Programme Document

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Duration of programme	Open-ended, but preliminary Business Plan drafted for 2017-2021
Current Investors	Australia, Belgium, Bill & Melinda Gates Foundation, Canada, European Commission, Germany, Japan, Norway, United Kingdom and Wellcome

Disclaimer: This document has not been brought to the CEPI Board. Its content is however in large part based on Board approved documents

Acronym and abbreviation list

- AFRO – WHO Regional Office for Africa
- AMRO – WHO Regional Office for the Americas
- BARDA – Biomedical Advanced Research and Development Authority
- CEPI – Coalition for Epidemic Preparedness Innovations
- CFPs – Call for Proposals
- COI – Conflict of Interest
- CMOs – Contract Manufacturing Organizations
- DTRA – Defence Threat Reduction Agency
- EC – European Commission
- EIDs – Emerging infectious diseases
- EMRO – WHO Regional Office for the Eastern Mediterranean
- EUAL – Emergency Use Assessment and Listing
- EURO – WHO Regional Office for Europe
- GAVI – Global Alliance for Vaccines and Immunisation
- GLOPID-R – Global Research Collaboration for Infectious Disease Preparedness
- IHME – Institute for Health Metrics and Evaluation
- IMI – Innovative Medicines Initiative
- JCG – CEPI Joint Coordination Group
- LMICs – Low and Middle Income Countries
- MDG – Millennium Development Goals
- MoU – Memorandum of Understanding
- NIH –National Institutes of Health
- OHCHR – Office of the High Commissioner for Human Rights – United Nations
- PAHO – Pan American Health Organization
- PDPs – Product Development Partnerships
- R&D – Research & Development
- SAC – CEPI Scientific Advisory Committee
- SDG – Sustainable Development Goals
- SEARO – WHO Regional Office for South East Asia
- SOPs – Standard Operating Procedures
- UNICEF – United Nations Children's Fund
- WEF – World Economic Forum
- WB – World Bank
- WG – Working Groups
- WHO – World Health Organization
- WPRO – WHO Regional Office for the Western Pacific

Content

I. Introduction

The Business Plan 2019-2022[1] sets out the mission, vision and scope of CEPI, as reframed and endorsed by the Board October 2018. The revised Business Plan built on the Preliminary Business Plan 2017-2022 published September 2016 – before CEPI was formally established. While the Business Plan gives a high-level overview of CEPI's strategic direction, this Programme Document gives a more detailed depiction of the *implementation* of our programmatic areas.

The purpose of this document is to provide coherent overview about this direction as it relates to CEPI's strategic objectives and operations. In addition to the revised Business Plans this document also builds on the board's investment decisions and processes, permanent governance arrangements and CEPI policies. The Programme Document also provides information around CEPI's theory of change and how it relates to achievement of goals and milestones depicted in the results framework. Moreover, a detailed risk assessment and description of the selection and decision process of the Calls for Proposals (CFP) is included.

[1] Expected publishing date: May 2019

2. About the CEPI programme

2.1 Situation analysis

Emerging infectious diseases (EIDs) pose a growing threat to global health security in a world of higher population density, increased mobility and ecological changes. Recent outbreaks of EIDs such as Ebola have claimed thousands of lives and inflicted billions of US dollars in losses for economies that were both directly and indirectly affected by the outbreak. A consensus emerged after the devastating 2014 – 16 Ebola Outbreak in West-Africa that the world must take steps to be better prepared for and respond more rapidly to future epidemics.

Following the 2000 Millennium Development Goals, government and philanthropic funding havesupported a growing community of product developers with pipelines for new vaccines, diagnostics and drugs for many high-burden diseases that primarily affect citizens living in the poorest countries. The importance of vaccine development, research and access was reiterated in the Sustainable Development Goals number 3, starting in 2015. However, effective biomedical tools such as vaccines and drugs are almost entirely lacking for EIDs despite their known disruptive potential. EIDs are characterized by limited market potential, and planning for these diseases is especially challenging due to the sporadic nature of their emergence and re-emergence. Better Research & Development (R&D) preparedness – through new or improved biomedical products, better R&D response speed, proactive planning for clinical testing, regulatory approval and delivery – is urgently needed.

As the SARS, MERS, Ebola, and Zika epidemics have demonstrated, new diseases can emerge quickly and unexpectedly. However, biomedical R&D is highly complex, lengthy, costly, and associated with high attrition rates. Devising new ways to accelerate development times is both difficult and necessary. New and better coordinated funding is essential to build and sustain an EID countermeasure program. Funding, however, is not enough. To succeed, it is necessary also to pair new funds with new institutional and technical platforms to improve the speed of development.

Box 1: Societal and Economic Impact of Epidemics

Ebola: 11 000 deaths and an estimated negative economic impact of USD 53 bn[2]. Health systems weakened resulting in significant decline in most maternal and child health indicators[2].

Spanish flu[3]: 50 million deaths and Gross domestic product (GDP) loss of 3% in Australia, 15% in Canada, 17% in the UK, and 11% in the USA.

SARS[3]: 774 deaths and global economic loss of USD52.2 billion

1: World Bank, 2: Lancet Glob Health. 2017 Apr; 5 (4):e448-e457, 3: Yamay et al, 2017: Financing of international collective action for epidemic and pandemic preparedness,

Vaccines – CEPI's focus today – are important tools in our effort to protect the world against EID outbreaks. Feasible vaccine candidates exist for some of the EIDs within CEPI's initial scope. When this is the case, it is possible, as we saw in the Ebola outbreak, to develop vaccines quickly, even in extremely challenging conditions. All major post Ebola reports[3] agree however, that this process must be improved. The current model, which relies on ad-hoc initiatives and the good will of a handful of biopharmaceutical companies, is insufficient for several reasons, including but not limited to:

- The vaccine pipeline is weak for most EIDs

[2] Huber, C., Finelli, L., & Stevens, W. (2018). The economic and social burden of the 2014 Ebola outbreak in West Africa. The Journal of infectious diseases, 218(suppl_5), S698-S704.
[3] WHO, LSHTM / Harvard / Lancet, NAM / Global Health Risks Framework, and UNSG High-level Panel (Moon, Sridhar et al. 2015, World Health Organization 2015, United Nations Secretary General 2016)

- Clinical trials suffer unnecessary administrative delays
- Ad-hoc initiatives for vaccine development are fragmented and unpredictable
- Unilateral, uncoordinated government efforts to fund R&D preparedness are inefficient and unsustainable in addressing global epidemic risks
- The global health community is operating without an insurance policy against a growing threat from EIDs

As described in more detail in the following chapters, CEPI's financing scope is initially focused on bringing vaccine for known and unknown emerging infectious diseases ready for efficacy trials (phase 2b/3). This is understood as the most important for ensuring an appropriate preparedness level for outbreak readiness. An explanation of the vaccine development processes and platform technologies is given in Box 2 and 3 below.

