involving political engagement, advocacy and communications (traditional and social media) was launched. Global platforms such as the G7, G20, World Health Summit, World Economic Forum, Munich Security Conference were leveraged and played a key role in rallying political support for CEPI 's replenishment through the creation of highly visible events, culminating in the Global Pandemic Preparedness Summit in London on 7th-8th March 2022. The Summit will mark a critical starting point upon which to build resource mobilisation efforts in 2022 and beyond.

The promotion of alternative funding models, including a proposed expansion in the use of the International Finance Facility for Immunisation (IFFIm)[23] for CEPI, and the exploration of new global public investment financing schemes has been kicked off to complement and diversify the replenishment approach.

By the end of 2021 had managed to already secure USD 263M as a down-payments towards CEPI 2.0.

1.3.1.1. Alignment of funding and scope with other organisatons

Outcome 3.1 – KPI 16: Agreements with downstream financing partners in place for each of CEPI's priority diseases

Baseline	Target 2021	Actual 2021	Status
0	3 (for 3 of these diseases Lassa, Nipah, MERS, Rift Valley Fever and Chikungunya)	• 0 • Good progress and lessons from COVAX experience. • Core pathogens now require focus at the appropriate time. Chikungunya is the 2022 focus.	**ACTION REQUIRED***

Comment:
CEPI is in active discussions with downstream financing partners about Chikungunya, other CEPI core priority pathogens are too early in development for such discussions.

***CEPI 2.0**

In CEPI 2.0, each CEPI core priority pathogen will have an end-to-end plan to enable equitable access to vaccines against that pathogen. These plans will be aligned with key stakeholders. The access plans will also connect with the sustainability initiatives under CEPI 2.0, including manufacturing. Access plans may include:

- Work with LMIC partners and WHO towards supporting the LMIC vaccine manufacturing industry.
- Facilitate technology transfer of one or more lead candidates to an LMIC based vaccine manufacturer for late-stage manufacturing, including ready reserves to enable equitable access for LMICs.
- Align with various stakeholders (Gavi, UNICEF WHO, National regulatory authorities, manufacturers etc.) on the vaccine deployment strategy in relevant scenarios and map out the pathway to use.

[23] The International Financing Mechanism for Immunization (IFFIm) is a financing tool based on bond issuance that has been developed for GAVI – The Vaccine Alliance, but which has shown willingness to consider CEPI as an additional candidate for its financing. For more information see Annex 1

Output 3.1 – KPI 17: USD 1B raised as multi-year contributions to CEPI			
Baseline	**Target 2021**	**Actual 2021**	**Status**
USD 630M	USD 1B (2019)	USD 834M	**ACTION MAY BE REQUIRED***

Comment:
Continued extenuating circumstances due to the COVID-19 pandemic resulting in delays in core programme progress, with consequent knock on effects on the levels of investment needed must be noted. In 2021, efforts were focused towards mobilising resources to meet needs of COVID-19 vaccine development and manufacturing work which is part of CEPI's second business cycle from 2022-2026. 2021 saw continued increase in the total number of sovereign, philanthropic and private sector investors joining the coalition, that included a few new sovereign investors that made one-off financial contributions to CEPI's core programme. A number of investors who had contributed previously also increased their funding amount in 2021. Despite this, the total funds accumulated for the core portfolio were slightly higher than the reported USD 735M in 2020.

***CEPI 2.0**
As CEPI is entering its second business cycle from 2022-2026, the forecasted financial needs for the successful completion of its three strategic objectives: Prepare, Transform, Connect is USD 3.5B. This amount includes funding to replace resources previously repurposed in the first business cycle to support COVID-19 activities.

Output 3.1 – KPI COVID-19: Resources fully mobilized to support the R&D&M COVAX investment case			
Baseline	**Target 2021**	**Actual 2021**	**Status**
N/A	Tentative target: USD 2.1B funding for core R&D; USD 5.7B for manufacturing and advanced purchase agreements (mainly recoverable loans, down payments to the COVAX Facility and blended finance; not all funding will flow through CEPI).	USD 1,5B	**ACTION MAY BE REQUIRED***

Comment:
The timely launch of the COVID-19 investment case in early 2020 sought to raise USD 2.1 billion over 18 months. This was followed by the Coronavirus Global Response Pledging Conferences in May and June 2020, which mobilised resources from existing and new investors. In 2021, CEPI continued to follow up on commitments to ensure that pledges were materialised worked towards new one-off commitments to COVAX which required extensive effort. However, the COVAX facility continues to face a large gap in the funding needed with R&D funding also facing shortfalls. The funding gap was considerably reduced by end of 2021 with a funding need of USD 256M moving into 2022.

1.3.2. Drives efficiencies to reduce costs across the end-to-end spectrum of vaccine development

There are numerous ways that CEPI seeks to drive efficiencies across the end to end spectrum including:

- Constantly striving for cost reductions and streamlining in all areas from R&D and vaccine manufacturing to regulatory process and stockpiling, and even through the deployment of vaccines. Supports the streamlining of processes related to vaccine development and regulatory approval that could reduce R&D timelines or extend the shelf-life of vaccines, thereby reducing the frequency of costly replenishments;
- Being committed to developing and deploying vaccines against emerging infectious diseases in a manner that demonstrates it is a responsible steward of public resources;
- Seeking to guarantee that the financial resources bestowed to CEPI are invested in a way that provides value.

In relation to COVID-19

- CEPI seeks to secure a supply of successful products through partnership agreements, that build in equitable access terms with right of first refusal of vaccines for the COVAX Facility (or alternative purchasing mechanism) from early stages of development.
- The COVAX Manufacturing Task Force set up in 2021 (see section 1.2.4.) contributed to identifying and resolving vaccine manufacturing challenges and bottlenecks impeding equitable access to COVID-19 vaccines and other human health products
- The COVAX Marketplace established in 2021 improves visibility and facilitates the transaction of critical, single-use consumables for COVID-19 vaccine manufacture.
- To support the deployment and expand access of COVID-19 vaccines CEPI has
  - Invested in mix-and-match clinical trials covering a wide range of vaccine combinations for heterologous prime boosts, heterologous boosters and fractional dosing;
  - Supported geographically-dispersed trials in countries across Africa, Asia, Europe, South America and Oceania and contributed to sustainable clinical trial capacity building for future preparedness.
- The MedInstill/INTACT technology and collaborations with Institut Pasteur de Dakar as well as Medigen (see section 1.2.3) are additional projects demonstrating CEPI's work to drive efficiencies and reduce costs across the end-to-end spectrum of vaccine development.
- The before mentioned CfP to develop heat-stable vaccine technology for use against epidemic and pandemic threats, launched in February 2022, is an example of how CEPI continues to focus on the development of innovative technologies to improve global access to vaccines in CEPI 2.0.

I.3.2.I. Managing the portfolio

Throughout 2019 and 2020 CEPI established core capabilities in R&D project management, risk management and portfolio management to actively monitor and manage the investments made in the portfolio of vaccine projects. These included:

- A common portfolio management cycle for systematic project identification, selection, management and evaluation (Figure 6);
- A dedicated portfolio governance committee – the Portfolio Strategy and Management Board (PSMB) – consisting of senior members of the CEPI leadership team and internal technical and subject matter experts);
- Standardized project and portfolio management practices to drive harmonization and comparability across the portfolio;
- Clear and consistent management and reporting of project and portfolio information;
- A dedicated R&D Programme Management Office to oversee aligned and disciplined execution of CEPI's vaccine projects.

CEPI's has adapted and modified its approach to portfolio management during 2020 and 2021 in response to the COVID-19 pandemic, to enable greater speed and flexibility in decision-making relating to COVID-19 portfolio investments.

During 2021, CEPI continued to oversee the progress and management of the R&D projects of both the core (non-COVID-19) portfolio and the COVID-19 portfolio. It has further strengthened portfolio management capabilities based on recommendations from the portfolio governance effectiveness review conducted in late 2020 (see below). CEPI has also worked on preparing for the transition to CEPI's second business cycle commencing from 2022 to 2026, including:

- Updating portfolio objectives and targets based on CEPI 2.0 strategy;
- Reviewing portfolio composition and performance through both internal and external portfolio reviews;
- Taking initial steps towards adapting portfolio governance to CEPI 2.0.

Figure 8: CEPI's Portfolio Management Cycle

Development of CEPI 2.O strategy and definition of new strategic targets

CEPI's goal during the first five-year business cycle (2017-2021: CEPI 1.0) was to establish a portfolio of vaccine candidates, technology platforms and enabling science programmes with the objectives of:

- Advancing vaccines against core (non-COVID-19) priority pathogens to evidence safety and efficacy in humans and to generate ready reserves of material for use in outbreak conditions;
- Establishing a diverse portfolio of rapid response platform technologies that can accelerate the development, manufacture, and clinical evaluation of vaccines in response to outbreaks of newly emerging pathogens, designated Disease X by WHO.

Further, in response to the COVID-19 pandemic CEPIs goal was to:

Rapidly advancing vaccine candidates against COVID-19 through to licensure with the aim to develop at least three safe and effective vaccines which can be distributed and deployed to the world through COVAX.

