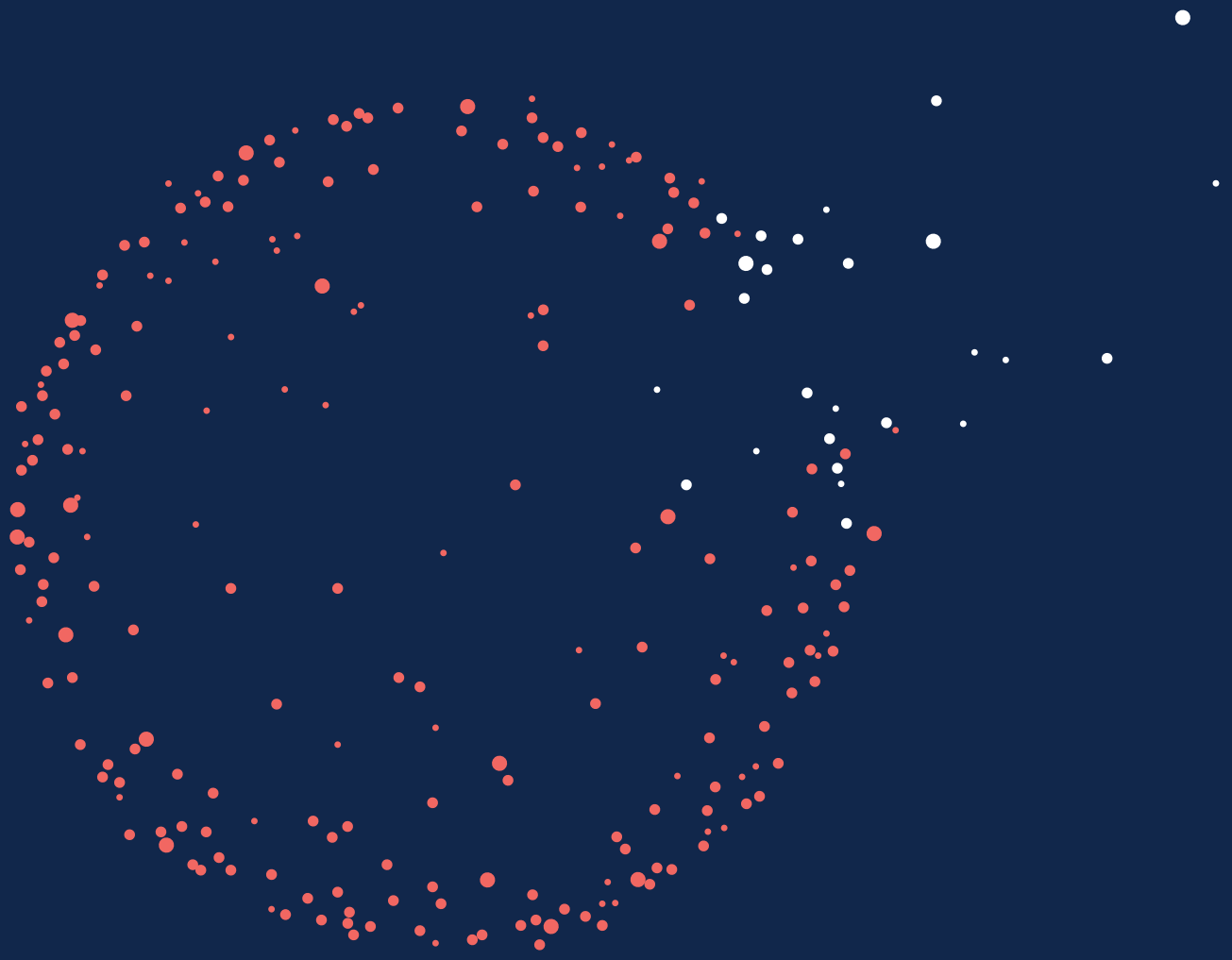
CEPI

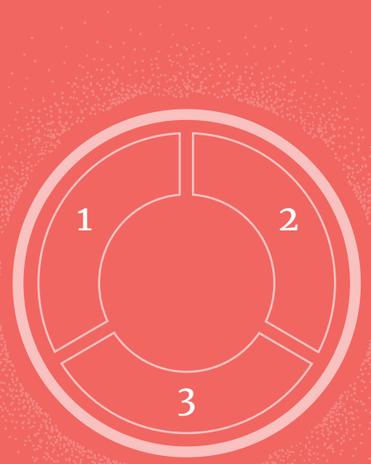
Business Plan 2019 - 2022



CEPI'S VISION

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

CEPI's mission - **to accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks -** is supported by three strategic objectives:



Preparedness

Advance access to safe and effective vaccines against emerging infectious diseases

Response

Accelerate the research, development and use of vaccines during outbreaks

Sustainability

Create durable and equitable solutions for outbreak response capacity

CONTENTS

INTRODUCTION

The Coalition for Epidemic Preparedness Innovations (CEPI) is an innovative global partnership where we envision a world where epidemics are no longer a threat to humanity. The global need for CEPI emerged after the devastating West Africa Ebola crisis in 2014–16 that caused over 11,000 deaths. The collective response to Ebola had fallen short, and it was evident that we needed a better system to produce vaccines—one of our most powerful public health tools—against known epidemic threats.

In response, following extensive public deliberation and consultation, CEPI was launched at Davos in January 2017 to speed up the development of vaccines against the most pressing known pathogens with epidemic potential and advance innovative technological platforms to develop vaccines rapidly in response to newly emerging infectious disease threats.

Founded by the governments of Norway and India, the Bill & Melinda Gates Foundation, Wellcome, and the World Economic Forum, CEPI is now a broad coalition of governments, international organisations , philanthropies, civil society partners, and the private sector.

While many organisations operate within the end-to-end space of vaccine funding and R&D implementation, CEPI was designed to fill a number of gaps. First, CEPI will advance vaccines against known threats through proof-of-concept and safety testing in humans and will establish investigational vaccine stockpiles before epidemics begin – 'just in case'. Second, CEPI will support innovative platform technologies with the potential to accelerate the development and manufacture of vaccines against previously unknown pathogens, commonly referred to as Disease X– 'just in time'.

Third, CEPI will support and coordinate activities to improve our collective response to epidemics, strengthen capacity in countries at risk, and advance regulatory science that governs product development.

Currently[1] focussed on the pathogens which cause Lassa fever, Middle East Respiratory Syndrome (MERS), Nipah, Chikungunya and Rift Valley fever, CEPI has already committed to investing up to $413 million to support the development of 18 vaccine candidates (Figure 1). The WHO R&D Blueprint for Action to Prevent Epidemics was the point of departure for CEPI when selecting priority diseases. Through our second Call for Proposals, we are also funding innovative platform technologies to speed the development and manufacture of vaccines against newly emerging pathogens – commonly referred to as Disease X.

In the discussions that led to the creation of CEPI, hundreds of experts from around the world advised on the key issues that CEPI should address. Their recommendations culminated in our Preliminary Business Plan, which served as the roadmap for CEPI's start-up phase. Now in our growth phase, a number of strategic documents have been developed, including a Programme Document and Annual Plans to reflect a renewed approach. Together with this Business Plan, these documents incorporate decisions made by CEPI's Interim and now Permanent Board and reflect lessons learned from the first two years of operations.

Three strategic objectives—preparedness, response, and sustainability—drive our efforts to accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks. This document provides details about these strategic objectives and outlines CEPI's approach to implementation.