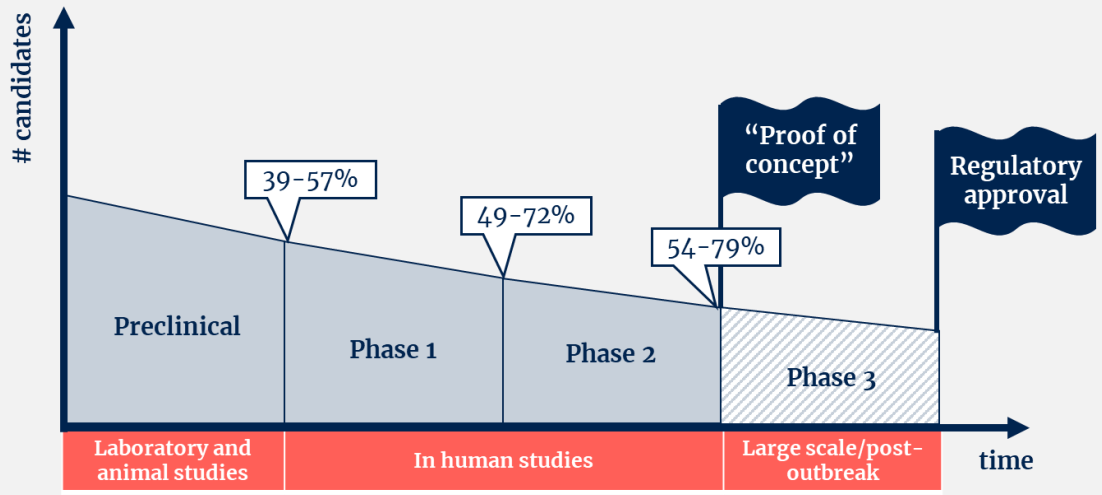
Box 2: Vaccine development explained

The R&D process for developing vaccines consists of a preclinical phase involving laboratory and animal studies, followed by clinical testing in humans.

Preclinical research and development are carried out in laboratories and is based on both *in vitro (e.g microorganisms, cells and biological molecules)* and, when necessary, *in vivo* studies (meaning animals).The data from the preclinical studies provide details of the development and production of a vaccine together with reports of control testing, which should be adequate to justify subsequent clinical studies in humans.

Clinical trials in humans 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 the 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, the study design of phase III trials implies that it cannot be conducted in advance of outbreaks. Phase II tested vaccines therefore have the potential of stopping the spread of disease during outbreaks, as well providing readiness 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, highlighting the areas that are covered in CEPI's financing scope – through proof of concept. The end of every stage is depicted by the average success rate, ranging from low to high. Depending on the success rate applied, it is expected that one needs 3-5 candidates starting in preclinical in order to have 1 successful phase II outcome.



Source: 1) WHO Technical Report, Series No. 924, 2004. Annex 1 Guidelines on clinical evaluation of vaccines: regulatory expectations. 2) Haire, B. G., & Folayan, M. O. (2017). Undue inducement, or unfair exclusion: considering a case study of pregnancy in an HIV prevention trial. Journal of medical ethics, 43(12), 829-830. 3) Davis Vaccine 201 4) Struck Nature Biotechnology 1996 5) Pronker Plos One 2013

Box 3: Platform technologies

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. The Call CEPI has launched will develop promising platform technologies to the end of phase 1 studies, and also look to reduce the vaccine development time significantly, thereby increasing the types of vaccine platforms that can be quickly adapted against emerging infectious diseases.

2.2 Establishment of CEPI

Recognizing the urgent need for a new approach to EID vaccine development, leading figures from governments, foundations, industry and civil society proposed a coalition for proactive R&D during the Annual Meeting of the World Economic Forum in Davos in January 2016. Since then, representatives from industry, governments, foundations, regulators, intergovernmental organisations, such as WHO and civil society organisations, have been closely collaborating to create a Coalition for Epidemic Preparedness Innovations (CEPI). CEPI has been separate from (but complementary to and strongly informed by) the WHO-led process to develop an R&D Blueprint for emergencies.

During its initiation phase (January 2016 – June 2016), CEPI consisted of a stakeholder group and a project management group that set up expert task teams to consider issues such as pathogen prioritisation, clinical development, manufacturing capacity and regulatory pathways, potential models for partnership, funding needs, resource mobilization and shared risk/reward arrangements between sectors. The three task teams recommended CEPI to focus its investments on vaccine development from preclinical to clinical Phase II development with pilot stockpiles, and that it makes use of rapid response technology platforms where possible. The task teams suggested that CEPI should coordinate vaccine development from an end-to-end perspective including alignment around plans for clinical Phase III studies, regulatory approval pathways, stockpiling and procurement should an epidemic occur.

Building on the recommendations of these groups, CEPI then transitioned into a start-up phase (July 2016 – December 2017) and evolved through a multi-sectorial dialogue between its members. A temporary structure was designed to ensure the start of implementation and also that all stakeholders could contribute their perspectives on CEPI's permanent organizational structure and governance.

To this purpose, an interim Secretariat of CEPI was set up at the Norwegian Institute of Public Health (NIPH), and a legal entity was established in the form of an international non-profit association. Subsequently, the interim Board, the Scientific Advisory Committee and the Joint Coordination Group convened for meetings in the lead up to CEPI's official launch that took place at the World Economic Forum in January 2017. A decision was made on the permanent Secretariat arrangements soon thereafter, with a multi-nodal Secretariat led and incorporated in Norway with a second node in London (hosted by Wellcome) and a small representation office in Washington D.C. CEPI's CEO Richard Hatchett led the establishment of the permanent Secretariat and took steps to implement a revised and permanent governance structure that was formally in place first quarter of 2018.

Figure 1 below depicts the main activities and events that have led to the establishment of CEPI.

Figure 1: Activities and events that have led to the establishment of CEPI

Establishment of CEPI	Timeline
SARS, MERS, Ebola, and Zika outbreaks	-> 2015
Post-ebola reports identified gaps	2015-2016
WEF 2016: Proposal to establish organization	Jan 2016
CEPI Initiation phase with stakeholder consultations and recommendations	Jan-Jun 2016
Interim Secretariat and CEPI association established	Jul-Aug 2016
Meetings of the interim Board, SAC and JCG	Aug-Dec 2016
WEF 2017: official launch	Jan 2017
Permanent Secretariat identified and permanent CEO appointed	Jan-May 2017
Permanent Governance structures in place	**Q1 2018**

As depicted in the timeline, 2018 was CEPI's first year in its "permanent" (fully established) phase; a governance model had been implemented, a secretariat structure was in place and the first contracts with vaccine developers had been signed. Although more staff is expected to be hired through 2019, CEPI is now a fully operational organisation with processes and procedures in place for managing a large portfolio of vaccine candidates.