Portfolio Review

On 4-5 November 2021, CEPI conducted a strategic review of its core and COVID-19 R&D portfolio. Over 70 CEPI coalition partners engaged in a technical review of portfolio progress and priority setting for the delivery of CEPI 2.0 objectives. Specific objectives for the portfolio review meeting were to:

1. Recap on CEPI's strategic portfolio positioning for each pathogen/area
2. Review CEPI's portfolio composition, investment and performance for each pathogen/area
3. Align on portfolio priorities and investment needs for CEPI 2.0

The meeting provided the opportunity for holistic review and discussion across the full scope of CEPI's R&D portfolio as well as an in-depth consideration of pathogen and platform-specific aspects of the portfolio, for both COVID-19 and the core portfolio pathogens - Lassa, Chikungunya, MERS-CoV, Nipah and Rift Valley Fever viruses.

Participants provided perspectives on CEPI's strategic positioning across COVID-19 and core portfolios, widely acknowledging that through CEPI the global community has both reinvigorated its interest and accelerated its commitment to emerging disease R&D preparedness and response. Participants recognised that CEPI had set high priority strategic objectives for the first five-year cycle in the aftermath of the West Africa Ebola epidemic, which provided a solid foundation for CEPI's rapid pivot to COVID-19, even though initial pathogen priorities focused on cross-border epidemic threats.

Participants noted that CEPI portfolio priorities needed to further evolve, especially with regards to:

- Balancing focus between epidemic and pandemic threats according to stakeholder interests and global needs changing after COVID-19;
- Re-positioning of focus between priority pathogens and Disease X, especially CEPI's rapid response platform strategy;
- Setting ambitious goals for future pandemic preparedness and response yet managing expectations about the likelihood of their attainment.

The portfolio review also incorporated findings and recommendations from a PSMB effectiveness review completed in early 2021, and an independently led RDMIC lessons learned exercise conducted in Q3.

Evolution of portfolio governance towards CEPI 2.0

As CEPI moves to CEPI 2.0, the approach to portfolio investment governance will be adapted to reflect the broader and more ambitious range of strategic portfolio objectives. CEPI anticipates launching a number of CfPs in 2022 which will increase the number and range of vaccine R&D projects in the portfolio. In addition, activities in manufacturing and therapeutics will likely expand the diversity of projects across the portfolio.

CEPI is in the process of reviewing the current framework for portfolio investment governance in view of these anticipated changes. This is part of a broader exercise to evolve CEPI's overarching governance structure along, guided by the following principles:

- Agile: To retain fast decision-making process despite larger scale and scope
- Holistic: To ensure decisions are made with consideration of broad context, beyond scientific and technical criteria
- Empowered: With decision-making capabilities spread across layers, ensuring speed at the appropriate oversight
- Transparent & clear: To create external accountability and ensure a fair process
- Leveraging broad expertise: To ensure the right expertise is pulled in for key decisions

Other recommendations for strengthening portfolio governance for CEPI 2.0 include delegation authority, remit, agenda & cadence, chair & membership, processes, external expertise and decision framework and are being developed for implementation in early 2022.

COVID-19 portfolio management – COVAX governance

As CEPI's COVID-19 portfolio transitioned into the COVAX pillar of the ACT-Accelerator, investment decision-making for the COVID-19 portfolio moved under the responsibility of a new R&D and Manufacturing Investment Committee (RDMIC) within the COVAX structure. The RDMIC and associated structures in CEPI came into effect in July 2020 with CEPI's Portfolio management team serving as the secretariat. The RDMIC has continued to be operational throughout 2021 as the pandemic evolved.

The RDMIC is a multidisciplinary decision-making group, led by CEPI, with industry expertise that provides portfolio strategy and investment decision recommendations to rapidly identify, develop and manufacture COVID-19 vaccines that can be deployed at scale to address global health needs. To that end, the RDMIC has defined the target composition, diversity, investment allocation and risk profile of the COVID-19 R&D portfolio of vaccine candidate projects and cross-cutting enabling projects. It also provides overall oversight of project progress and serves to:

- Endorse new projects;
- Provide resolution of significant project issues escalated by the Technology Review Group (TRG);
- Endorse recommendations for project progression through Stage Gate Reviews provided by the Technical Review Group.

New project proposals coming to the RDMIC are reviewed from a scientific and technical perspective through the TRG and associated processes. The RDMIC then reviews these recommendations in the context of the broader portfolio and funds available for investment. In order to achieve the strategic COVID-19 R&D portfolio objectives, RDMIC has, in 2021, applied the following investment priorities:

- Maximise doses of existing vaccines to COVAX in 2021 and 2022;
- Pursue clinical research to maximise access of existing vaccines;
- Invest in new vaccines with optimized profiles, including for new variants;
- Continue to invest in enabling sciences.

The CEPI Board is accountable for decisions, following advisory guidance from RDMICs. Vaccine candidates within the COVID-19 R&D portfolio are assessed for inclusion by the COVAX Facility – the global procurement mechanism of COVAX. The Facility pools the purchasing power from participant countries (including self-financing economies and the Gavi AMC economies) to secure procurement of COVID-19 vaccines from the COVID-19 R&D portfolio and other available vaccines.

The Independent Product Group (IPG) established by Gavi makes recommendations to the Office of the COVAX Facility on the inclusion of vaccines in the COVAX Facility. The IPG is advisory in nature and serves to make recommendations on vaccine candidate prioritization and portfolio balance within the overall COVAX Facility portfolio. To ensure an effective and efficient end-to-end procurement process, a One Deal team2[24] operates across the partner organisations.

To support COVID-19 vaccine development CEPI established SWATs in 2020. SWATs are groups of experts focused on resolving technical issues and challenges common across all COVID-19 vaccine development projects to promote and accelerate vaccine development. SWAT core members represent diverse stakeholders in the vaccine development ecosystem, providing expertise in enabling sciences; clinical development and operations; and manufacturing to scale. A Regulatory Advisory Group (RAG) provides guidance for regulatory science challenges and interdependencies escalated by all three SWAT disciplines. The RAG, composed of regulators representing all global regions, works to resolve and provide guidance for harmonized pathways to address regulatory science challenges, in order to accelerate vaccine development.

The objectives for all SWAT teams and the RAG are to:

- Focus on resolving common technical cross project questions and challenges at speed;
- Act as an open source of information for Vaccine Teams and COVID-19 vaccine developers more broadly;
- Promote harmonization and comparability across projects, and;
- Bring together different stakeholders and coordinate with other players in the ecosystem to maximise efforts.

The benefits of this organisational structure are such that CEPI envisions that the SWAT/RAG model can be used moving forward with core pathogens to address advanced development challenges, particularly in enabling sciences, regulatory approval pathways and harmonization. Lessons learned and gaps identified in all SWATs can be leveraged for future response preparedness and the end-to-end process of responding to epidemics and pandemics with COVAX partners.

[24] One Deal Team is a cross-partner COVAX workstream / team that reviews COVAX vaccine portfolio strategy, APA deal terms and the product supply volumes. It includes representatives from all COVAX partners

1.3.2.2. Sustainable manufacturing and clinical trials

CEPI continues to engage in a broad approach to 'scaling-up' and 'scaling-out' manufacturing, which includes supporting technology transfer, reserving manufacturing capacity for CEPI-funded vaccine developers, and securing supplies of materials ahead of time such as glass vials to minimise the number of bottlenecks during the production process. CEPI co-hosted a supply chain summit and as a result of the event, the COVAX Marketplace was launched.

CEPI's partnership with the Stevanato Group, an Italian-based pharmaceutical glass producer, has secured 100 million medical-grade glass vials that could store and deliver up to two billion doses of COVID-19 vaccines. CEPI donated 70 million vials to Clover. This partnership has deliberately been kept flexible as not all COVID-19 vaccine candidates will successfully make their way through the development process, so if vaccine programmes fail, the glass vials can be repurposed for another COVID-19 vaccine programme.

CEPI has advanced its support for the evaluation of a novel technology for filling, transporting, and delivering vaccines particularly suitable for use in low-resource settings, the MedInstill/INTACT Solutions multi-dose pouches. Key areas within CEPI have been expanded to include CMC leads to each vaccine development programme, and completion of a manufacturing facility survey across LMIC regions to map manufacturing capacity and capability to support future network activities. In addition, outreach in support of sustainable manufacturing has included in excess of 40 external presentations across a variety of audiences.

Output 3.2 – KPI 18: Percent of priority actions taken to achieve efficiencies

Baseline	Target 2021	Actual 2021	Status
N/A	50%	N/A	N/A

Comment:

- Due to resource reallocation to continue supporting COVID-19 key deliverables, the scoping exercise to identify and prioritize actions to drive efficiencies in the end-to-end spectrum has not been completed. It is therefore difficult to say whether 50% of the priority actions to achieve efficiencies have been reached. An area where efficiencies were achieved, specifically with regard to sustainable manufacturing, is outlined in the narrative above.
- As CEPI advances to its 2.0 strategy, creating efficiencies in the end-to-end spectrum of vaccine development will be critical to progressing its 100-day aspiration.

1.3.3. Develop contingency plans to reduce risks so that successful products are available to support outbreak response

CEPI looks at every way possible to develop vaccines in a manner that enables them to be available, affordable and accessible, from supporting enabling science that benefits the entire field, facilitating manufacturing in multiple geographies by different manufacturers to mitigate the risk posed by a single source and vaccine nationalism, to striving for ease of delivery in low-resource settings. For later-stage vaccine candidates against Chikungunya, for example, CEPI is supporting the development of vaccines suitable for endemic countries and has undertaken matchmaking between developers and Contract Development Manufacturing Organisations (CDMO)[25], funded scale-out to secondary manufacturers' sites to enable vaccine security, and provided support for endemic country licensure and WHO prequalification activities.