Richard Hatchett, CEO

1 Correct at time of publication.

CEPI's mission is to accelerate the development of vaccines against emerging infectious diseases and enable access to these vaccines for people during outbreaks

Figure 1: CEPI's progress since inception leading up to the revision of the Business Plan

Jan 2017
CEPI is officially launched at the World Economic Forum's annual meeting in Davos. Oslo HQ established

Jan 2017
Launch of CEPI's first Call for Proposals to develop vaccine candidates against MERS-CoV, Nipah and Lassa viruses

Apr 2017
Richard Hatchett starts his position as CEO of CEPI

Nov 2017
CEPI established office in Washington D.C., USA

Oct 2017
CEPI established office in London, UK

Sep 2017
Launch of CEPI's second Call for Proposals for platform technologies to enable rapid vaccine development against unknown pathogens

Feb 2018
CEPI announces new permanent board

Feb 2018
CEPI held a first-of-its-kind workshop looking at the challenges, opportunities and possiblilities of developing vaccines against Chikungunya in Delhi, India

Mar 2018
CEPI announces its first partnership with Themis Bioscience worth up to US$ 37,5 million to advance vaccine candidates against Lassa fever and MERS-CoV

May 2018
CEPI announces partnership with Profectus Biosciences and Emergent Biosolutions worth up to US$ 25 million to advance the development and manufacture of a vaccine against Nipah virus

May 2018
CEPI announces partnership with IAVI worth up to US$ 54,9 million to advance Lassa fever vaccine development

Apr 2018
CEPI announces partnership with Inovio worth up to US$ 56 million to advance vaccine development and manufacturing against Lassa fever and MERS-CoV

Aug 2018
CEPI announces partnership with Profectus Biosciences and Emergent Biosolutions worth up to US$ 36 million to advance the development and manufacture of a vaccine against Lassa virus

Aug 2018
CEPI announces partnership with IDT worth up to US$ 36 million to advance MERS-CoV vaccine development

Sep 2018
CEPI announces partnership with Oxford University and Janssen Vaccines worth up to US$ 19 million to develop MERS, Lassa and Nipah vaccines

Jan 2019
CEPI announces partnership with the University of Queensland worth up to US$ 10,6 million to develop a "molecular clamp" platform technology

Jan 2019
CEPI launches its third Call for Proposals to develop vaccines against Rift Valley fever and Chikungunya virus

Dec 2018
CEPI announces partnership with Imperial College London worth up to US$ 8,4 million to develop a transformative rapid-response technology to create vaccines against unknown pathogens

Feb 2019
CEPI awards contract worth up to US$ 31 million to The University of Tokyo to develop vaccine against Nipah virus

Feb 2019
CEPI awards US$ 34 million contract to CureVac to advance The RNA Printer™ - a mRNA vaccine platform that can rapidly combat multiple diseases

June 2019
CEPI awards up to US$ 21 million to Themis Bioscience for Phase 3 Chikungunya vaccine development

July 2019
CEPI awards up to US$ 23,4 million to Valneva for late-stage development of a single-dose Chikungunya vaccine

July 2019
CEPI awards funding agreement worth up to US$ 9,5 million to Colorado State University to develop a human vaccine against Rift Valley fever

July 2019
CEPI awards contract worth up to US$ 12,5 million to consortium lef by Wageningen Bioveterinary Research to develop a human vaccine against Rift Valley fever

Business Plan published

THE CHALLENGE

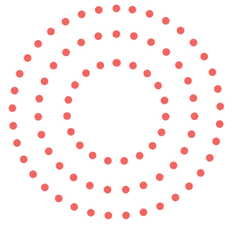
Scope and initial priorities

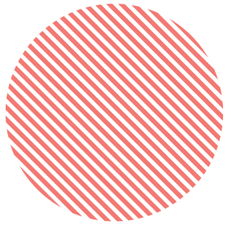
The tragic West Africa Ebola outbreak in 2014-16—the largest and longest outbreak of Ebola in history to date—galvanised global leaders behind a goal of developing systems and tools to fight future outbreaks of Ebola and other severe infectious pathogens.

In addition to the devasting human costs, the socioeconomic burden caused by this outbreak was in excess of $53 billion.[2] It created severe shocks to investment, production, and consumption throughout the region, coupled with commodity price shocks in affected countries.[3] Healthcare systems in affected countries were also weakened, resulting in a significant decline in most indicators of maternal and child health as well as many other health system outputs.[4]

To better prepare for future outbreaks, the World Health Assembly endorsed the World Health Organization (WHO) R&D Blueprint for Action to Prevent Epidemics[5], a global strategy and preparedness plan to reduce the time between the declaration of a public health emergency of international concern and the availability of effective diagnostics, therapeutics, and vaccines that can be used to respond to such a crisis.

For the diseases highlighted in the WHO R&D Blueprint, development of vaccines is an especially important and complex endeavour (Box 1). Market forces have proved insufficient to bring such products forward and other incentives for advancing the development of medical countermeasures against emerging infectious diseases (EIDs) were poorly coordinated or lacking altogether.





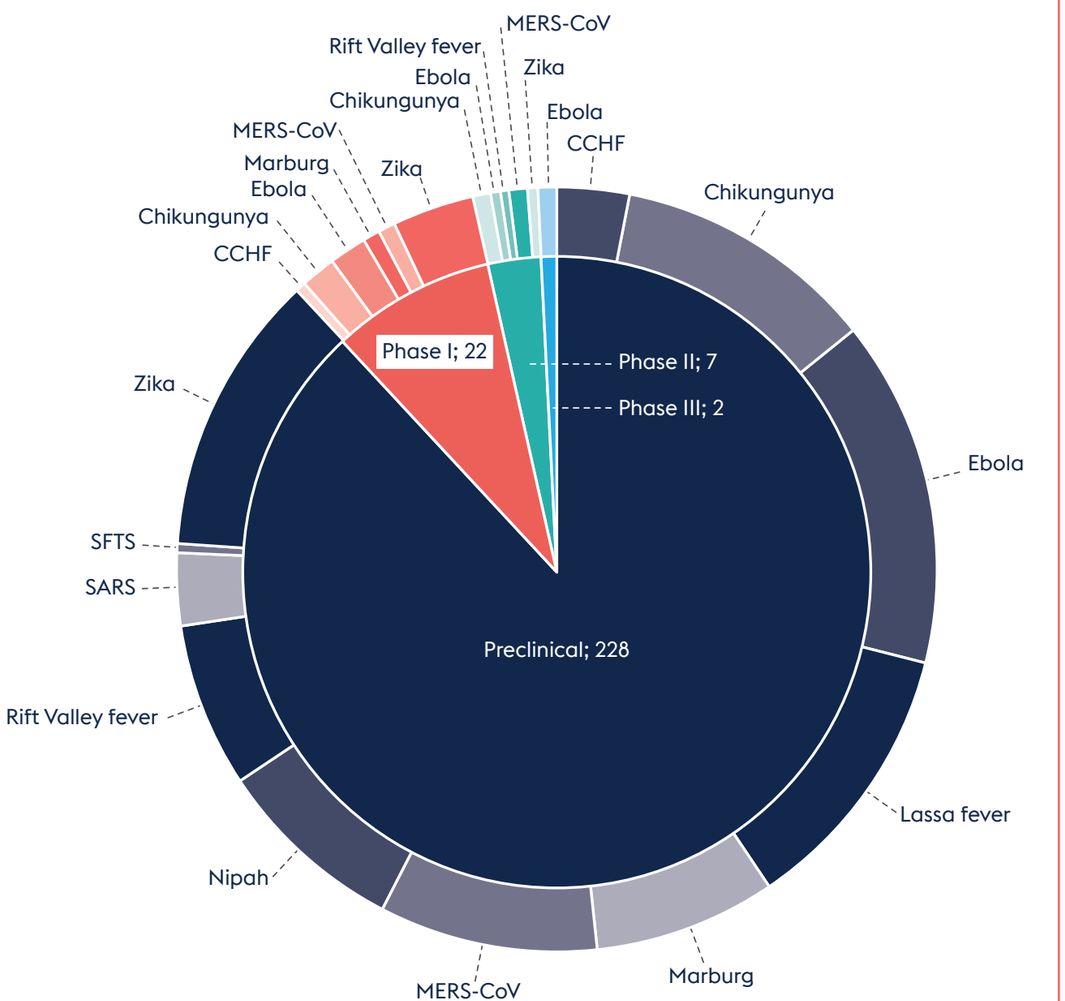
2 https://academic.oup.com/jid/article-abstract/218/suppl_5/S698/5129071
3 http://www.worldbank.org/en/topic/macroeconomics/publication/2014-2015-west-africa-ebola-crisis-impact-update
4 https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(17)30078-5/fulltext
5 www.who.int/blueprint