3. CEPI vaccine priorities

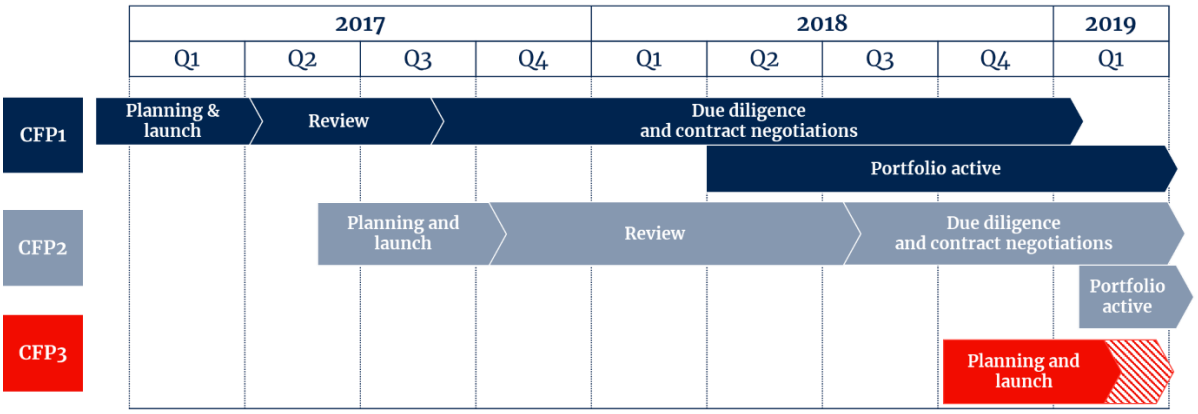
In selecting its priority diseases and funding scope, CEPI has benefited from the evidence base and recommendations generated through the WHO R&D Blueprint process. Ever since the Ebola epidemic, the WHO has proactively undertaken a set of important functions based on its roles and responsibilities as the global normative body of health to design a new R&D blueprint and emergency response framework to EIDs. This includes pathogen prioritization, product requirements and roadmap setting, regulatory coordination, and platform technology assessments. This wealth of evidence and analysis informs CEPI's approach to prioritization and coordination. Collaboration between WHO and CEPI leverages the strengths of each partner from the outset, avoids duplication, and maximises complementarity.

Since its establishment, CEPI has launched three Calls for Proposals (CFP) for vaccine development projects in addition to calls for cross-cutting supportive activities like epidemiology and standards and assays:

- **CFP1 on priority pathogens for EIDs**: Launched January 2017 for the diseases Lassa, Nipah and MERS. The decision on priority diseases departed from pathogens identified by the WHO Blueprint for Action, followed by an in-depth assessment by the SAC. In recommending priority diseases to the CEPI Board, the SAC applied criteria related to 1) public health impact (potential of outbreak, transmissibility, burden of disease) and 2) feasibility (current scientific knowledge, pipeline candidates available). CEPI expects to finalise its first contracts for CFP1 by end of March 2018 and the remainder by Q2. Link to CFP1 call text.
- **CFP2 on platform technologies:** Launched October 2017 to enable rapid vaccine development against both known and unknown pathogens that trigger infections with epidemic potential. A requirement is to produce sufficient vaccine doses to impact an emerging outbreak and that the platform demonstrates versatility one of the priority pathogens from the WHO Blueprint list. The first contracts are expected to be finalised in Q4 2018. Link to CFP2 call text. An overview of the three CEPI priority diseases are given in Box 4.
- **CFP3 on priority pathogens:** Launched January 2019 for the diseases Rift Valley Fever (RVF) and Chikungunya. The broadening of CEPI's vaccine portfolio to include these viruses has been based on wide consultation and advice from CEPI's Scientific Advisory Committee and on three main criteria: the public health impact of these diseases, that no vaccines are currently available for human use, and the feasibility of vaccine development. Link to CFP3 call text.

Timelines for the first phases of the three different calls are depicted in figure below. Note that these timelines reflect the portfolios and not the different projects, where there is/have been more variation.

Figure 2: Indicative project timelines for CEPI Calls for Proposals



A common denominator for CEPI's priority pathogens is that no effective vaccines currently exist – the reason being too a large extent, lack of market incentives. The lack of market incentives is in large part

due to the unpredictable nature of outbreaks, as well as the types of countries that stand to be the biggest beneficiaries of the funded vaccines; low- and middle income countries. With the associated lack of purchasing power, companies cannot defend the large investments when the likelihood of making a profit is slim-to-none.

Box 4: CEPI priority diseases

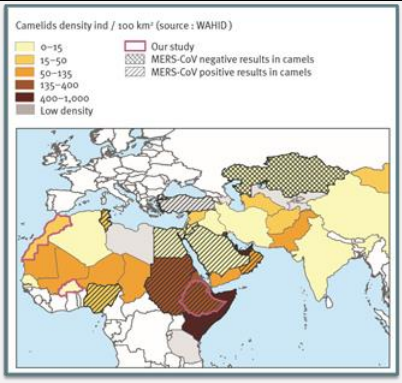
MERS

Disease burden

- Total 2 040 cases
- Endemic cases, outbreaks
- Transmission via camels and human-to-human infections in health care
- ~35% CFR among those diagnosed
- Confirmed global cases of MERS COV 2012-2017

Key countries

Middle East (Saudia Arabia), as well as at risk countries: Jordan, UAE, Egypt, Somalia, Ethiopia, Sudan



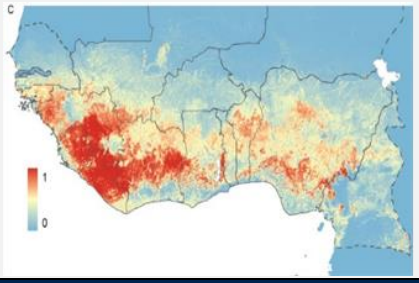
Lassa

Disease burden

- Endemic, annual outbreaks
- Estimated up to 300,000 cases/year
- Case fatality rate in hospitalized patients is 15-20% but can reach as high as 50% during epidemics

Key countries

Sierra Leone, Liberia, Ivory coast, Nigeria



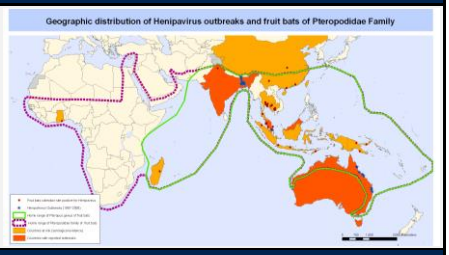
Nipah

Disease burden

- Annual outbreaks in Bangladesh/India
- Up to 80% Case fatality rate
- Human-human transmission and via intermediate hosts (pigs)

Key countries

Bangladesh, India, Malaysia



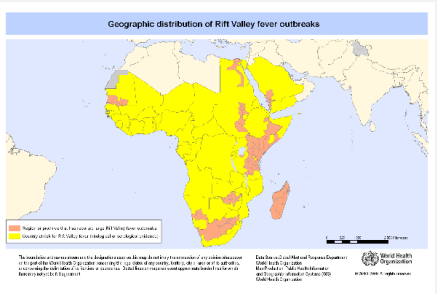
Rift Valley Fever

Disease burden

- Case fatality rate has been less than 1% in documented epidemics
- Substantial outbreaks almost annually since 2000
- No human-to-human transmission of RVF virus has been documented

Key countries

Egypt, Saudi Arabia, Yemen, Mauritania, Senegal, the Gambia, Sudan, South Sudan, Kenya, Tanzania, Zambia, Zimbabwe, Mozambique, Madagascar, Namibia, South Africa

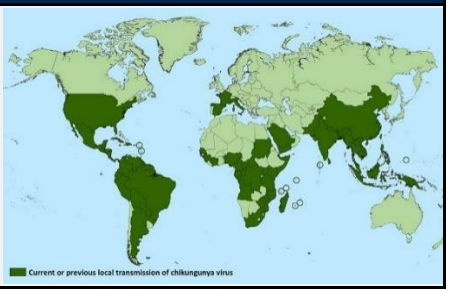


Chikungunya

Disease burden

- Viral disease transmitted to humans by infected mosquitoes.
- It causes fever and severe joint pain. Other symptoms include muscle pain, headache, nausea, fatigue and rash.
- The disease mostly occurs in Africa, Asia and the Indian subcontinent. However a major outbreak in 2015 affected several countries of the Region of the Americas.