CEPI's Chikungunya programmes also include commitments to tiered pricing frameworks that are sustainable for the manufacturer and affordable (taking into account the country's income), as well as commitments to seek appropriate marketing approvals in endemic countries within a reasonable period of time.

Minimising the impact of vaccine nationalism

Whilst the KPI below relates to CEPI's core portfolio CEPI has taken contingency planning for manufacturing further with its COVID portfolio and has reserved manufacturing capacity in geographically diverse locations, funded the inventory build at risk, procurement of raw materials at risk and has provided financial support to scale out manufacturing to multiple sites. Conditions for this financial support has been provided on basis of forgivable loans and on the basis that where R&D efforts fail, prior to the use of materials or capacity that those materials or capacity be fungible between CEPI projects.

Output 3.3 – KPI 19: Percentage of vaccine Partnership Agreements in place that contain contingency plans for manufacturing

Baseline	Target 2021	Actual 2021	Status
N/A	100%	100%	ON TRACK

Comment:
Each partnership agreement contains manufacturing plans that take into account the potential for a break in continuity of supply. All of CEPI's partnership agreements include an ability to enable continuity of supply. The more advanced projects include specifics as to where and how that contingency will be activated. Earlier projects have the right to require it and a timeline to agree the plan.

[25] A contract development and manufacturing organization (CDMO) is a company that serves other companies in the pharmaceutical industry on a contract basis to provide comprehensive services from drug development through drug manufacturing.

2. Finance and Funding

2. Finance and Funding

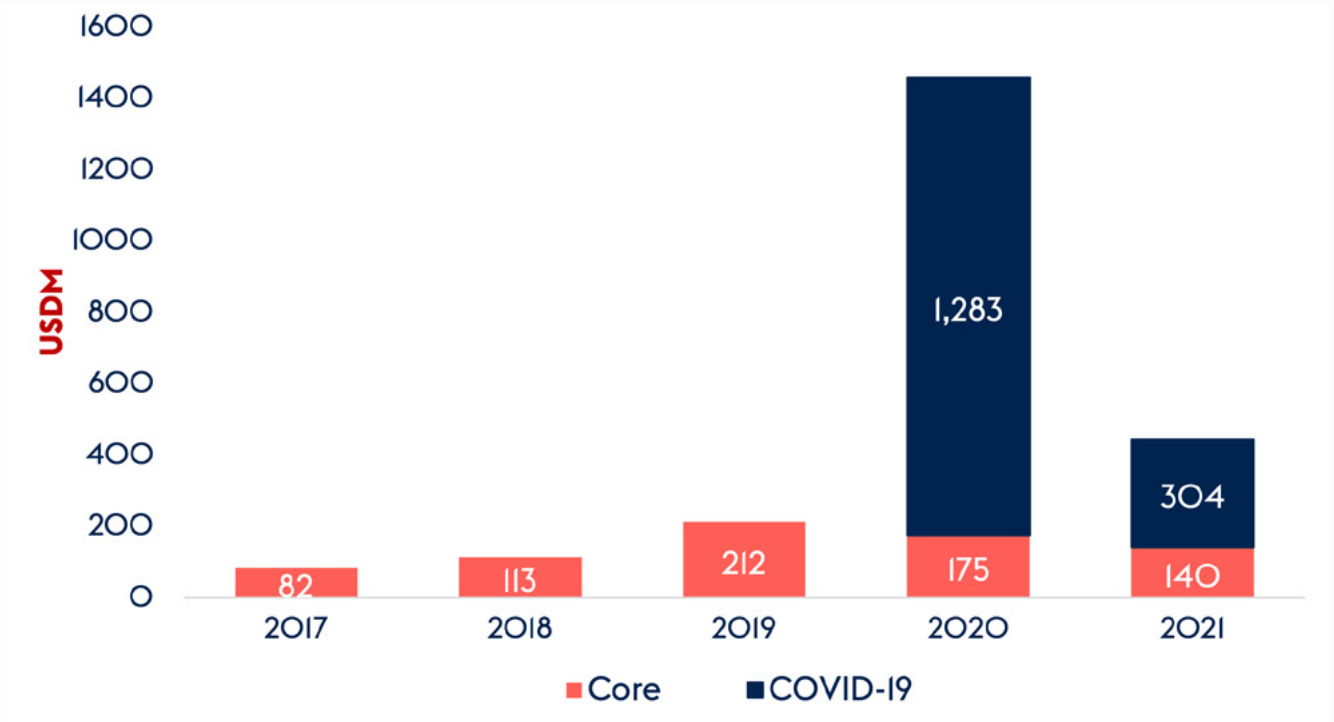
Figures presented in the finance section are expressed in USD equivalents using actual exchange rates for the years 2017-2021 and 2022 budget rates for years beyond 2022. Further details on CEPI finances can be found in Appendix 2: Finance. Reference is also made to CEPI's Annual Audited Accounts and Board of Directors Report 2021.

2.1. Contributions from Investors

Support from investors continued to grow during 2021, and by year-end more than USD 2.3B had been pledged to CEPI 1.0 since its launch in 2017, including USD 1.5B for CEPI's original COVID-19 investment case[26]. In addition to this, CEPI has received pledges of close to USD 0.3B as a down-payment for continued COVID-19 investments under CEPI 2.0[27]

Out of the USD 2.6B pledged during 2017 to 2021, the contributions received by CEPI by year-end 2021 were USD 2.2B. The remaining funds pledged are expected to be received in years 2022-2024. In 2021, CEPI received USD 444M in contributions.

Figure 9: Total Contributions per Year[28]



[26] Out of the USD 2.3B, 93% is secured through contribution contracts.

[27] Out of USD 263M, 92% is secured through contribution contracts.

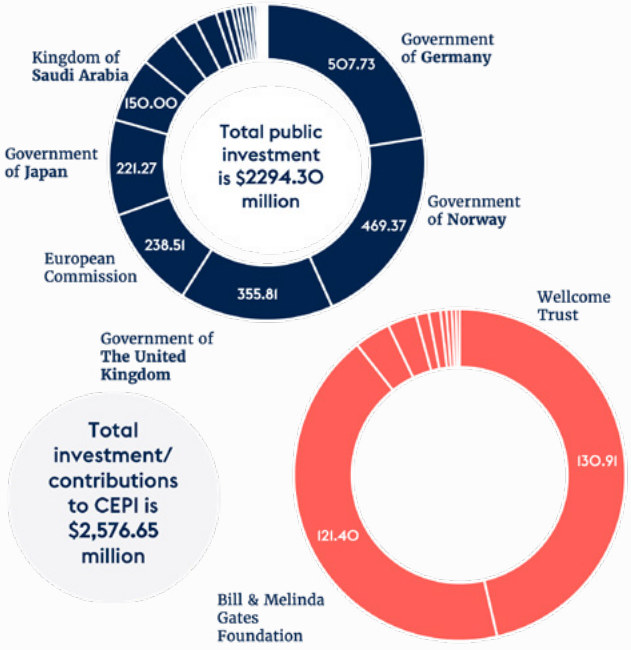
[28] Contributions/pledges may be received by CEPI in years different to those for which the contribution/pledge is secured. The figure shows funds received/proceeds up until December 2021.

CEPI receives contributions from sovereign investors, the European Commission, philanthropies and private organisations. Sovereign public investors represent the largest investor group (89%) and grew rapidly during 2020. In 2021, two new sovereign investors joined the coalition and overall CEPI now has contributions and pledges from 34 countries.

The overall number of individual contributors has grown from 14 by the end of 2019, to 80 by the end of 2021[29] (see figure 8 below). Traditionally, most donations have been pledged to CEPI's common/core pool of funds, while in the last couple of years, CEPI has also received earmarked donations directed to the COVID-19 pandemic. Earmarked funds are pooled and spent on eligible groups of projects[30].

In 2020, the CEPI Board allowed for a substantial redirection of "core" funding to COVID-19 investments, whereof part of the funds (USD 110M) was considered permanently repurposed[31]. So far, the COVID-19 funds have been sufficient to cover CEPI's COVID-19 investments, and the Board, therefore decided in 2021 that the funds should be repurposed back to "core", with the possibility to spend on COVID-19 if needed.

Figure 10: Snapshot CEPI's Investors and Contributions as of 31 December 2021



Full list of public sector investment (USD millions)			
Government of Australia	10.03	Government of Mexico	0.90
Government of Austria	2.36	Government of Netherlands	58.64
Government of Belgium	6.04	Government of New Zealand	10.82
Government of Canada	88.80	Government of Norway	469.37
Government of Denmark	1.45	Government of Panama	0.02
Government of Ethiopia	0.27	Government of Portugal	0.34
Government of Finland	6.63	Government of Philippines	0.01
Government of Germany	507.73	Government of the Republic of Korea	9.00
Government of Greece	1.78	Government of Romania	0.24
Government of Hungary	0.84	Government of Serbia	1.23
Government of Iceland	1.92	Government of Singapore	2.01
Government of Indonesia	1.00	Government of Spain	85.25
Government of Italy	17.67	Government of Switzerland	10.28
Government of Japan	221.27	Government of the United Kingdom	355.81
Government of Kuwait	10.00	Government of the United States of America	20.00
Government of Lithuania	0.11	Kingdom of Saudi Arabia	150.00
Government of Luxembourg	0.94	European Commission	238.51
Government of Malaysia	3.00		

[29] Including sovereign, philanthropic, and private sector contributions.