Box 1: Market deficiencies in vaccine development

Vaccine development for emerging infectious diseases (EIDs) is challenging for many reasons, including the difficulty of demonstrating vaccine effectiveness, the unpredictability of epidemics, the substantial complexity of conducting clinical trials in the midst of an outbreak, and the substantial costs associated with development efforts.[6] For a variety of reasons, EIDs have predominantly affected low- and middle-income countries and are much more likely to evolve into large epidemics in such settings. These countries have limited means to finance or drive vaccine development on their own. As a consequence of these factors, the development of commercial vaccines against epidemic threat pathogens happens infrequently, if at all.

Of the 259 treatments[7] that are being developed for use against WHO R&D Blueprint pathogens, most are in early phases of development and are not ready for use during outbreaks. This paucity of available treatments underscores how unprepared the world is for future outbreaks of EIDs.

The figure below shows the stage of development for vaccine candidates against 11 epidemic infectious diseases, from preclinical through to Phase III[7]



6 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518734/

7 Gouglas et al (2018) Lancet Global Health and Secretariat analysis

The WHO R&D Blueprint was the point of departure for CEPI when selecting priority diseases (Box 2). Criteria including the risk of an outbreak occurring, burden of disease, and feasibility of vaccine development were also applied. In addition to the known pathogens - where a threat has been identified - there are numerous other pathogens that also have the potential to cause epidemics and extensive human suffering and distress: the so-called "Disease X". By supporting the advancement of platform technologies that can rapidly be adapted to such threats, we seek to further strengthen the world's ability to respond to the broadest set of challenges in the realm of EIDs (Boxes 3 and 4).

CEPI has a focussed funding scope to invest in vaccine candidates and innovative platform technologies against emerging epidemic diseases, and use "enabling science" to support their advancement (Box 2).

Box 2: Prioritised areas for funding

- Development of vaccine candidates against Lassa, Nipah, and MERS-CoV for stockpiling prior to large-scale efficacy testing (through Phase II).
- Development of vaccine platform technologies tested against several pathogens (through Phase I).
- Development of vaccine candidates for Chikununya and Rift Valley fever.
- Enabling science and technologies that support the advancement of such vaccines.
- Finishing the job of developing vaccines against Ebola.

By the end of 2022, we aim to have completed Phase II clinical trials and established investigational stockpiles for four candidates against at least two of our priority pathogens. These investigational vaccines will then be ready for large-scale efficacy testing in the event of future outbreaks. To achieve this ambitious target, CEPI will need to secure $1 billion to accomplish the strategic objectives we have set for our first 5 years of operation[9]. Our success will not only improve our collective ability to prepare for and respond to epidemics but will prevent the devastation they can cause and reap societal, public health, and economic benefits for everyone.

9 CEPI Preliminary Business Plan 2017-2021

Box 3: CEPI priority diseases

Lassa

Lassa virus belongs to the *Arenaviridae* family and causes Lassa fever, also known as Lassa haemorrhagic fever (LHF). It is a haemorrhagic illness that occurs between one and three weeks after infection. The natural host of Lassa virus is the rodent *Mastomys natalensis*, otherwise known as the Natal multimammate mouse or rat.

Lassa virus can pass from person to person via bodily fluids, and can spread in healthcare settings if suitable precautions are not taken.

Nipah

Nipah virus belongs to the *Paramyxoviridae* family of viruses, genus Henipavirus, alongside Hendra virus.

The natural hosts of the virus are fruit bats (also known as flying foxes) of the genus *Pteropus*. Nipah virus can be spread to people from infected bats, infected pigs, or infected people.

MERS

MERS-CoV is the virus that causes Middle East Respiratory Syndrome (MERS). It is a coronavirus, part of the same family of viruses that causes the common cold and SARS (Severe Acute Respiratory Syndrome). It is thought that camels are a major source of infection in people. Raising camels, eating undercooked camel meat, and drinking raw camel milk or urine are risk factors for the disease in humans. MERS-CoV can spread from person to person, usually through close contact.

Chikungunya

WHO has highlighted Chikungunya as a major public health risk and has stated that further research and development is needed to mitigate the risk it poses.

It causes fever, severe joint pain, muscle pain, headache, nausea, fatigue and rash. Joint pain is often debilitating and can vary in duration.

The disease shares some clinical signs with Dengue and Zika viruses and can be misdiagnosed in areas where they commonly occur.

Rift Valley fever

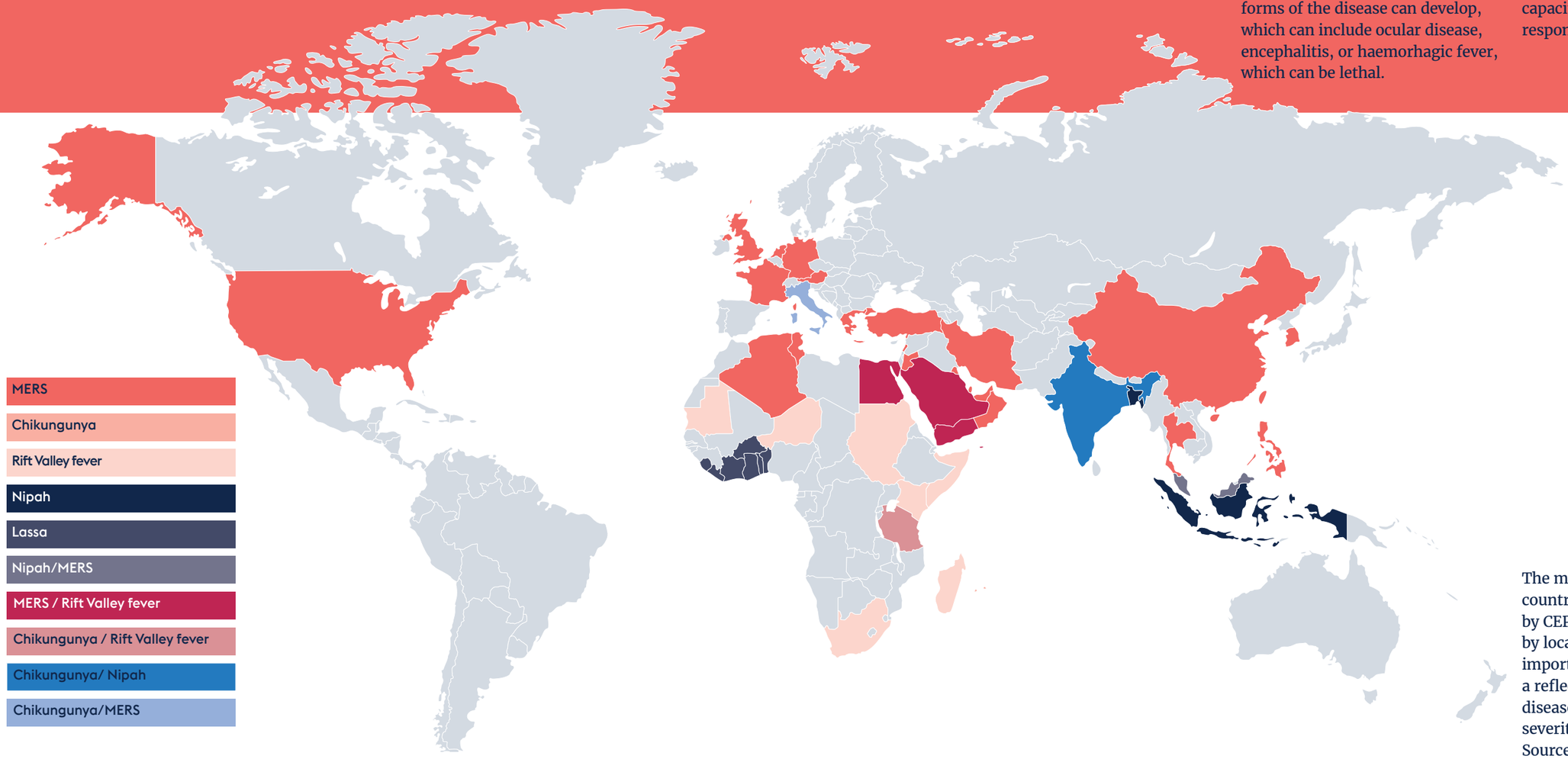
Rift Valley fever has been listed in the WHO R&D Blueprint of priority pathogens in view of its epidemic potential. Most human infections result from contact with the blood or organs of infected animals but can also result from the bites of infected mosquitoes. The virus was first identified in 1931 during an investigation into an epidemic among sheep on a farm in the Rift Valley of Kenya. Multiple outbreaks have been reported across the African continent and in Saudi Arabia and Yemen.