See complete list of countries on cdc.gov/chikungunya/geo/index.html



4. Governance and accountability

4.1 Governance structure

CEPI's organizational structure includes governance, management, coordination, and advisory functions. The set-up has been established to ensure that organizational, political and scientific elements are addressed and that participation of investors and relevant partners in governing bodies is ensured. CEPI's Articles of Association includes the following organizational structures:

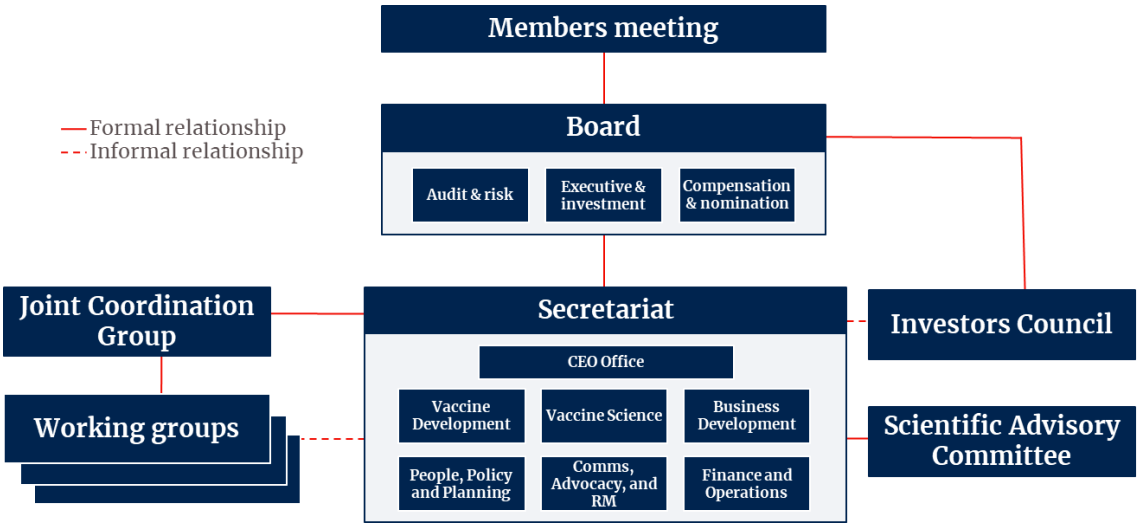
- Four permanent institutional bodies: the CEPI Members Meeting, the CEPI Board, the CEPI Investors Council and the CEPI Secretariat.
- Two other organizational structures to fulfil advisory and coordination functions: the CEPI Scientific Advisory Committee (SAC) and the CEPI Joint Coordination Group (JCG).
- Optionally, the CEPI Board may establish other committees or advisory task teams to address specific issues.

A more exhaustive explanation of the institutional bodies is given in the subsequent sections and in attachments.

Table 1: Overview of Permanent CEPI Governance arrangements

Body	Detail
Members Meeting	The Members of CEPI are the voting members of the CEPI Board and the members of the Investors Council.
Board	12 Board members – 4 investor representatives and 8 more technically oriented + 5 observers. The Board has three sub committees; • Nominations and Compensations Committee • Executive and Investment Committee • Audit and risk Committee See this link for current Board members and subcommittee composition.
SAC	Capped at 25 individuals with attention to geographic, technical expertise and gender diversity. Reporting to Secretariat strengthened
JCG	The purpose of the JCG is to address barriers to advancing and delivering vaccines and to align priorities between member institutions. To address such challenges the JCG can establish dedicated task forces, independently or in with support from the Secretariat. These task forces report to the JCG and provide recommendations for action. Examples of task forces that have already been formed include a regulatory task force, stockpiling task force, a standards and assays task force and a sustinable manufacturing task force.
Investors Council	Investor Council established to allow for investor engagement in CEPI's governance without inflating the size of the Board

Figure 3: Governance model for CEPI



4.2 Governing bodies of CEPI

CEPI is an international association registered in Norway. The head office (node) is hosted by the Norwegian Institute of Public Health (NIPH) in Oslo, with an additional node hosted by Wellcome in London. CEPI also has a small representation in Washington DC, USA. This secretariat structure facilitates recruitment, enables close collaboration with host institutions (ie, NIPH and Wellcome) and provides closer geographical proximity to some developers, normative bodies, and funders.

Board:
CEPI's board is composed of eight independent members and four representatives of our Investors Council (three representatives of sovereign investors, and one of the foundations). Additionally, four observers sit on the board;the Chair of the scientific advisory committee, the Chair of the Joint Coordinating Group, CEPI's CEO, and a representative from CEPI's fund holder (The World Bank). The independent members represent the expertise needed to advance vaccines: from product development, regulatory approval, and field delivery. 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 Board sub-committees are i) Compensation and Nomination Committee, ii) Executive and Investment Committee and iii) Audit and risk Committee.

Members meeting:
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 members meeting is CEPI's highest formal body, somewhat equivalent to a general assembly.

Investors Council:
This council is composed of all legal entities contributing to CEPI's general fund. It provides guidance to CEPI in areas relevant for management and oversight of CEPI activities. The council also approves any single investment worth more than $100 million, before it is presented to the Board for final decision. The Investors Council selects four members to represent it on the Board: one member from philanthropic foundations and three from governments. Members of the Investors Council are entitled to access the same information as CEPI Board members and may attend Board meetings as observers.

Scientific Advisory Committee (SAC):
The main function of the committee is to provide technical advice to the Secretariat on disease prioritisation, vaccine candidate selection, portfolio management, and vaccine science. They meet on a

quarterly basis, either in person or virtually, but may decide to have additional meetings if new investment opportunities or scientific challenges are encountered by the Secretariat. The committee consists of 24 scientific experts who have been selected on the basis of their knowledge in different areas of vaccine development, including knowledge of CEPI's priority diseases. An additional five non-voting members, who represent industry perspectives, ensure that recommendations are guided by challenges encountered by vaccine developers. The criteria guiding selection of members include technical expertise (vaccine R&D, manufacturing, public health, vaccine licensure, and implementation), diversity of stakeholders, geographical representation, and gender balance.