[30] COVID-19 funds are either earmarked through contract, or funds intended for COVID-19 investments.

[31] "Core" refers to CEPI's pre COVID-19 investment priorities.

2.2. R&D Project Investments

To date, CEPI has entered into partnership agreements with total investment requirements of up to USD 2.5B[32]. The biggest investments are in vaccine candidates, but CEPI also invests in an array of cross- cutting enabling projects to develop standards and assays, preclinical models, centralized lab networks, clinical studies, and multi-country epidemiology studies. CEPI has also invested in manufacturing capacity and materials for COVID-19, with some of these investments being structured as forgivable loans[33]. Disbursements are made in tranches, dependent on the completion of pre-specified project milestones.

Out of USD 2.5B worth of investments, USD 1.8B are COVID-19 investments (including Broadly Protective SARS-CoV-2 projects) of which USD 0.6B was committed during 2021. CEPI has paid out USD 563M on COVID-19 projects in 2021, and USD 1.1B in total since the start of the pandemic.

For CEPI's core portfolio, the total investment value at year-end 2021 was USD 703M. Most of these investments are longer term, multi-phased investments, not all of which are expected to be committed, as these will be contingent on key milestones that candidates will have to meet as they transition between phases of development. Accounting for expected phase-to-phase attrition, CEPI expects to spend USD 604M on its current portfolio of core projects.

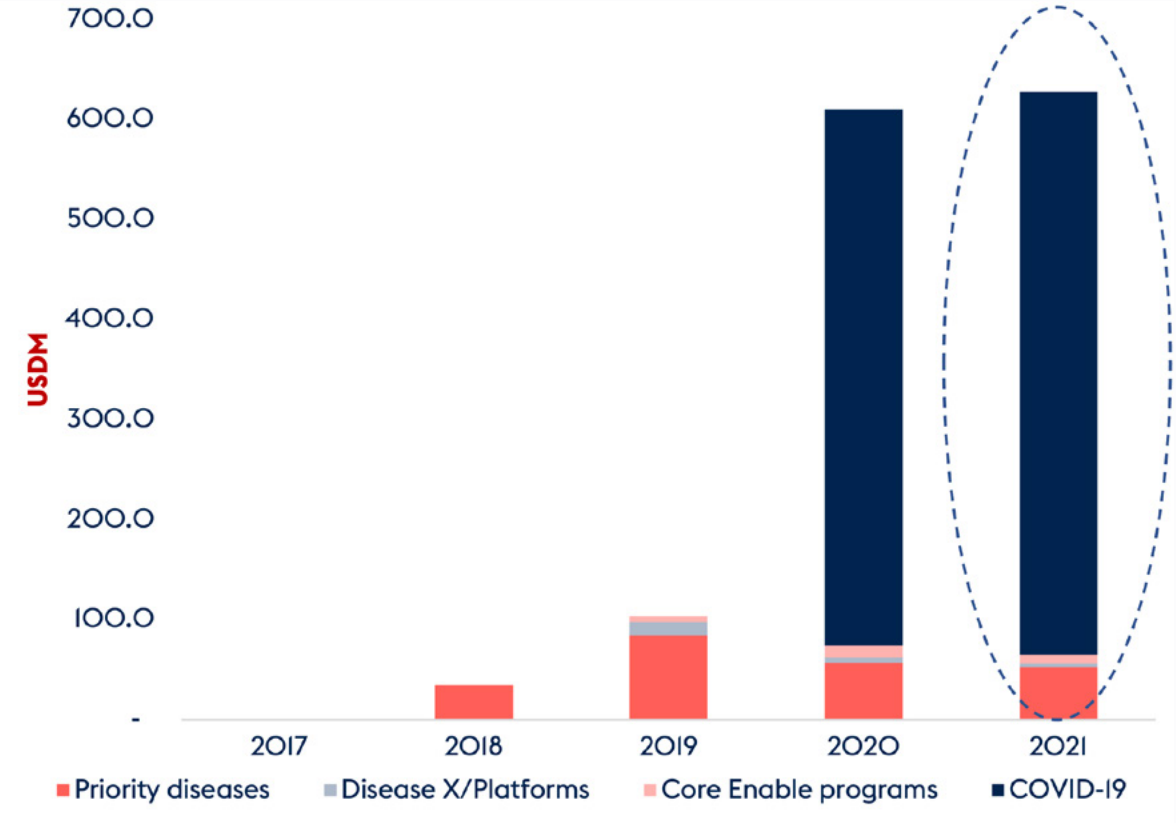
In addition to the current portfolio, multiple new investments or change requests to existing projects have been approved by CEPI governance and are to be signed. This includes USD 75M for COVID-19, USD 94M for broadly protective Betacoronavirus projects, as well as a reduction in existing platform technology projects of USD 19M.

The COVID-19 pandemic has caused significant delays to CEPI's "core" portfolio projects, reflected in adjusted project timelines and reduced payment forecasts throughout 2020 and 2021. Out of budgeted disbursements of USD 196M, only USD 65M was disbursed during 2021. Part of this relates to the fact that CEPI postponed the planned call for further development for Chikungunya and Rift Valley Fever, part of it relates to "normal" progression delays vis-a-vis original project plans (administrative delays in reporting and late disbursement requests from CEPI's awardees), but a major part is a direct effect of the pandemic (e.g., lock-downs, supply issues, shifting focus towards COVID-19 etc.). In total, USD 277M has been paid out on "core" projects by the end of CEPI's first business cycle.

[32] This figure includes only current contract value of signed contracts (signed as of 31.12.2021).

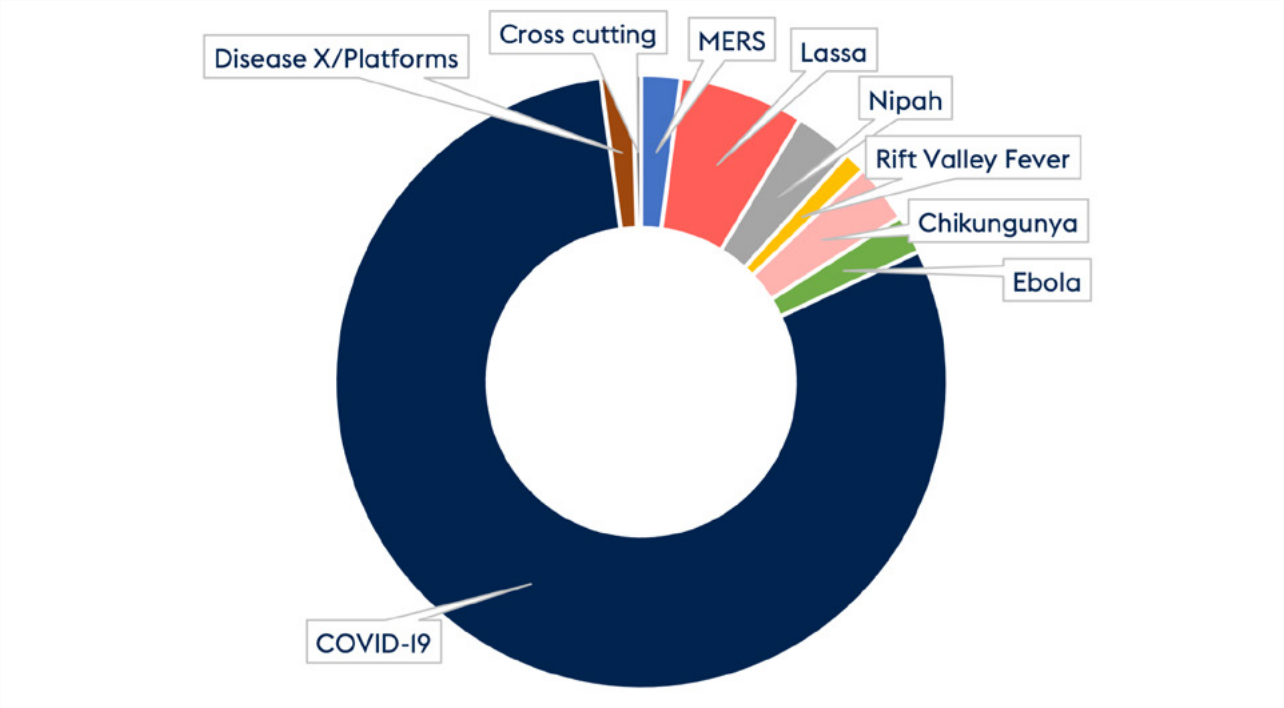
[33] Forgivable loans constitute USD 537M of total current COVID-19 investments. The repayment of loans is triggered by contractual requirements. By year-end 2021, CEPI considered it likely that USD 470M would be repaid, of which USD 35M had been received. USD 6M has been ascertained as unrecoverable, while there is still significant uncertainty regarding the remaining USD 61M.

Figure 11: R&D Project Disbursements 2017-2021



Apart from COVID-19, the largest disbursements by end of 2021 have been on Lassa and Chikungunya vaccine development projects, while Lassa, MERS and Nipah projects are the largest in terms of total investment commitments.