Most human cases are mild but in a small proportion of patients severe forms of the disease can develop, which can include ocular disease, encephalitis, or haemorhagic fever, which can be lethal.

Disease X

Disease X represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease. In February 2018, Disease X was included in the updated WHO R&D Blueprint list of priority diseases.

What we do know is that new diseases emerge all the time, from locations all around the world. Developing countries, particularly those with high rates of biodiversity, are at heightened risk because of the increased risk of outbreaks and the limited capacity for surveillance and response in these countries.



The map to the left shows all the countries that have been affected by CEPI's priority diseases, either by local disease transmission or importation of cases. It serves as a reflection of global spread of the diseases rather than their relative severity across countries.
Source: WHO

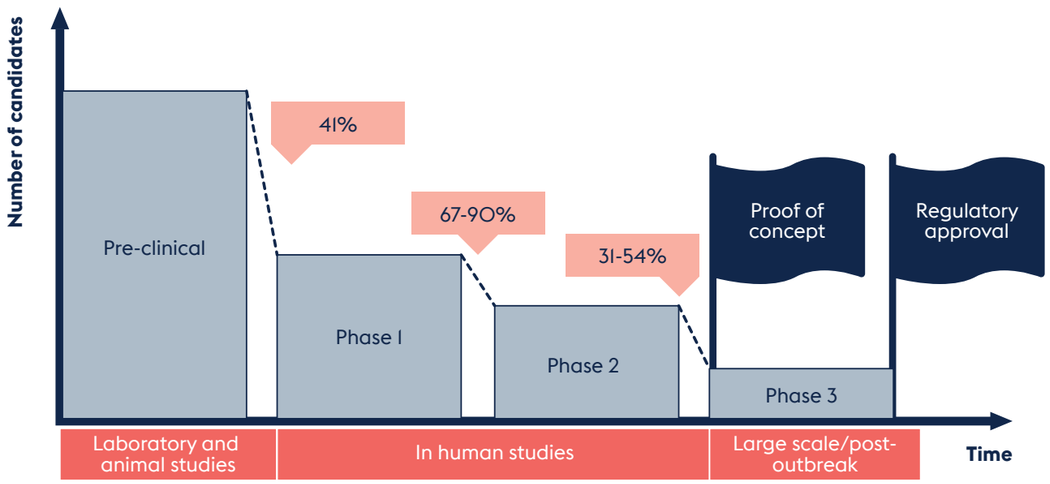
Box 4: Vaccine development explained

The R&D process for developing vaccines consists of preclinical and clinical phases.

Preclinical research and development is carried out in laboratories and based on both in vitro (e.g. microorganisms, cells and biological molecules) and, when necessary, in vivo (e.g. mice and non-human primates) studies. The data from the preclinical studies provide details of the development and production of a vaccine which need to be adequate to justify subsequent clinical studies in humans.

Clinical trials are classified into three phases: Phase I, Phase II and Phase III. The Phase I clinical studies carry out initial testing of a vaccine in small numbers (e.g. 20) of healthy adults, to test the properties of a vaccine, its tolerability, and, if appropriate, clinical laboratory and pharmacological parameters. Phase I studies are primarily concerned with safety. Phase II studies involve larger numbers of subjects and are intended to provide preliminary information about a vaccine's ability to produce its desired effect (usually immunogenicity) in the target population and its general safety. Together, Phase I and II trials establish "proof-of-concept". To fully assess the protective efficacy and safety of a vaccine, extensive Phase III trials are required. The Phase III clinical trial is traditionally the pivotal study on which the decision on whether to grant a licence is based and sufficient data have to be obtained to demonstrate that a new product is safe and effective for the purpose intended. For many EIDs, Phase III trials cannot be conducted in advance of outbreaks due to the sporadic nature of their emergence and re-emergence. Phase II tested vaccines therefore have the potential of stopping the spread of disease during outbreaks, as well as being ready for Phase III testing. Depending on the study design, one may choose to conduct a "Phase IIb" trial between Phase IIa and Phase III. The purpose of this trial is to essentially conduct a small-scale efficacy trial. For many EIDs this may be the most realistic trial to consider prior to some form of emergency use listing.

The figure below depicts these different stages of development. The end of every phase is depicted by the average success rate, ranging from low to high. Depending on the success rate applied, it is expected that 3-5 preclinial candidates are needed to have 1 successful Phase II outcome.



Sources: 1) WHO Technical Report, Series No. 924, 2004. Annex 1 Guidelines on clinical evaluation of vaccines: regulatory expectations. 2) Pronker, Plos One 2013 3) Hay, Nature biotechnology 2014 4) Wong, Biostatistics 2019

Box 5: Platform technologies explained

Platform technologies can be understood as building materials ("platforms") that can be applied for developing a multitude of vaccines against different pathogens. Vaccines based on different platform technologies induce different types of immune responses, and the immune response required for protection against a certain disease varies. As such, one does not need to know the exact disease a platform is being developed for, allowing it to be potentially used for novel, as well as known pathogens.

The WHO R&D Blueprint process has identified several platform technology proposals for human vaccine development that have the potential to rapidly develop vaccines against known or unknown pathogens in the event of an epidemic. CEPI is developing promising platform technologies through to the end of Phase I studies. Successful development of these platform technologies could reduce vaccine development time significantly, thereby increasing the number and types of vaccine platforms that can be quickly adapted against EIDs.

The vaccine ecosystem

Development and delivery of vaccines is a costly and complex process that involves many steps and numerous partners. The vaccines CEPI helps develop are therefore not CEPI vaccines, but the *World's* vaccines.

CEPI thus also assesses both opportunities and challenges/ bottlenecks that other organisations face in the discovery and delivery – either those that hinder a health pipeline of early candidates or those that impede delivery and access to vaccines. CEPI coordinates its efforts with WHO and other major institutional partners, and works closely with like-minded funders to allocate resources for the greater good. Acknowledging the important work of other stakeholders, CEPI approaches all of its investments by taking an end-to-end approach, acting as either a facilitator or funder as required to drive change and help fill the critical gaps that still exist (Figure 2).