Joint Coordination Group (JCG):
The purpose of the JCG is to address barriers to advancing and delivering vaccines and to align priorities between member institutions and the broader ecosystem engaged in developing and implementing vaccine policies and strategies. To address such challenges the JCG can establish dedicated task forces, independently or with support from the Secretariat. These task forces report to the JCG and provide recommendations for action. Examples of task forces that have already been formed include a regulatory task force, stockpiling task force, sustainable manufacturing task force and a standards and assays task force. The JCG is composed of nine permanent member institutions; WHO, European Medicines Agency, Federal Drug Administration, African Vaccine Regulatory Forum, Médecins Sans Frontières, International Federation of Red Cross and Red Crescent Societies, National Institute for Biological Standards and Control, Wellcome, and UNICEF. Other members can be invited on a non-permanent basis to address challenges specific to the stage of development that CEPI's portfolio is in.

Secretariat:
While the Board sets our strategy, provides guidance and make decisions on CEPI's investments, the Secretariat operates on the basis of sound scientific, financial, and operational assessments. The Secretariat is structured to be nimble while possessing the capabilities needed for effective operations, sound investment management, and active engagement with development partners. The Secretariat presently consists of five teams: the Vaccine Development team (responsible for advancement of CEPI's product portfolio); the Vaccine Science team (provide technical advice and supports science that tackle barriers to rapid advancement of vaccine); Legal and Business Development team (responsible for engagement with private-sector partners, negotiating partner agreements, and for the legal aspects of CEPI operations; the Finance and Operations team (responsible for the day-to-day operations of the Secretariat); and the People, Policy and Planning team (responsible for HR, project management and investor relations functions). Additionally, some staff are part of the office of the CEO.

The Secretariat proposed on October 2018 an increased headcount from 42 to 66. Evidence to support the proposal included a breakdown of the activities of each CEPI department, existing and planned workload and the corresponding staff capacity they would need. The proposal was also benchmarked against other PDPs. Subsequent to Board's approval of the proposal, the Secretariat proceeded to advertise and recruit new members of the team. A revised organizational chart has been developed (Figure 4) and job descriptions are developed for all identified roles. All roles are expected to be filled by Q3 2019. Finally, the secretariat is also supported by a strong team of consultants that can support in highly specialized areas where building in-house capacity does not make sense or in peak periods.

***Figure 4**: Secretariat structure*

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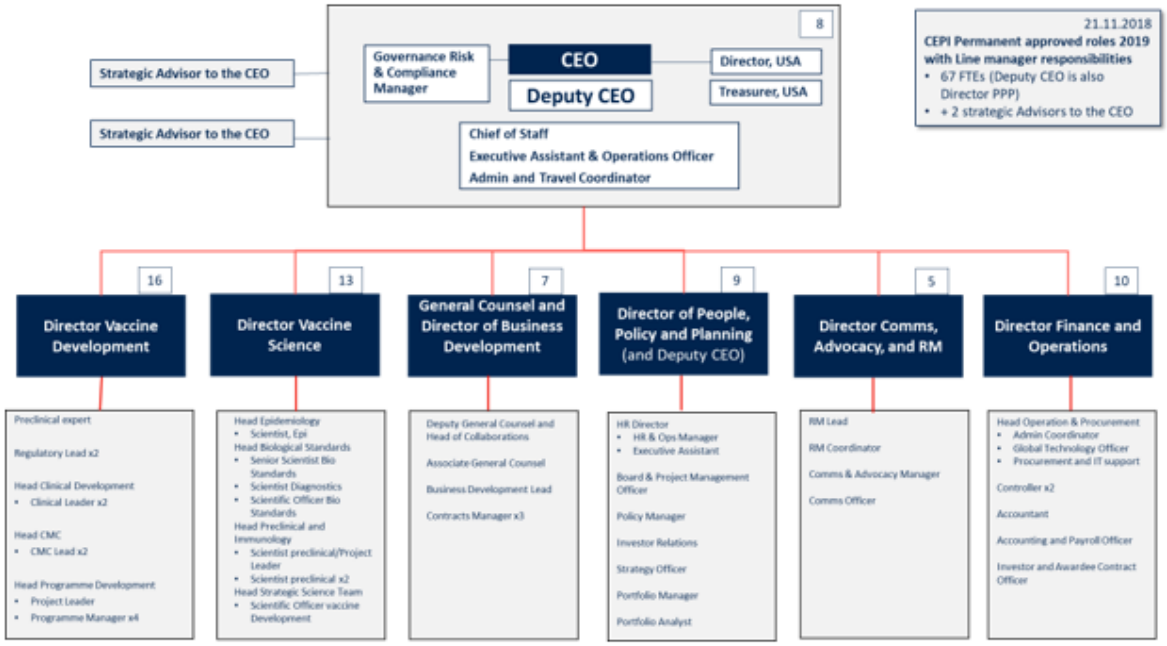