Figure 12: R&D Investment Disbursements Lifetime-To-Date



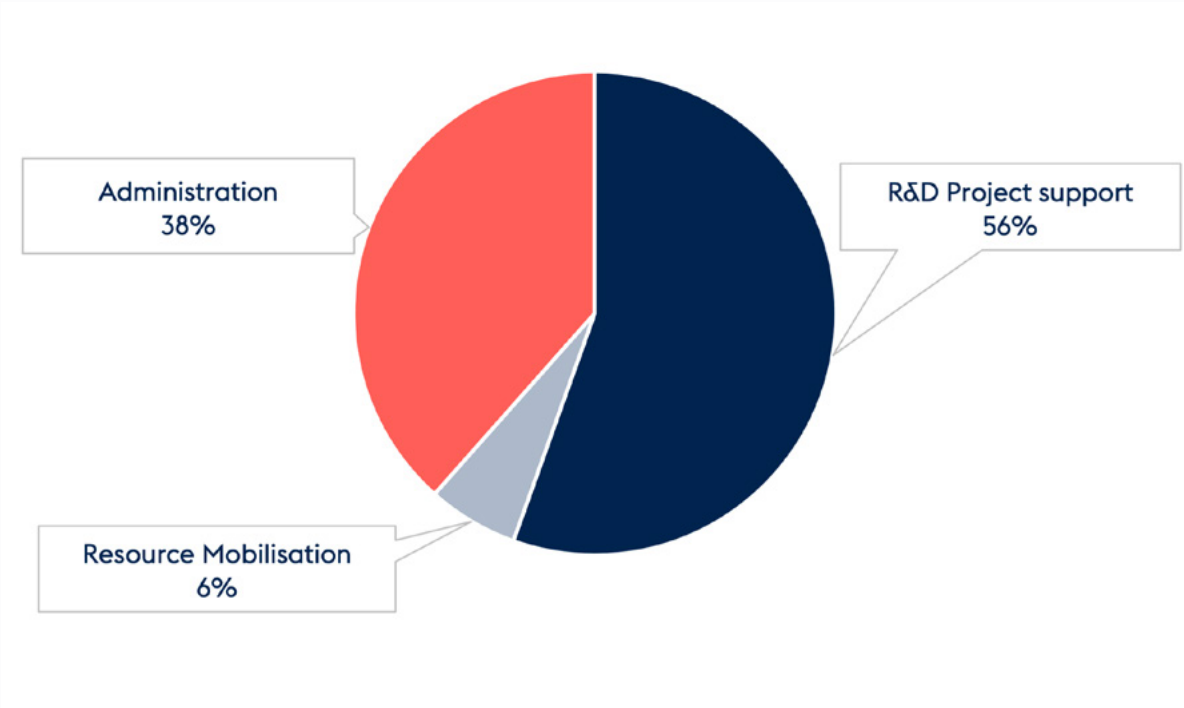
2.3. Operating and Total Costs

Of total costs and investments for 2021 (Appendix 2), CEPI spent 97% on its main activity, vaccine research & development, leaving a spend of 3% on overhead (resource mobilisation and administration).

Since its inception, CEPI has had a significant year-on-year increase in staff. This was also the case in 2021 as CEPI continued to prepare for the expanded scope under CEPI 2.0. Operating costs amounted to USD 45M in 2021, an increase of 30% over 2020 and 2% over the 2021 budget (see Appendix 2 for details). The increase in operating costs in 2021 was a result of continued hiring, full-year effect of increased headcount in 2020 and operational expenses related to Oslo HQ office move, development of business support processes, and development of CEPI's new operating model. The increase over the 2021 budget was communicated and approved by the CEPI Board early in the year.

Operating costs are depicted below by activity and refer to whether an expense is channelled towards R&D project support, resource mobilisation[34] or administration[35]. This provides insight into whether operating expenses are directed towards adding value to the portfolio of investments through project support, or to raising funds or managing the organisation administratively. The last two are typically labelled overhead costs. Of CEPI's operating costs, 56% relates to R&D project support which is largely driven by CEPI's R&D department, staffed with technical experts responsible for launching CfPs and conducting technical follow-up of CEPI's portfolio of projects.

Figure 13: 2021 Operating Costs by Activity



[34] Refers to CEPI's efforts to increase ongoing, and secure new funding commitments.

[35] Shared costs like IT, Office facilities, Finance & Operations and HR are not distributed to the different activities but are fully included under Administration. Total shared costs for 2021 were USD 8.6M.

2.4. Procurement

The CEPI procurement policy and procedure include general rules and principles, eligibility criteria for tenderers, specification of tender procedure types and duration of contracts. It also defines a set of thresholds that trigger different procurement processes (lowest level/simple tender/full tender), whereby the number of steps and scrutiny undergone reflect the value and type of procurement.

Together, the policy and the procedure reflect international best standards and EU directives. They were also drafted in close consultation with CEPI's investors, ensuring the approach was in line with legal requirements. The policy and procedure are currently under review, with the aim to simplify and adjust procurement thresholds. The new versions are likely to be implemented by the end of Q1 2022.

In 2021, CEPI continued to strengthen its procurement capability through specific developments in the areas of people & skills, processes, and system support. The procurement team maintains a strong focus on cross-functional collaboration and knowledge sharing, particularly with the legal team.

Furthermore, CEPI has mapped procurement processes and harmonized the ways of working across CEPI locations, as well as clarified roles and responsibilities between procurement, legal, compliance and other departments. CEPI is also working on improving the controls within procurement throughout the full life cycle of a contract. The current and planned contract life cycle management software enables the procurement managers to store and track signed contracts and ensure that CEPI always has valid contracts for all purchases.

During 2021, 50 tender processes and around 60 low-level procurements were undertaken and completed in accordance with CEPI's Procurement Procedure. Table 4 below gives an overview of CEPI's procurement levels across the different procurement processes, according to the estimated value. As noted above, these thresholds are currently under review.

Table 4: Overview of Procurement Thresholds in NOK (Norwegian Kroner)

Type of procurement processes
Lowest-level procurement (value below NOK 100,000)
Simple Procurement (value between NOK 100,000-500,000)
Full Tender (value above NOK 500,000)

3. Risk Management

3. Risk Management

Risk management, compliance and internal audit processes are key components in assuring that proper governance and monitoring are in place and continuously improved in CEPI. Monitoring of risk in CEPI is carried out by the CEPI Board, the Board Audit and Risk Committee and the CEPI Leadership Team, with the support of the Governance, Risk and Compliance function (GRC).

3.1. Risk Management

CEPI's risk management framework was designed to manage risks in order to achieve the coalition's strategic objectives. The framework provides reasonable, but not absolute, assurance for CEPI to reach its goals, through processes and activities embedded in the secretariat and the governing bodies of the coalition. CEPI's current risk management framework was developed in 2018; managing risks has been ingrained in CEPI's way of operating.

The continued growth of CEPI and the significant scale-up required in response to the COVID-19 outbreak has resulted in significant change in the risk landscape for CEPI. As CEPI grows and becomes a more complex operation, the approach to managing risks has evolved. CEPI has gradually improved and established new processes to stay abreast of changes, but the strategic shift to CEPI 2.0 requires that the approach to risk management needs to evolve and mature.

In December 2021, the CEPI Board endorsed the need to revise CEPI's risk management framework.

As the organisation is implementing strategic and organisational changes to deliver the 2.0 strategy, including a revised operating model, the risk framework review is in particular considering the following:

Change of scope: The new strategy proposes a significant growth in spending and range of activities. It proposes following more products through to licensure, taking on manufacturing in a more aligned and assertive fashion, some initial activity (with potentially future ambitions) in therapeutics; working on monoclonal antibodies and evidence generation platforms; a focus on prototypic vaccines for viral families, broadly protective vaccines, as well as the flagship ambition of supporting, corralling, and contributing towards the 100-day mission. This collection of activities moves CEPI from a relatively constrained agenda within R&D to something broader and more sophisticated. While offering tremendous opportunity, potential and excitement, this move establishes a different scope for the organisation which requires different thinking about risk.

New operating model: The organisation is dynamic and expanding rapidly. With a revised operating model and a larger organisation, the importance of an effective risk review framework increases and is a strategic as well as an organisational exercise.

Resource mobilisation: CEPI is looking to raise an ambitious USD 3.5B, which generates different considerations of how investors are engaged, how their expectations are managed, but also highlights the importance of ensuring the right safeguards, thresholds, and frameworks around CEPI's financial operating processes, such as audits, reporting and compliance.

Partnership and ecosystem: CEPI is operating in a highly dynamic ecosystem. In some parts of the world, countries are making national investments to develop their domestic R&D capacity. In other parts, regional groups are being set up which could be seen to challenge or overlap with the work of CEPI. At the same time, the competition for funds in the global health environment is notable, and there is considerable positioning going on as the world works through what sort of architecture is needed in the future, and where CEPI fits. Therefore, with a dynamic ecosystem and reliance on others, CEPI needs to evolve its risk strategy to address this new complexity.

Increased visibility: CEPI has evolved from a new organisation to a key part of the global health architecture in less than five years. Prominence is powerful, and the basis for CEPI's ability to influence the action of others. But greater attention also means that CEPI should expect greater scrutiny and higher expectations. This could be from investors, the public, and sectors such as civil society. It will be critical to have a robust risk framework that is able to anticipate the challenges, and can proactively prepare for and manage them.

Portfolio management: With more multiple lines of activity and investment, the importance of managing the portfolio holistically, judging how all the parts contribute to the overall objective, how funds are allocated, and how risks integrate and support this thinking is critical. CEPI's enhanced scope and objectives mean that the approach to risk management not only needs to be scaled up, but also needs to add a layer of reflective review across the different components of activity.