To be responsive and effective in our mission, we forge partnerships with local and regional institutions and involve the scientific community in affected countries. This is also an integral part of our organisational model and our governance structure, whereby the broadest set of experts, funders and institutions working in the field are consulted and take part in decision-making.

Figure 2: CEPI's funding and facilitating role

1 DISCOVERY	2 DEVELOPMENT/ LIECENSURE	3 MANUFACTURE	4 DELIVERY/ STOCKPILIING	5 LAST MILE
Academia	Industry	Industry	GAVI	Countries
Governments	Governments	BARDA	UNICEF	WHO
Wellcome Trust	Regulators	CMOs	PAHO	UNICEF
NIH	Wellcome Trust	Regulators	Governments	Responding
IMI	NIH	Governments	WHO	Organisations
GLOPID-R	EC	WHO	Industry	(eg. MSF)
Industry	IMI	GHIF	Pandemic Emergency	
Regulators	BMGF		Facility (World Bank)	
Biotech	BARDA/DTRA etc.		WHO Contingency	
	WHO		Fund	
	Biotech			
	PDPs			

VISION, MISSION AND STRATEGIC OBJECTIVES

CEPI's vision is a world in which epidemics are no longer a threat to humanity. Our mission is to accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks.

To achieve this mission, CEPI has three strategic objectives: preparedness, response, and sustainability. To measure progress and success towards these objectives, CEPI has developed a results framework (see Appendix).

All our strategic objectives encompass the principle of equitable access – our most important priority. To CEPI, equitable access to epidemic vaccines in the context of an outbreak means;

that appropriate vaccines are available when and where they are needed to end an outbreak or curtail an epidemic, and that they are accessible to all populations that need them, without financial constraints, to achieve that objective. Moreover, as part of its funding agreements, CEPI will pursue the principle that once a vaccine is licensed, price should not limit necessary access to a vaccine it has funded while at the same time ensuring the sustainability of vaccine manufacturing and distribution.

Accordingly, equitable access is a commitment that drives every aspect of our work and is key to our success as a global health organisation.

Price should not limit necessary access to a vaccine CEPI has funded while at the same time ensuring the sustainability of vaccine manufacturing and distribution.

Strategic objective I: Preparedness

Advance access to safe and effective vaccines against emerging infectious diseases

Our ability to advance vaccine candidates against our priority pathogens is the ultimate test of our ability to deliver on our mission.

However, vaccine development is a lengthy process. Advancement of vaccines—especially epidemic diseases—is a complex endeavour requiring active involvement by industry, academic and public health experts.

To support preparedness against EIDs, CEPI engages in the following areas of work:

- Investing in promising candidates targeting EIDs to drive development of vaccines where markets incentives are insufficient.
- Facilitating the establishment and maintenance of investigational stockpiles and development of robust plans to allow for trials and eventual deployment of vaccines during outbreaks.
- Providing expert assistance and funds enabling science and technologies to enhance vaccine development efforts.

Plans and targets (see Appendix)

- Advance 3 candidates each against Lassa, Nipah, and MERS through Phase II testing by end of 2022.
- Have 4 vaccine candidates against at least 2 pathogens in investigational stockpiles by end of 2022.
- Ensure that development partners seek early engagement with regulators and agree to terms that are consistent with CEPI's Equitable Access policy.

Investing in promising candidates targeting EIDs to drive development of vaccines where markets incentives are insufficient

CEPI supports the development of vaccines against priority pathogens and works with partners to ensure that promising vaccine candidates are ready for large-scale field trials when an outbreak occurs. CEPI carefully manages its portfolio of vaccine candidates. We continuously assess the performance of our vaccine portfolio and add additional investments based on its progress. As part of our investments, we work with our development partners to develop domestic clinical-trial capacity in countries where we will deploy our vaccines.

While initial investments have been made in vaccines against Lassa, Nipah, MERS, Chikungunya and Rift Valley fever as priority diseases, new diseases may be added to CEPI's portfolio in response to reassessments of existing threats and new emerging diseases. Depending on the success rate of our vaccine portfolio, CEPI might also choose to invest in additional vaccine candidates for existing priority diseases or co-invest in large-scale efficacy trials when a vaccine candidate is ready.

Strategic objective 2: Response

Accelerate the research, development and use of vaccines during outbreaks

Response to an unknown pathogen requires the necessary tools to expedite vaccine development, and innovative technologies can make uptake and delivery of the vaccine more effective.

Importantly, history has shown us that the R&D and delivery response will not be effective unless it has been tested and planned for in preparedness mode. To support the epidemic response, CEPI is:

- Investing in platforms to speed up the development and manufacture of vaccines.
- Supporting the development of technologies to facilitate use of vaccines in the field and rapid response to epidemics.
- Engaging end-to-end partners to plan for the deployment of vaccines during outbreaks.

Facilitating the establishment and maintenance of investigational stockpiles and developing robust plans to allow for trials and eventual deployment of vaccines during outbreaks

CEPI will facilitate the establishment of investigational stockpiles of successful vaccine candidates. This activity is designed to enable a response to an outbreak and the fast-tracked execution of large-scale efficacy trials (Phase III clinical studies) during the initial stages of an outbreak.

If a vaccine is deemed to be safe and effective, trials must be followed by regulatory approval and licensure. Manufacturing plans will also need to be devised to allow for eventual large-scale deployment. In view of these manufacturing needs, all vaccine candidates supported by CEPI will have manufacturing plans and associated quality controls in place to increase production capacity of these vaccines if more doses are needed. These manufacturing capabilities will also be required to replenish unused stockpiles of vaccines that have expired.

Providing expert assistance and funds enabling science and technologies to enhance vaccine development efforts

CEPI provides substantial technical support to its partners and serves as a liaison with WHO, other institutional partners, and countries at-risk, to increase the likelihood of success and expedite clinical testing. CEPI's partners face an array of challenges in developing vaccines against epidemic diseases. The epidemiology of CEPI's target diseases has not been well characterised. Preclinical models for these diseases are underdeveloped and the international standards and assays needed for vaccine development have not been established. Much work remains to be done to optimise the design of clinical trials suitable for testing candidate vaccines during public health emergencies, and a great deal of preparatory work will be required if vaccine trials are to be conducted under such circumstances.

CEPI staff, external experts, and members of its Scientific Advisory Committee (SAC) contribute subject-matter expertise in support of partners. CEPI also promotes and funds enabling science. Examples of enabling science include the validation of animal models required for vaccine proof-of-concept, the development of correlates of protection, providing support for diagnostics, and the preparation of biological standards and assays critical for the evaluation of vaccine candidates. CEPI also works closely with regulators and authorities in developed countries and developing countries to promote regulatory harmonisation and to ensure that regulatory requirements are addressed.

Plans and targets (see Appendix)

- Have at least 2 vaccine platform technologies by end of 2022 that can be rapidly adapted to develop vaccines against unknown pathogens for use in humans.
- Have at least 8 candidates through preclinical by 2020 and 6 vaccine candidates through Phase I by end of 2022.
- Ensure that development partners have necessary agreements in place for vaccines to be deployed and tested during an outbreak.

Investing in platforms to speed the development and manufacture of vaccines

CEPI invests in platform technologies that can be rapidly adapted to new and unknown pathogens, to reduce the time required for vaccine development to as little as 16 weeks.
In addition to expediting vaccine development, our platform technologies will be adaptable for use across different viral families.

The goal of CEPI's investments in vaccine platforms is to accumulate data on the performance of these platforms in a variety of settings, to characterise the human immune response to vaccines developed on these platforms to the greatest extent possible, and to work with regulators to streamline pathways for the approval of vaccines emerging from these platforms in the event of an emergency.