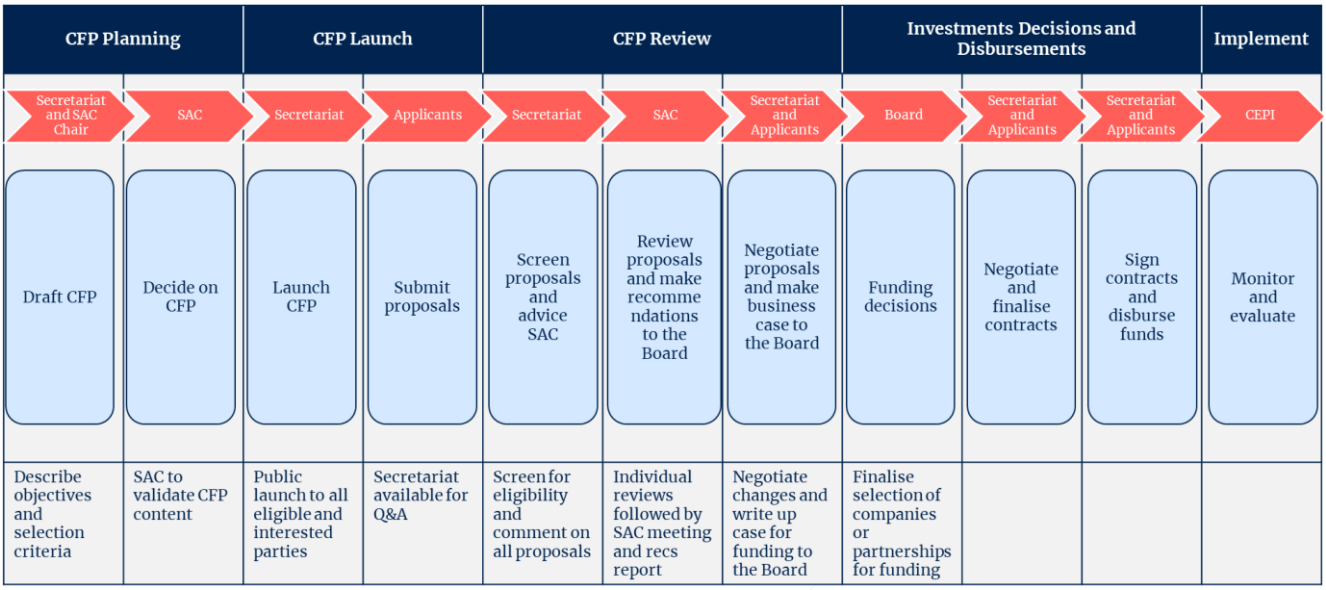
4.3 CFP procedures and review

All investment decisions are derived from CEPI's Strategic Objectives, as covered in section 2.1. Using the WHO Blueprint as point of departure, CEPI then assess which diseases to prioritise, considering likelihood of outbreak, consequences of any such outbreak and feasibility of developing a vaccine against the disease in question. In most cases, projects eligible for funding will be identified and assessed through Calls for Proposals (CFPs). CFPs can range from broad announcements made in the public domain (e.g. CEPI's website) to restricted announcements targeted to organizations with known capabilities. Rolling calls are also in planning, whereby CEPI accepts applications over longer periods of time, assessing to what extent a given project fits with CEPI's existing portfolio and strategic direction. Announcements and associated decisions will follow applicable rules and procedures on procurement for CEPI. Although CEPI will make assessments for each CfP on exactly how the CFP will be implemented, including on roles, review process and criteria applied for assessments, the main steps and principles remain largely unchanged ensuring impartial expertise and peer review of the proposals. Since the first CfP that was launched in January 2017 CEPI has acted on lessons learned, reducing the time from decision to launch, to actual signing of contracts for CfP2 and CfP3 .

CEPI's Scientific Advisory Committee (SAC) has an advisory role in the design of CFP technical content, including criteria and methods for assessment of applicants for CEPI funding. Secretariat staff will screen proposals for eligibility and forward proposals for assessment to the SAC. Eligibility criteria and methods for proposal assessments will be specified in the respective CFPs, according to SAC directions. In exceptional circumstances – e.g. in emergency situations - CEPI investments could be executed through direct contracting, requiring rapid assessments and decisions to support vaccine development or clinical testing. The Board has also directed the Secretariat to develop a targeted strategy on rapid response. The strategy should ensure that CEPI does not duplicate existing efforts but rather depart from its portfolio when identifying roles, responsibility, and investments.

Over time, CEPI may diversify its tools for channelling investments to include proactive scanning and soliciting relevant projects. The core steps of the application process are depicted in figure 3 below and expanded upon in the following sections.

Figure 5: CEPI's investment process



4.3.1 CFP launch and review

CEPI will make assessments on a case by case basis for how CFPs will be implemented, including on roles, review process and criteria applied for assessments. The first two calls that were launched followed a two-step process, while the recently launched CFP3 followed a one-step process. The main difference relates to the two-step process doing an initial high-level assessment based on a shorter application before shortlisted applicants then are then invited to submit a longer proposal. Through these processes, applications have been and are assessed according to criteria including feasibility, anticipated potential use, manufacturing scalability, experience and track record, cost and time to completion. The criteria are formulated in a way that allows applications to be assessed according to the extent they respond to overarching strategic objectives for CEPI and the objectives of the specific call.

In CFP1 process, applications in the Step 1 that met the eligibility criteria of the Call were reviewed by both the Scientific Advisory Committee and independent experts. Based on the reviews, shortlisted applicants were invited to submit a full proposal through the Step 2 process. The Step 2 review process was similar to that of the Step 1, but having drawn on additional expertise and consultants to contribute to the evaluation of the proposal, as deemed necessary. The recommendations from the review process were presented by the Secretariat to the SAC for their considerations. The SAC provided their funding recommendation to the CEO, and the CEPI Board made the final investment decisions, building upon SAC and CEO recommendations, as well as business and strategic considerations. More information on the review processes for the CFP1, CFP2 and CFP3 can be found here.

Secretariat staff will screen proposals for eligibility and forward proposals for assessment to expert reviewers. Experts will be a combination of external experts, SAC experts and internal experts, ensuring impartiality and topic expertise. Eligibility criteria and methods for proposal assessments will be specified in the respective CFPs, according to SAC directions. Eligible applications are assessed according to criteria such as feasibility, anticipated potential use, manufacturing scalability, experience and track record, cost and time to completion. Applicants may be invited for interviews if beneficial to ensure that any outstanding questions are resolved prior to concluding the full review. Proposals and budgets will be subject to a cost challenge undertaken in the context of the applicant's

projects and CEPI's policies and cost guidance. The SAC will make the final short list of candidates based on a proposal developed by the Secretariat on the basis of expert reviews. Based on the inputs from the SAC the CEPI CEO will then present his recommendations to the Board for funding decisions.

4.3.2 Investment decisions, disbursements and implementation

When the funding decision is made by the CEPI Board, an extensive internal due diligence is conducted on all potential awardees of CFP funding before contract negotiations commence. The due diligence process consists of both technical, legalas well as financial/integrity due diligence, as initiated in CFP1. While these have been conducted sequentially before, more recent CfPs have undertaken these steps with greater overlap – and sometimes in paralell – to further shorten the time required prior to contract signature. The technical due diligence will review the scientific implementation plan of the awardees and prepare a technical report with a recommendation based on a three category assessment; "go", "conditional go" or "no-go". The report will also include a revised scope of work, planning and cost estimates, with proposed payment per milestones/stage gate, for each project. Both the technical and the financial due diligence will consist of a review of written feedback from awardees on identified questions from the due diligence team, in addition to review of awardee technical and financial capabilities and procedures, and site visits.

All investments are governed by partnership agreements, including project governance, payment terms and conditions, reporting and compliance with CEPI policies, including our equitable access policy. These partnership agreements also regulate CEPI's oversight of the product-development life-cycle through ongoing reporting and established stage-gate reviews, allowing CEPI to implement measures to mitigate risks or withhold funding in the event of non-compliance or inadequate progress. CEPI reserves the right to terminate agreements according to mutually agreed "go/no-go" decision criteria. CEPI will negotiate with each awardee to optimize and reach an agreement on the ownership and management of intellectual property. Optimal management will safeguard against the use of intellectual property in a manner that impedes equitable access to the vaccine.

More details on award conditions – including policies and contract templates - are available online under CEPI policies and CEPI CfPs. A few of specific interest are listed below:

- Equitable access policy, including data sharing
- Clinical trial policy
- Scientific Intergrity policy

4.3.3 Reporting, monitoring and stage gates (go/no-go) decisions

Monitoring, reporting and evaluation of project deliveries will be ongoing throughout the funding cycle. The Funding Agreement establishes frequency[4] and guidelines for the awardees for project management, monitoring and reporting. CEPI also ensures that the reports include information and results according to agreed-upon indicators, as reflected in CEPI's results framework. The content requirements will be set forth in templates for progress and financial reporting, reflecting the assessment criteria from the application review, to ensure a timely and coherent flow of information from awardees to CEPI. The templates will include risk assessments, results frameworks, time period for project milestones, amongst others. At the end-of-project cycle, a review with decisions on termination or continuation of the investment, will be carried out on the basis of the scientific progress that has been made according to the agreed upon milestones.