The risk framework review will consider the context in which CEPI will operate for the next strategic period and the new operating model. The review work will specifically consider:

- Risk governance and control;
- Ensuring an enterprise view on risk management;
- Developing a risk appetite framework;
- Ways of working, decision-making and risk reporting.

3.2. Compliance

In 2021, CEPI continued to evolve its compliance programme. This section addresses activities undertaken and developments throughout the year:

Awardee management: In 2021, an improved integrity due diligence (IDD) process was successfully implemented in awardee management. The IDD process was established as a fully in-house process and was formally included alongside other pre-investment assessment activities such as technical, regulatory, and financial due diligence. A compliance screening and monitoring tool was successfully implemented. The tool enables screening and monitoring of all relevant entities, key individuals, ownership structures and ultimate beneficial owners, and sends automated alerts if there are any relevant changes related to ownership, directors, adverse media, and sanctions.

Sanction compliance programme: To ensure compliance with sanction regimes, in particular the US, EU, UK, and the UN regimes, as well as complying with requirements of CEPI's funders, CEPI started developing a sanctions compliance programme in 2020. CEPI continued the work in 2021. The screening and monitoring tool (mentioned under awardee management) ensures that CEPI does not engage with any sanctioned entities or individuals. In 2021, a sanction risk assessment was conducted, and a process of updating the sanction policy, as well as developing a sanction compliance procedure, was initiated.

Business integrity training: In 2021, all employees and long-term consultants (engaged more than three months), received business integrity training. The training addressed topics such as code of conduct, modern slavery, corruption and bribery, gifts and hospitality, confidential information, whistleblowing, and sanction requirements.

Human rights programme: CEPI's human rights programme was further improved in 2021. The IDD process in awardee management has been key in identifying potential human rights infringements. A human rights impact assessment (HRIA) was initiated in Q4 2021 with support from BSR, a non-profit advisory organisation. The HRIA will be concluded at end of Q1 2022 and inform how CEPI continued to address human right aspects in its operations.

Policy management: CEPI's current policy framework is comprehensive and covers a broad range of organisational subjects. To further strengthen the policy framework, as well as ensuring that changes in both CEPI's external and internal environment are addressed, a policy review was conducted in 2021. The 2021 policy review process included a revised approach to conduct regular policy reviews as well as strengthen CEPI's ability to ensure it complies with all investor requirements.

3.3. Internal Audit

The Internal Audit Function reports to a subset of the Leadership Team for operational purposes and to the Board Audit and Risk Committee for its oversight role. Internal audit plays a role in assisting the Leadership Team and Audit and Risk Committee in the performance and discharge of their functions and duties. In 2021, the internal audit activities continued to focus on CEPI awardee activities by carrying out four awardee audits in total. The awardee audit activities identified relevant findings and areas of improvement to be resolved and implemented by awardee management. The recommended improvements are outlined in the form of an action plan and agreed with the awardee to facilitate continuous improvement of the awardee's management of granted funds. CEPI monitors the status of the awardee's progress on the agreed-upon action plan until the action items are considered effectively implemented or resolved.

APPENDICES

Appendix 1: Organisational Update

CEPI 2.0 Operating Model – Transitioning the organisation to deliver CEPI 2.0

Given the ambitions of the new strategy, CEPI management decided to focus on what the organisation needed in place to make sure it could deliver CEPI 2.0. This consideration was initiated in advance of embarking on the work of CEPI 2.0 to ensure the organisation could hit the ground running. There were three main contextual drivers for this work:

1. **Increased size and scale:** CEPI will have increased spending (tied to the USD 3.5 billionstrategy), increased organisational size and number of employees, as well as expanded size and diversity of investor base;

2. **Expanded scope and focus areas:** CEPI will expand its focus from core vaccine development into other domains (e.g. manufacturing), take on ambitions across a larger set of priority pathogens, and require a greater need for matrixed horizontal capabilities to achieve its strategic goals (e.g. 100-day target, continued emphasis on equitable access);

3. **Changed external context and expectations:** Coming out of the pandemic, CEPI has achieved an elevated position and higher expectations of its performance within the broader global health ecosystem. Achieving CEPI's objectives (particularly Connect) will require engaging with a broader range of partners with more ambitious goals.

In that context, in late 2021, a project was initiated to review and update CEPI's operating model – how the organisation works to deliver its strategy. This was supported by the Boston Consulting Group, which also supported CEPI's initial organisational governance design in 2017. This project was predicated on the view that a refined model to deliver against CEPI's strategy and address the changed context would require building on the successful foundations to date and retaining CEPI's culture at its core. It was initiated in lockstep with the continual evolution of the CEPI 2.0 strategy - i.e. accounting for decisions on CEPI's ambition-levels tied new areas of scope (e.g. Therapeutics, Manufacturing) and the development of more granular objectives underpinning the strategic pillars of Prepare, Transform and Connect.

The operating model project focusses on five key areas: structure, people, governance, ways of working, and systems and processes. A set of principles for the operating model design were identified in order to guide the overall approach to the work, as follows:

- Take a holistic view of the operating model, extending beyond structure alone;
- Be well informed through robust diagnosis that gets more detailed over time;
- Be thoughtful in sequencing, acknowledging interdependencies across operating model elements;
- Use this opportunity to resolve areas of difficulty/ uncertainty to design a model that lasts;
- Propose a manageable level of change, preventing "change for change's sake";
- Take a flexible decision-making process to balance speed and required input.

There are three phases to the work: diagnosis, design, implementation. There was significant engagement with the CEO and Leadership team to make adjustments to enable the organisation to be able to effectively deliver the 2.0 strategy. A few key requirements for success were identified, including:

- To ensure the right structure and capabilities and capacity of staff;
- An empowered strengthened focus on manufacturing, supply chains, innovations and capacity – with an enhanced team to work in partnership with R&D;
- An integrated approach to partnerships, with a strong focus on influencing partners, the ecosystem, and delivering Connect with equitable access at the core;
- To scale-up the organisation, growing and integrating CEPI's internal functions to provide CEPI with the stability and agility it requires to do its work;
- To ensure delivery of the strategy through an enhanced CEO's office with a focus on cross-cutting strategic issues and integration;
- To preserve the key factors in CEPI's success: culture, agility, mission focus;
- Ensuring the governance set up is evolved to be able to provide the appropriate strategic challenge, oversight, and guidance – with decisions made in the right place, at the right time, in the right way. This includes ongoing work relating to the delegations and internal governance groups;
- Ensuring CEPI's systems and processes are as effective and efficient as possible. Focus has been placed on updating on the processes relating to procurement, calls for proposals, and evolving CEPI's process architecture, with implementation in 2022.

Final work on design in some areas, and implementation in all areas, is ongoing through to the April 2022 Board where the project will be concluded. A summary of the changes CEPI has made to structure, governance, staffing, and systems and processes will be shared with investors.

Increase in size of the organisation and description of the work through HR

The CEPI workforce has continued to grow, from 96 full time permanent and fixed-term employees in January 2021 to 155 a year later. The increase has come as a consequence of CEPI's COVID-19 portfolio and the build-up of CEPI's project management capabilities and the decision to expand its support beyond Phase IIa for three pathogens and to strengthen its capabilities in manufacturing scale-up, and scale-out, in responding to COVID-19.

As a growing organisation, it has also increased the overall demand for support functions in CEPI. Among those is CEPI's IT function where a dedicated cyber security role is of particular importance and will be responsible for driving CEPI's IT security operations, strategy, and implementation to maintain the appropriated cyber resilience for CEPI.

In addition to supporting the current priority pathogen programmes and products through late stage development, CEPI was preparing itself to be ready for CEPI 2.0 and to be able to: (i) expand support to products beyond vaccines; (ii) increase CEPI's role and coordination in outbreak rapid response; and (iii) provide more enabling sciences support to accelerate development.

All teams are also supported by a strong cadre of international expert consultants that serve to broaden CEPI's global reach, diversity, and operational flexibility.

Establishing a new manufacturing group

To reach CEPI 2.0 goals, a new Manufacturing and Supply Chain division has been established. The group will support vaccine development projects, implement new innovative technologies and, establish sustainable development-manufacturing facility-and supply chain networks to rapidly deliver equitable vaccine access where and when needed.

The division is divided into four functions/ departments:

1. **Innovations** is responsible for identifying innovations required to achieve CEPI2.0 and M&SC division strategic goals, publishing and coordinating associated CfPs, and leading technology development projects towards implementation in collaboration with vaccine developers and manufacturing facilities.

2. **Manufacturing and Quality Control development** is responsible for CMC support to all vaccine development projects, implementing innovative technologies, acting as subject matter experts in CfP and due-diligence processes, establishing process related steering groups, ensuring quality and regulatory compliance of process and assay's, manufacturing clinical trial material, early scale-up, comparability strategy.

3. **Manufacturing and supply chain networks** is responsible for related country and stakeholder engagements to coordinate CEPI's vaccine manufacturing and supply chains together with external developers-manufacturers, critical consumable suppliers, global initiatives, managing the vaccine development/manufacturing facility network, run the COVAX/CEPI Marketplace, model supply chains particularly in LMICs, develop innovative manufacturing solutions/networks and, perform vaccine facility surveys, analysis and data leverage.

4. **Commercial Manufacturing** is responsible for technical due diligence, transfer and oversight of process from clinical to commercial supply phases, scale-up/out, support large scale manufacture in LMIC, establishing a process related steering group.