Supporting the development of technologies to facilitate field use and rapid response

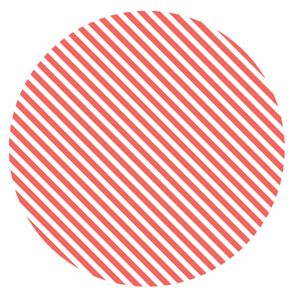
Where appropriate, and often in conjunction with other partners, CEPI will support the development of technologies that enable rapid testing and delivery of vaccines in the field. Examples of these technologies we could support in the future include thermostabilisation technologies to enhance the stability of vaccines in a variety of storage conditions, needleless injection devices, and other vaccine delivery systems that can make it easier for healthcare workers to administer vaccines.

Engaging end-to-end partners to plan for the testing and deployment of vaccines during outbreaks

CEPI proactively coordinates with a range of end-to-end partners that enable testing and delivery of vaccines to affected populations during an outbreak situation.

This means working with partners to design and implement clinical trials, engaging relevant regulators and ethics review boards prospectively, ensuring the security and reliability of the supply chain (including any needed cold-chain logistics), and preparing for potential large-scale administration of vaccines once trials are complete and the vaccine has been shown to be safe and effective.

Our Joint Coordination Group (JCG)—composed of normative bodies, regulators, funders, stockpilers, and first responders—plays a key role in this effort. Under their guidance, CEPI maps roles and responsibilities in relation to the vaccines it is funding, identifies potential gaps in preparedness, and develops plans to address these gaps. These may include ensuring that development partners have necessary agreements in place for vaccines to be deployed and tested during an outbreak. CEPI also works with WHO and other partners as needed to coordinate its response activities.



Strategic objective 3: Sustainability

Create durable solutions and equitable for outbreak response capacity

While preparedness and response are key priorities for an organisation working on EIDs, sustainability is a key component within all priorities and investments will ultimately ensure that the products we help develop stand the test of time.

This means that CEPI will organise and prioritise such that the investments we make are robust to tackle the unpredictable nature of epidemics, and that they can 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 is:

- Improving the predictability of financing for vaccine development to address end-to-end market failures.
- Driving efficiencies in vaccine development to reduce costs.
- Developing contingency plans to reduce risk so that successful vaccines are available during outbreaks.

Plans and targets (see Appendix)

- Raise $1bn as multi-year contributions to CEPI.
- Have agreements in place with downstream partners on life-cycle financing a of CEPI-funded products.

Improving the predictability of financing to address end-to-end market failures

We work closely with public-sector and private-sector partners to coordinate the development and procurement of our vaccine candidates. By improving the predictability of such financing, and establishing long-term mechanisms for the maintenance of stockpiles, we can ensure that successful vaccines can reach affected populations during an outbreak.

CEPI collaborates with organisations, whose missions intersect with our own, to proactively identify and fill funding gaps for vaccine R&D. Such collaboration could manifest as funding opportunities for large-scale vaccine efficacy studies or support for development of financial incentives such as prizes, advance purchase commitments, or vouchers. We continue our efforts to secure multi-year financial contributions for vaccine research and development.

These contributions allow us to operate flexibly in uncertain environments, such as during outbreak situations, and to increase financial predictability for our vaccine development partners. This approach requires CEPI to work closely with other actors and funders to align organisational priorities.

Driving efficiencies to reduce costs across the end-to-end spectrum of vaccine development

CEPI constantly strives for cost reductions and streamlining in all areas: from R&D and vaccine manufacturing to regulatory process and stockpiling, and even through to deployment of vaccines. CEPI also 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 stockpile replenishments.

CEPI is committed to developing and deploying vaccines against EIDs in a manner that demonstrates it is a responsible steward of public resources. CEPI must therefore guarantee that the financial resources, bestowed to CEPI by our investors, are invested in a way that provides value for money.

Developing contingency plans to reduce risk so that successful products are available to support outbreak response

CEPI establishes contingency plans with our partners for key aspects of epidemic responses, including those related to manufacturing and delivery of vaccines.

In practice, this means that if there is a failure of "plan A" (i.e. a vaccine manufacturing partner goes out of business), we have "plan B", which will enable continued vaccine manufacturing and distribution.

CEPI is committed to developing and deploying vaccines against EIDs in a manner that demonstrates it is a responsible steward of public resources.

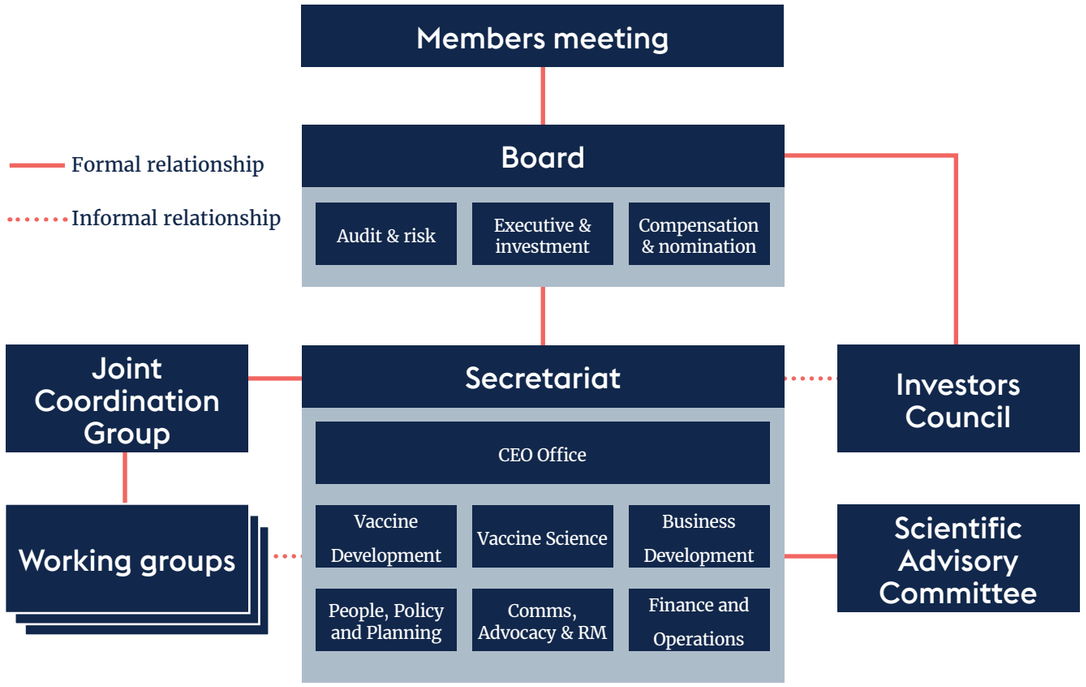
IMPLEMENTATION[10]

Governance

CEPI's governance structure has been developed to embed sound scientific assessment, and evidence based decision-making as well as ensure the highest operational standards and rigour in awarding of funds (Figure 3).

- The members' meeting is CEPI's highest body, equivalent to a general assembly. This meeting includes all independent Board members and all Investors and is responsible for adopting the annual accounts and approving revisions to the CEPI's Articles of Association.
- The Board is composed of 8 independent members and four representatives of the Investors Council — a body composed of all Investors in CEPI. While the Board is CEPI's ultimate decision-making authority, three sub-committees of the Board gives the Secretariat guidance on issues critical for the progress of CEPI, but which do not require full Board approval.
- The Investors Council also provides oversight and guidance to the Secretariat in areas relevant for management.
- The Scientific Advisory Committee (SAC) provides technical advice to the Secretariat on disease prioritisation, vaccine candidate selection, portfolio management, and vaccine science.
- The Joint Coordination Group (JCG) is composed of normative and regulatory agencies, funders, procurers and delivery institutions. The JCG addresses barriers to advancing and delivering vaccines and works to align priorities between member institutions. It can also establish working groups for issues requiring dedicated attention.