Once projects have been selected and initiated (through a kick-off meeting), it customarily follows a monitoring and decision model whereby the following bodies engage at different levels

[4] As CEPI's Funding Agreements, the awardee shall provide written reports to CEPI at least quarterly during the course of the Award, and shall provide regular reports to CEPI after the completion of the Award in order to allow CEPI to determine the impact of its funding.

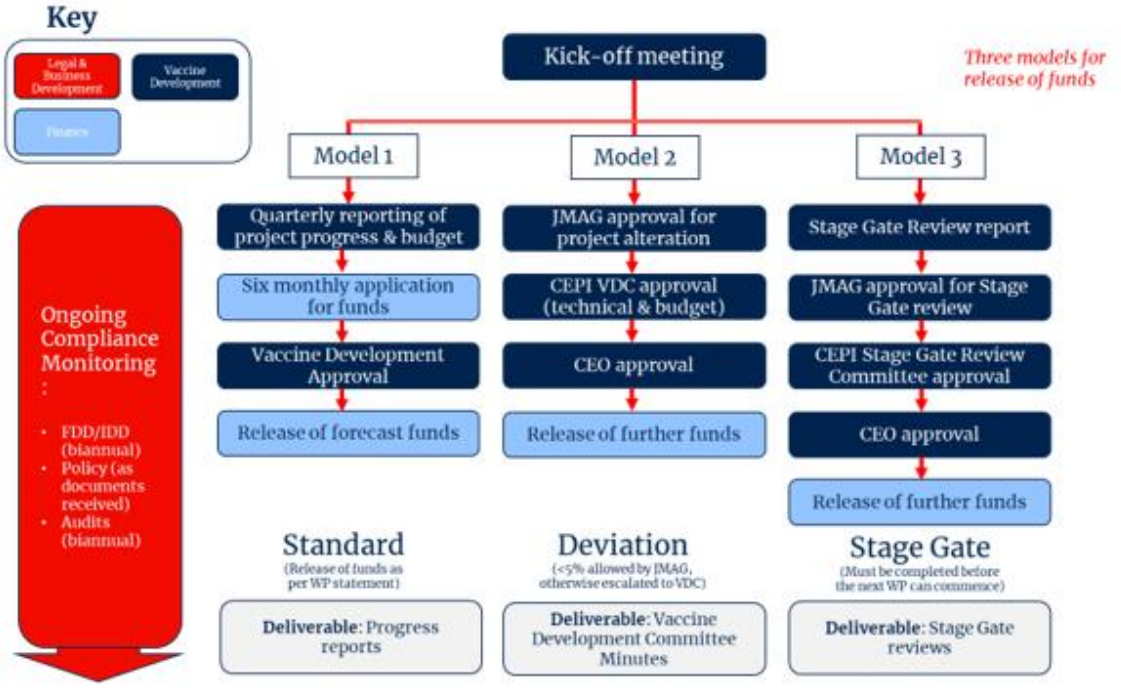
- **General project management within the secretariat**: A team is formed, from members of the Secretariat, with a dedicated leader for each project. At a bare minimum this team comprises experts covering budget and project management as well as project specific expertise (eg CMC, preclinical etc). This team does the ongoing monitoring and evaluation of progress and addresses issues that arise that do not require elevation to other governance levels. In the case of a clinical trial, the project team will also provide an observer for the Trial Steering Committee and the Data and Safety Monitoring Board.
- **Joint monitoring and evaluation committee (JMAG)** is constituted with both CEPI staff and representatives of the awardee. This may be further supplemented with external experts if required (depending on subject matter). The purpose of the group is to carry out day to day management of the project. It will further propose project alterations to the Vaccine Development Committee (VDC) and, if required, to a Stage Gate Review Board on completion of a particular work package.
- **Vaccine development committee (VDC)** is an internal CEPI body which reviews alterations to the agreed project plan. It is anticipated that learnings gathered during project execution may lead to changes to the initial plan. Such changes are unlikely to be cost-neutral and so CEPI will carry out an internal review to decide if such proposals are justified before informing the JMAG.
- **Stage gate review committee (SGRC)**, is usually carried out at the end of a workpackage before initiation of a subsequent one. In the current CfP it is not anticipated that more than one workpackage will be funded for each project. However, should subsequent funds become available, a Stage Gate Review would be held before more funds were released.

Depending on where a given project finds itself in a work package, the different bodies engage according to the following models. A figurative depiction is given further down.

Model 1: all awardees are pre-funded through work-packages, but the entire funding for that work package is not disbursed at once. Awardees have quarterly reporting to CEPI and apply for additional funding within that work package every 6 months. These forecasted funds are customarily released following a quick review from the vaccine development committee within CEPI, as there are no milestones set.

Model 2: If an awardee wants to make alternations to a project plan, it has to be assessed by the JMAG if the deviation is within 5% of the budget, and otherwise escalated to the Vaccine Development Committee before ultimate approval is made by the CEO.

Model 3: At the end of a work package when an awardee has reached a stage gate, an in-depth review of the technical progress, given budgetary implications, is reviewed by the JMAG and the stage gate review committee before the CEO approves the release of funds for the next work package.



NB: JMAG= Joint Management Advisory Group (50% Awardee : 50% CEPI)
VDC= Vaccine Development Committee (CEPI only)

Additional to these three models for the release of funding, CEPI monitors general compliance on an ongoing basis. This takes the form of monthly project management interaction, quarterly scientific reports and six-monthly budget review. Collectively, this ensures that CEPI has a strong interaction with their Awardees.

CEPI will also conduct annual portfolio reviews to assess the performance across projects, providing a periodic strategic review of CEPI's overall progress. Thus review will help identify future priorities and engage both internal (secretariat, SAC, Board) and external (CEPI partners and awardees) key stakeholders. A portfolio review is a core part of CEPI's portfolio management cycle for holistic review across the full portfolio.