Appendix 2: Finance

Table 5: Total Contribution and Pledges by 31 December 2021 with expected received year (in USDM)

Investors USDM	2017-2020	2021	2022-2026	Total contributions & pledges[1]	% of Total contributions & pledges
Government of Australia	7.42	1.35	1.26	10.03	0.39%
Government of Austria	1.16	1.20	-	2.36	0.09%
Government of Belgium	6.04	-	-	6.04	0.23%
Government of Canada	40.94	45.91	1.95	88.80	3.45%
Government of Denmark	1.45	-	-	1.45	0.06%
Government of Ethiopia	0.10	0.07	0.10	0.27	0.01%
Government of Finland	4.34	1.16	1.14	6.63	0.26%
Government of Germany	342.65	165.09	-	507.73	19.71%
2 Government of Greece	-	1.78	-	1.78	0.07%
Government of Hungary	0.84	-	-	0.84	0.03%
Government of Iceland	-	1.92	-	1.92	0.07%
Government of Indonesia	1.00	-	-	1.00	0.04%
Government of Italy	5.96	11.71	-	17.67	0.69%
Government of Japan	196.27	25.00	-	221.27	8.59%
Government of Kuwait	10.00	-	-	10.00	0.39%
Government of Lithuania	0.11	-	-	0.11	0.00%
Government of Luxembourg	0.94	-	-	0.94	0.04%
3 Government of Malaysia	-	1.00	2.00	3.00	0.12%
Government of Mexico	0.60	0.30	-	0.90	0.03%
Government of Netherlands	58.64	-	-	58.64	2.28%
Government of New Zealand	-	10.82	-	10.82	0.42%
Government of Norway	358.00	111.37	-	469.37	18.22%
Government of Panama			0.02	0.02	0.00%
Government of Portugal	-	0.34	-	0.34	0.01%
Government of Philippines	-	0.01	-	0.01	0.00%
Government of Romania	0.24	-	-	0.24	0.01%
Government of Serbia	1.23	-	-	1.23	0.05%
Government of Singapore	0.81	0.60	0.60	2.01	0.08%
Government of Spain	-	-	85.25	85.25	3.31%
Government of Switzerland	10.28	-	-	10.28	0.40%
Government of the Republic of Korea	3.00	-	6.00	9.00	0.35%
Government of the United Kingdom	333.91	21.90	-	355.81	13.81%
Government of the United States of America	-	8.00	12.00	20.00	0.78%
Kingdom of Saudi Arabia	140.00	10.00	-	150.00	5.82%
European Commission	124.40	-	114.12	238.51	9.26%
Total Public investors	**1,650.33**	**419.54**	**224.43**	**2,294.30**	**89.04%**

Investors USDM	2017-2020	2021	2022-2026	Total contributions & pledges[1]	% of Total contributions & pledges
Avast	8.00	-	-	8.00	0.31%
Bill and Melinda Gates Foundation	101.98	19.42	-	121.40	4.71%
Fidelity Charitable gift funds	1.49	-	-	1.49	0.06%
Goldman Sachs Gives	1.63	-	-	1.63	0.06%
Nestle	1.04	-	-	1.04	0.04%
Sumitomo Mitsui Banking Cooperation	1.14	-	-	1.14	0.04%
The Paul G. Allen Familiy foundation	3.50	-	-	3.50	0.14%
UN Foundation	10.00	-	-	10.00	0.39%
Wellcome Trust	84.99	3.42	42.50	130.91	5.08%
4 Other Private Investors and Philanthropies	1.89	1.34	0.00	3.23	0.13%
Total Private investors & Philantropies	**215.66**	**24.19**	**42.50**	**282.35**	**10.96%**
Total Contributions & Pledges	**1,865.99**	**443.73**	**266.93**	**2,576.65**	**100.00%**

1) Includes pledges made through 31.12.2021. Contributions received are expressed in USD equivalents using the exchange rates on the dates funds are received. Contributions Funds pledged but not yet received are expressed in USD equivalents using CEPI Budget 2022 exchange rates.

2) Includes EUR 5M contribution in 2021 received via the International Finance Facility for Immunisations (IFFIm).

3) Includes contributions of NOK 600M frontloaded in 2019 through IFFIm, and NOK 2B frontloaded through IFFIm for COVID-19 in 2020

4) Private Investors with contributions of less than $1M are grouped under “Other Private Investors and Philanthropies”.

Table 6: R&D Investment Disbursements 2021

Investment area USDM	2021 Actual	2021 Budget	2021 Variance
Priority pathogens	52.7	149.1	-96.4
Disease X/Platforms	3.3	16.6	-13.3
Core Enabling Science programmes	8.7	30.1	-21.4
COVID-19*	563.0	475.4	87.6
Total R&D projects/investments	**627.8**	**671.2**	-43.5

Disease USDM	2021 Actual	2021 Budget	2021 Variance
MERS	5.7	25.4	-19.8
Lassa	20.8	63.0	-42.1
Nipah	11.1	22.6	-11.5
Rift Valley Fever	4.5	15.6	-11.1
Chikungunya	8.5	27.2	-18.6
Ebola	9.9	15.3	-5.4
COVID-19*	563.0	475.4	87.6
Disease X/Platforms	3.3	17.3	-14.0
Cross-cutting	0.8	9.5	-8.6
Total R&D projects/investments	**627.7**	**671.2**	-43.5

* Due to a high level of uncertainty, Budget 2021 included only figures for signed contracts. COVID-19 figures incl. Enabling Science activities.

Table 7: R&D Investment Disbursements Lifetime-To-Date

Disease USDM	2017-2021 Actual
MERS	28.6
Lassa	90.7
Nipah	41.9
Rift Valley Fever	15.9
Chikungunya	42.9
Ebola	27.9
COVID-19*	1099.3
Disease X/Platforms	23.0
Cross-cutting	6.1
Total R&D projects/investments	**1376.4**

Table 8: Operating Costs 2021

Operating costs USDK	Actual 2021	Budget 2021	Variance 2021
Employment cost	**20,120**	**21,104**	**984**
Senior Management incl. CEO and Board remuneration	3,490	3,844	354
Policy, Strategy and Governance	1,600	1,786	186
Advocacy & Communication	545	561	16
Finance and Operations	1,483	1,612	129
Legal, Financial Awards & Business Development	1,784	1,661	-122
Portfolio Management	779	636	-143
Human Resources	813	799	-14
R&D	8,979	9,301	322
Investor Relations & Resource Mobilization	647	903	256
Consultants / Consultancy / Secondees	**17,959**	**11,753**	**-6,206**
Policy, Strategy and Governance	2,277	1,507	-770
Advocacy & Communication	273	259	-14
Finance and Operations	609	16	-593
Legal, Financial Awards & Business Development	3,738	2,654	-1,084
Portfolio Management	506	246	-260
Human Resources	42	50	8
R&D	9,628	6,602	-3,026
Investor Relations & Resource Mobilization	886	420	-466
Travel	**295**	**1,879**	**1,584**
Department travel expenses	295	1,666	1,371
Board, Committees, Conferences		213	-82
Infrastructure	**4,789**	**5,329**	**539**
IT consultancy	2,510	928	-1,582
Office costs & Insurance	557	1,404	847
Software & Licenses	549	493	-56
IT Operating costs & maintenance fees	552	1,557	1,005
IT development	125	173	48
Hardware	343	602	258
Cellphone	153	172	19
Service providers/Other	**2,063**	**2,152**	**89**
Accounting fees	339	338	-1
Board, Committees, Conferences, Meetings	-	347	347
Audit fees (External & internal)	601	658	58
Staff social	-	11	11
Miscellaneous	156	315	159
Media & Communication	291	183	-108
Recruitment expenses	677	300	-377
Discretionary fund		**2,000**	**2,000**
Total	**45,227**	**44,218**	**-1,009**

Management of Financial Risk

CEPI currently receives its donations predominately in USD, NOK, GBP and EUR, and investments are made in USD. CEPI has entered into a Trustee agreement with the World Bank through which the majority of committed funds to CEPI are channelled. Available funds are invested in the World Bank or with selected commercial banks, with the main investment goal being capital protection. To cover operational costs, CEPI is keeping cash in the donated currency for natural hedging purposes.

CEPI has an established hedging facility with its current commercial bank, hence is in a position to enter into forward contracts as means of minimising currency risk caused by a mismatch between funding received and grant currencies.

In 2021, CEPI had a return on World Bank investments of USD 1.9M. The net impact of foreign exchange revaluation was a loss of USD 0.8M

Annual Accounts and Board of Directors Report

CEPI's Annual Accounts and Board of Directors Report can be found on CEPI's website.
In the Annual Accounts, revenue and costs are recognised in accordance with the Norwegian Accounting Act and Generally Accepted Accounting Principles for Non-profit Organisations. As CEPI usually prepares its internal and external reporting based on a cash flow principle for revenue and investments, the Annual Accounts profit and loss deviate from CEPI's other financial reports, including the Annual Progress Report.

Appendix 3: Human Resources

The CEPI workforce has continued to grow to meet an expanded scope and increased expectations from its partners. At the end of 2021, the current workforce composition was as follows:

- The organisation had 155 permanent and fixed-term employees
- The gender balance among staff: 61% female and 39% male
- The gender balance in the CEPI Leadership Team: 50% female and 50% male

The 155 employees originate from 45 different countries, of which 25% are from LMICs.