Figure 3: CEPI's governance model



10 More details on CEPI's operating model is provided in CEPI's Programme Doccument and can be found on www.cepi.net

Portfolio management

Research shows that to successfully move one vaccine candidate from preclinical assessment to Phase II, one will involve at least three product failures.[11] As the development of our portfolio progresses, we anticipate that there will be a high rate of attrition. Therefore, to meet our strategic objectives, we require an appropriately sized portfolio of vaccine candidates, with a robust framework for portfolio management.

Rigorous investment decisions and trade-offs will need to be made on an ongoing basis to reach our ambitious targets, as outlined through our Strategic Objectives. Therefore, CEPI employs a consistent portfolio management system in place that includes the following aspects:

- A common portfolio management cycle to enable disciplined identification, selection, management and evaluation of vaccine candidate and platform projects in line with strategic objectives
- Effective portfolio governance enabling timely and high quality decision-making, overseen by a dedicated Portfolio Strategy & Management Board (PSMB), consisting of senior members of the CEPI leadership team and internal technical and subject matter experts
- Standardised project and portfolio management practices to drive harmonisation, consistency and comparability across the portfolio
- Clear and consistent management of project and portfolio information and analyses to enable effective decision-making in terms of portfolio value, cost, time, risk and diversity

CEPI's PSMB, with advice from its SAC and external experts, defines the target portfolio of vaccine candidate, platform technology and enabling sciences projects, and manages delivery of the portfolio according to a standard portfolio management cycle (Figure 4). The ultimate funding decisions are then made by the Board. In advance of entering into partnership agreements, CEPI performs financial, technical, and legal and business due diligence to ensure that development partners possess the necessary scientific, financial, and overall management expertise to advance products and are able to manage significant sums of money. The partnership agreements also provide a mechanism for ensuring compliance with our Equitable Access policy, and the Secretariat regularly publishes reports on the implementation of the policy.

CEPI manages projects through active engagement and routine monitoring and reviews. Approval criteria are applied to support periodic "stage-gate" reviews for partners seeking the next tranche of funding to advance to the next stage of development.

A Joint Monitoring and Advisory Group (JMAG) consisting of key Secretariat staff and representatives of vaccine development partners continually assess progress of individual projects, approve plans, and make recommendations to the PSMB concerning project continuation and the extension of additional funding through the formal stage-gate review process.

At the portfolio level, CEPI uses a range of analytical approaches as part of our annual strategic reviews to monitor risk and the value of our portfolio. Following close evaluation of our portfolio's progress, and of other unmet needs for vaccine R&D for EIDs, CEPI plans for future additional investments. This is informed by screening of new potential areas for funding, including analyses of vaccine research.

Figure 4: Porfolio management

11 Gouglas D, Tung TL, Henderson K, et al. Estimating the cost of vaccine development against epidemic infectious diseases. The Lancet Global Health. (in press)

Management of funds

The funds received by CEPI from its investors are usually received and kept in a Financial Intermediary Fund managed by the World Bank, with some investors having chosen to transfer funds directly to CEPI's bank accounts.

The Secretariat maintains most of its funds in US dollars and currently makes all grants in this currency. The Secretariat has commercial bank accounts for disbursement to CEPI's development partners or operating expenses. Funds held for either contingency or cash-management purposes are conservatively invested to ensure capital preservation and liquidity.

CEPI's annual reporting is informed by progress reports from our development partners. This information enables CEPI to measure progress towards our strategic objectives and financial targets.

CEPI policies, procedures, and risk mitigation

CEPI is guided by a commitment to effective, ethical operations and investment practices. For each vaccine development project, the CEPI Secretariat creates a "Risk and Follow-up Report". Risks are described in detail in funding applications, integrated product development plans, and by CEPI during technical, financial, legal, and integrity due diligence. Significant risks are included in the CEPI Risk Register, which is shared with the Board on a quarterly basis. Risk mitigation measures, policies, and procedures are critical, especially in view of CEPI's fiduciary, operational, and indirect development responsibilities. These measures are also important because the projects we fund might involve testing new vaccines in vulnerable populations during an outbreak. To ensure compliance with all relevant regulations and the highest ethical and quality standards, CEPI's policies[12] reflect:

i) Legal, ethical, and regulatory requirements including those required by global regulatory agencies and authorities in the geographies in which CEPI operates.

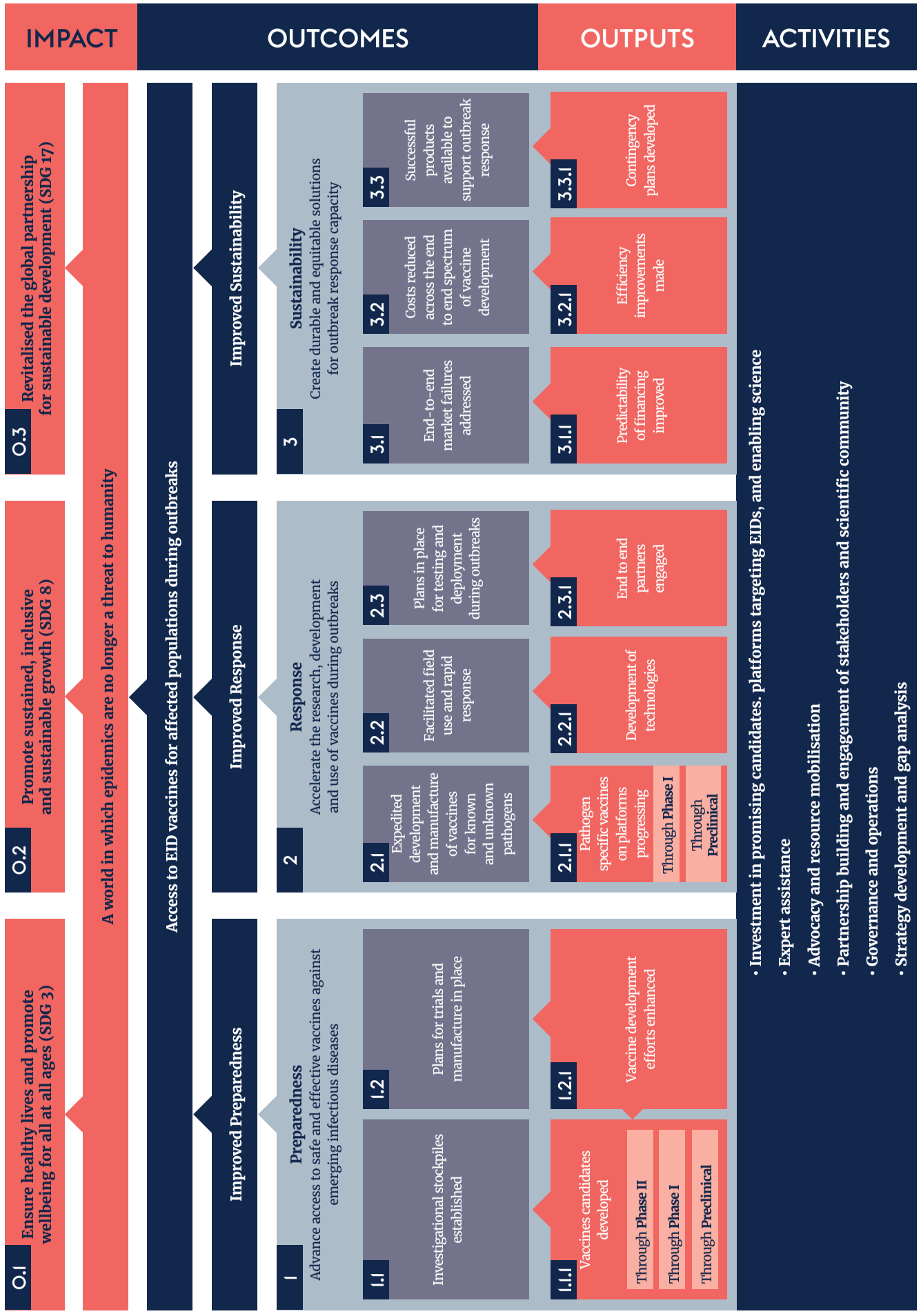
ii) Industry standards and best practice for conducting R&D and ensuring that it is ethical, effective, and transparent.

iii) Operational and financial requirements investors have asked CEPI to follow.