CEPI aims to attract and recruit high-performing staff committed to supporting CEPI's mission. CEPI's global Human Resources (HR) policy and recruitment procedures focus attention on attracting and retaining a diverse workforce and highlight its commitment to promoting diversity, equity, and fostering inclusion.

All staff at CEPI must be given the same opportunities with regard to salary, promotion, and professional and personal development.

When recruiting, CEPI carefully details skills, experience, qualifications, and attributes essential for the role to ensure job profiles and advertisements do not discriminate against candidates, either directly or indirectly. Deliberate and continuous efforts have been made and have contributed to developing CEPI's staff into an international group of employees.

CEPI's HR team aims to support the growth and overall development of the Organisation. In 2021, efforts were focussed on recruitment, culture and values, diversity and inclusion, internal communications, Organisational and people development. Among others, the team has provided both courses and lunch talks for leaders and employees, with the purpose of strengthening the culture and ways of working at CEPI. In addition, CEPI has closely monitored the impact of the COVID-19 pandemic on the workforce with a particular focus on health and well-being, and has established internal well-being opportunities for employees. A flexible working concept is in place.

Appendix 4: CEPI Board Summary

CEPI's Board met five times in 2021, and there were over 20 CEPI Board Committee meetings.

Administrative items

In the March Board meeting

- Jane Halton was renewed as a Board Member and as Board Chair for 5 years until 2026
- David Reddy and John Nkengasong were renewed as Board members for 5 years until 2026
- Patricia Garcia resigned as an independent Board member
- Veronika Von Messling was appointed as an Investor Board member, for a 3-year term until 2023

In the September meeting:

- Nisia Trinidade Lima was appointed to join the CEPI Board as an independent member, for an initial term of two years
- Juan Pablo Uribe was appointed by the World Bank as its new representative for its non-voting member seat
- At the end of the year, the Board and Committees conducted a light touch Board effectiveness review. Findings are to be shared by the Board Effectiveness Lead with the Chair in Q1 2022.

CEPI Board Members as of December 2021 Organisation/Affiliation Independent Members	Name	Position
	Jane Halton	(Board Chair)
Africa, Centres for Disease Control and Prevention	John Nkengasong	Director
The Wellcome Trust Research Laboratory	Cherry Kang	(Board Vice-Chair) Professor
London School of Hygiene and Tropical Medicine	Peter Piot	Director
Oswaldo Cruz Foundation (Fiocruz)	Nisia Trindade Lima	President
Medicines for Malaria Venture	David Reddy	Chief Executive Officer
Nigeria, International Fund for Agricultural Development	Nadine Gbossa	Regional Director
Vaccine Business Unit, Takeda	Rajeev Venkayya	President
Investor Representatives		
Wellcome Trust	Jeremy Farrar	Director
German Federal Ministry of Education and Research	Veronika von Messling	Director-General
Japan National Institute of Infectious Diseases	Ichiro Kurane	Former Director-General
UK Foreign Commonwealth and Development Office	Charlotte Watts	Chief Scientific Advisor
Non-voting Members		
Coalition for Epidemic Preparedness Innovations	Richard Hatchett	Chief Executive Officer
Wits Reproductive Health and HIV Institute	Helen Rees	(Chair SAC) Executive Director
American Association for the Advancement of Science	Peggy Hamburg	(Chair JCG) Chair of the Board
World Health Organization	Soumya Swaminathan	(WHO representative) Chief Scientist
Health, Nutrition and Population	Juan Pablo Uribe	(World Bank representative) Global Director

Appendix 5: Members of the Scientific Advisory Committee

In 2021, the Scientific Advisory Committee (SAC), a key independent body within the CEPI governance structure, continued its role in supporting CEPI's COVID-19 response, while advising on strategy for CEPI 2.0, incorporating lessons learned during the pandemic.

Although continued travel restrictions precluded physical gatherings, SAC met virtually four times and provided significant support and guidance to CEPI related to both the COVID-19 portfolio and the core portfolio. During the regularly scheduled meetings of the year, SAC provided essential feedback on key elements of the CEPI 2.0 strategy, including the Disease X and mRNA initiatives. The last meeting of the year was an ad-hoc meeting called quickly after the emergence of the omicron variant, to update on CEPI's activities and seek SAC guidance.

Activities undertaken by SAC are outlined below.

Activity	Comment (Aim)	2021 Update
Virtual Meetings	The SAC meetings are critical vehicles for garnering scientific guidance from the group of experts.	SAC met four times and provided essential advice on CEPI's COVID-19 portfolio, non-COVID-19 portfolio, enabling science projects, and CEPI 2.0.
Support review of calls for proposals	SAC members are invited to peer review applications received in response to calls for proposals on a volunteer basis.	Some SAC members were called upon to conduct expert peer reviews of proposals that were received for the 8 Calls for Proposals launched during 2021.
Stage Gate Review Committee (SGRC) work	SAC members are part of CEPI Stage Gate Review Committee, evaluating the progress of the CEPI vaccine portfolio and advising on next steps for the candidates	Eight SGRC meetings were conducted during 2021, where SAC members gave important input and recommendation for further development of the vaccine candidates in the CEPI portfolio.
SWAT teams	SWAT teams were established to tackle challenges arising in the precompetitive space related to COVID-19 vaccine development and manufacturing.	The Manufacturing SWAT benefited from participation of a SAC member during their regular meetings.
Other ad hoc consultations	SAC members with expertise in a particular area may be consulted outside of the regularly scheduled meetings as the needs arise	Several SAC members were consulted individually to give input on various programs, including epidemiologic modelling as well as Disease X.

The first SAC's term expired in March 2021. A call for new members was released at the beginning of the year, and existing members were invited to reapply for a second term. The new SAC was selected with the aim of achieving a broad spectrum of competencies relevant for CEPI 2.0, as well as good global representation and gender balance. The new SAC, composed of 10 renewed members and 25 first-time members, met for the first time in July 2021.

Members of CEPI Scientific Advisory Committee (SAC) as of May 2021	
Organization / Affiliation	Name
Wits Reproductive Health and HIV Institute	Helen Reese (SAC Chair)
University of Texas Medical Branch	Alan D. Barrett
Institute of Human Virology	Alash'le Abimiku
Imperial College London	Azra Ghani
Institute of Virology, Charité	Christian Drosten
Consultant	Dominique Maugeais
Malaghan Institute of Medical Research	Francis Priddy
Modex Therapeutics	Gary Nabel
Chinese Center for Disease Control and Prevention	George Gao
US Centers for Disease Control and Prevention	Inger Damon
Wellcome Trust	Josie Golding
University of Tokyo	Ken J. Ishii
Sanofi Pasteur	Kent Kester
Universidad Nacional Autónoma de México	Laura Palomares
Duke – NUS Medical School	Linfa Wang
Council on Foreign Relations	Luciano Borio
Consultant	Mahmudar Rahman
Harvard T. H. Chan School of Public Health	Marc Lipsitch
Santa Casa de Sao Paolo School of Medical Sciences	Marco Safadi
Consultant (SAC Vice Chair)	Michael King
MEVOX & VaxEquity Ltd	Michael Watson
MDM Consultant, LLC	Michel De Wilde
US National Institutes of Health	Paula Bryant
Bill & Melinda Gates Foundation	Peter Dull
Paradiso Biologics Consulting LLC	Peter Paradiso
London School of Hygiene & Tropical Medicine	Peter Smith
US Food and Drug Administration	Phil Krause
Epicentre	Rebecca Grais
GSK Vaccines	Rino Rappuoli
Nigerian Presidential Task Force on COVID-19, Federal Government of Nigeria	Sani Aliyu
University of Pennsylvania	Stanley Plotkin
SUNY Upstate Medical University	Stephen Thomas
Bharat Biotech	V. Krishna Mohan
World Health Organization	Vaseeharan Sathiyamoorthy
Indian Institute of Science Education and Research	Vineeta Bal

Appendix 6: Members of the Joint Coordination Group

Members of CEPI Joint Coordination Group (JCG) as of December 2021	
Organization / Affiliation	Name
American Association for the Advancement of Science	Peggy Hamburg (JCG Chair)
AVAREF	Diadie Miaga
European Medicines Agency	Marco Cavaleri
US Food and Drug Administration	Gruber Marion
US Food and Drug Administration	Peter Marks (joined September 2021)
GAVI the Vaccine Alliance	Aurelia Nguyen
International AIDS Vaccine Initiative (IAVI)	Mark Feinberg (Advisor)
International Federation of Red Cross and Red Crescent Societies	Emanuele Capobianco
International Federation of Red Cross and Red Crescent Societies	Petra Khoury (joined October 2021)
Médecins Sans Frontières	Sidney Wong
National Institute for Biological Standards and Control	Mark Page
United Nations Children's Fund	Robin Nandy
United Nations Children's Fund	Ephrem Lemango
Wellcome Trust	Charlie Weller
World Health Organization	Ana Maria Restrepo
World Health Organization	Vasee Moorthy
Working Group (Regulatory)	Rogerio Gaspar
Working Group (Regulatory)	Daniel Brasseur
Working Group (Regulatory)	Murray Lumpkin

Reporting Period and Contact Information

Reporting period:	1 January 2021 – 31 December 2021
Relevant Strategic period	CEPI 1.0 – from 2017 to 2021
Date report submitted:	31 March 2022
Contact name:	Samia Saad, Executive Director Resource Mobilisation and Investor Relations
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