APPENDIX: RESULTS FRAMEWORK

This Appendix provides an overview of all the indicators and their targets. A Theory of Change outlines how elements within our Strategic Objectives respond to the results hierarchy. CEPI's Programme Document provides more detail on how each indicator is monitored and measured. To complement this Framework, CEPI will continue to develop its monitoring plan by the end of 2019 to support timely and accurate follow-up of achievements towards our strategic objectives. This is deemed particularly important for the Theory of Change levels 2.2, 2.3.1, 3.2 and 3.3 which currently do not have dedicated indicators.

12 See www.cepi.net/about/governance for an up-to-date list of CEPI policies



Indicator number	TOC number	Indicators	Baseline YO	Target 2018	Target 2019	Target 2020	Target 2021	Target 2022
1	0,1	3.B.2 Development assistance to medical research & basic healthcare	N/A	N/A	N/A	N/A	N/A	N/A
2	0,1	3.D.1 Health emergency preparedness	N/A	N/A	N/A	N/A	N/A	N/A
3	0,2	8.1.1 GDP per capita growth rate	N/A	N/A	N/A	N/A	N/A	N/A
4	0,3	17.6.1 Science and technology cooperation	N/A	N/A	N/A	N/A	N/A	N/A
5	1,1	Number of vaccine candidates in investigational stockpile for outbreak situations and ready for efficacy studies and emergency use	0	0	0	0	0	4 candidates for at least 2 priority pathogens
6	1,2	Percent of vaccine partnership agreements that have manufacturing plans in place to enable vaccine production in response to an outbreak	N/A	100%	100%	100%	100%	100%
7	1,2	Percent of vaccine development partners agreeing to terms that are fully consistent with CEPI'S Equitable Access Policy and implementation guidance	N/A	100%	100%	100%	100%	100%
8	1,1,1 a	Number of vaccine candidates advanced through preclinical trials	Lassa: 0	Lassa: 1	Lassa: 3	Lassa: 4	Lassa: 4	
8	1,1,1 a	Number of vaccine candidates advanced through preclinical trials	Nipah: 1	Nipah: 1	Nipah: 3	Nipah: 4	Nipah: 4	
8	1,1,1 a	Number of vaccine candidates advanced through preclinical trials	MERS: 1	MERS: 1	MERS: 2	MERS: 3	MERS: 4	
8	1,1,1 b	Number of vaccine candidates advanced through PI trials	Lassa: 0	Progress towards targets reported	Lassa: 2	Lassa: 3	Lassa: 3	
8	1,1,1 b	Number of vaccine candidates advanced through PI trials	Nipah: 0	Progress towards targets reported	Nipah: 0	Nipah: 3	Nipah: 3	
8	1,1,1 b	Number of vaccine candidates advanced through PI trials	Nipah: 0	Progress towards targets reported	Nipah: 0	Nipah: 3	Nipah: 3	
8	1,1,1 b	Number of vaccine candidates advanced through PI trials	MERS: 0	Progress towards targets reported	MERS: 1	MERS: 2	MERS: 3	
8	1,1,1 c	Number of vaccine candidates advanced through PII trials	Lassa: 0	Progress towards targets reported	Progress towards targets reported	Lassa: 0	Lassa: 2	Lassa: 3
8	1,1,1 c	Number of vaccine candidates advanced through PII trials	Nipah: 0	Progress towards targets reported	Progress towards targets reported	Nipah: 0	Nipah:1	Nipah:3

Indicator number	TOC number	Indicators	Baseline YO	Target 2018	Target 2019	Target 2020	Target 2021	Target 2022
8	1,1,1 c	Number of vaccine candidates advanced through PII trials	MERS: 0	Progress towards targets reported	Progress towards targets reported	MERS: 1	MERS: 1	MERS: 3
9	1,2,1	Number of available biological standards and validated assays (including standard operating procedures) for evaluation of vaccine candidates against CEPI's priority pathogens	0	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	1 biological standards developed for each of priority pathogens	At least one validated assay available each of priority pathogens
10	1,2,1 a	Percent of vaccine candidates in clinical development (e.g. being tested in humans), with relevant engagement from national authorities—including regulators—in at-risk countries (End preclinical/move to Phase I (Stage Gate 1): Scientific advice for CTA/Pre-IND package)	0	Subject to successful completion of preclinical: 100%	Subject to successful completion of preclinical: 100%	Subject to successful completion of preclinical: 100%	Subject to successful completion of preclinical: 100%	Subject to successful completion of preclinical: 100%
10	1,2,1 b	Percent of vaccine candidates in clinical development (e.g. being tested in humans), with relevant engagement from national authorities—including regulators—in at-risk countries (End of Phase I, type C meeting/ scientific advice)	0	Subject to successful completion of PI 100%	Subject to successful completion of PI 1 100%	Subject to successful completion of PI 100%	Subject to successful completion of PI 100%	Subject to successful completion of PI 100%
10	1,2,1 c	Percent of vaccine candidates in clinical development (e.g. being tested in humans), with relevant engagement from national authorities—including regulators—in at-risk countries. (for Phase II, submission of CTA to NRAs in affected countries)	0	Subject to successful completion of PII 100%	Subject to successful completion of PII 100%	Subject to successful completion of PII 100%	Subject to successful completion of PII 100%	Subject to successful completion of PII 100%
11	2,1	Number of vaccine platform technologies that can be rapidly adapted to develop vaccines against unknown pathogens for use in humans	0	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	2 or greater, including at least one novel (innovative) platform, i.e., that has no prototyped licensed vaccine
12	2,3	Percent of vaccine development partners with necessary agreements in place for vaccines to be deployed and tested during an outbreak	0	100%	100%	100%	100%	100%
13	2,3	Percent of vaccine development partners with plans in place for equitable access fully consistent with CEPI's Equitable Access Policy	0	100%	100%	100%	100%	100%
14	2,1,1 a	Number CfP2 vaccine candidates progressing through preclinical	0	Progress towards targets reported	Progress towards targets reported	8 candidates		

Indicator number	TOC number	Indicators	Baseline YO	Target 2018	Target 2019	Target 2020	Target 2021	Target 2022
14	2,1,1 a	Number of CfP2 vaccine candidates	0	Progress towards targets reported	Progress towards targets reported	8 candidates		
14	2,1,1 b	Number of CfP2 vaccine candidates progressing through preclinical	0	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	6 candidates	
15	2,2,1	Number of CfP2 vaccine candidates progressing through preclinical	N/A	Annual update	Annual update	Annual update	Annual update	Annual update
16	3,1	Agreements in place with downstream partners on life-cycle financing a of CEPI-funded products, by disease area	0					3 agreements in place
17	3,1	$1bn raised as multi-year contributions to CEPI	$630 m	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	$1 bn
18	3,2,1	Percent of priority actions taken to achieve efficiencies	0	0	50%	50%	50%	50%
19	3,3,1	Percent of vaccine partnership agreements in place that contain contingency plans for manufacturing	N/A	100%	100%	100%	100%	100%

Epidemics affect us all. They do not respect borders.
A virulent respiratory virus spreading as fast as flu
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Vaccines are one of our most powerful tools
in the fight to outsmart epidemics.

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