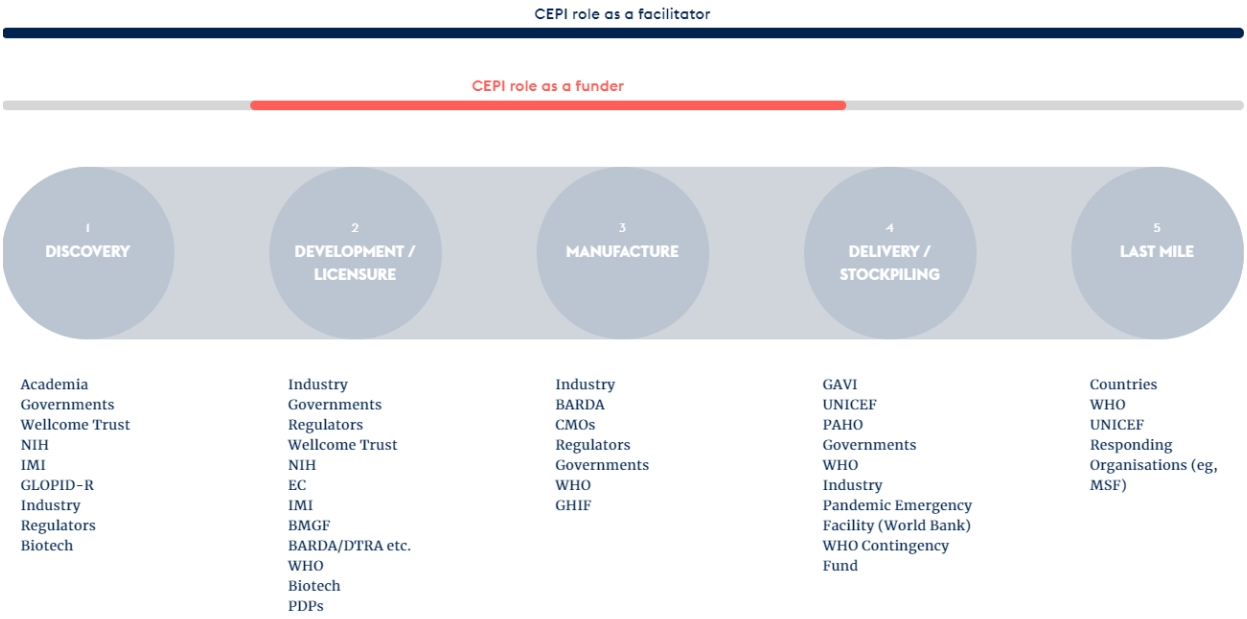
4.4 Partnerships and coordination

CEPI is building capabilities through a mix of partnership models in its "end-to-end" approach of vaccine development – from discovery to delivery.

There are already many actors in the "end-to-end space" of vaccine funding and R&D implementation and there is broad agreement that CEPI should avoid duplication and focus funding on the critical gap i.e. the lack of capability to move vaccine candidates from the preclinical stage through phase 2 (see Figure 6). However, this is not simply a question of funding the development activities required for proof of principle. It also requires CEPI to facilitate coordination activities between R&D and regulatory pathways, ensuring that a vaccine candidate can be successfully deployed in the event of an outbreak, supported by regulatory advice along critical checkpoints. The CEPI Joint Coordination Group serves as an important platform to take this work forward (see details in Chapter 0).

Through coordination with others, including the WHO, CEPI will fill R&D gaps as needed and coordinate with other entities to set priorities, pathogen specific road maps, plans to accelerate clinical testing and approval of products in epidemic situations. CEPI will also coordinate with others on vaccine stockpiling and distribution.

Figure 6: CEPI's scope and fit with other initiatives



5. Expected results

5.1 Introduction

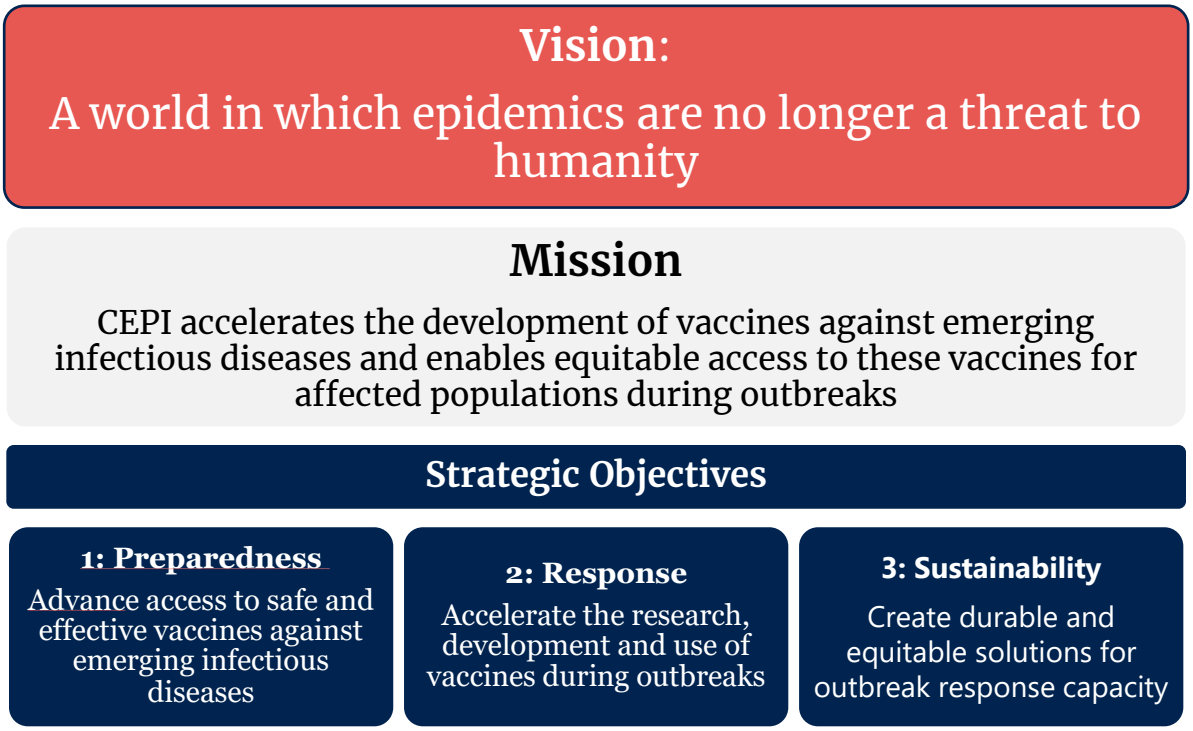
CEPI's response and investments will be directed towards preparing for future health crises by advancing vaccines for known and unknown pathogens. This will dramatically increase the world's ability to respond quickly and mitigate the spread of disease, thereby ensuring healthy lives and alleviating the associated negative economic consequences of outbreaks.

Additionally, CEPI will address systemic challenges in vaccine development, both outside and during epidemics. This includes working closely with stakeholders across the end-to-end scope of vaccine development to ensure a clear path to licensure and delivery.

An overarching objective for all of CEPI's activities is ensuring affordability and availability for populations in need in Low and Middle Income Countries (LMICs) for the vaccines CEPI helps develop. This is CEPI's ultimate target group. Additionally, CEPI will work closely together with key partners within the end-to-end scope of vaccine development, including public, private, philanthropic and civil organisations.

CEPI's priorities and guiding principles are derived from CEPI's Preliminary Business Plan for 2017-2021 and further adapted October 2018 to better reflect the current priorities. These updates will be incorporated in the revised CEPI Business Plan, to be published 2019. The associated vision, mission and strategic objectives guides the Coalition's approach, summarised in Figure 7**Error! Reference source not found.** below.

Figure 7*: CEPI's Vision, Mission and Strategic Objectives*



The next part of this section will provide a "theory of change" overview. The purpose is to give an outline of the current status of CEPI's activities, the outputs and outcomes they lead to, and subsequently how they relate to the overarching impact level of ensuring healthy lives, counteracting negative economic impacts resulting from epidemics and promoting public private partnerships and cross sectorial collaboration. It will moreover highlight the cross-cutting nature of CEPI's operations, and how one activity can lead to a multitude of outcomes.

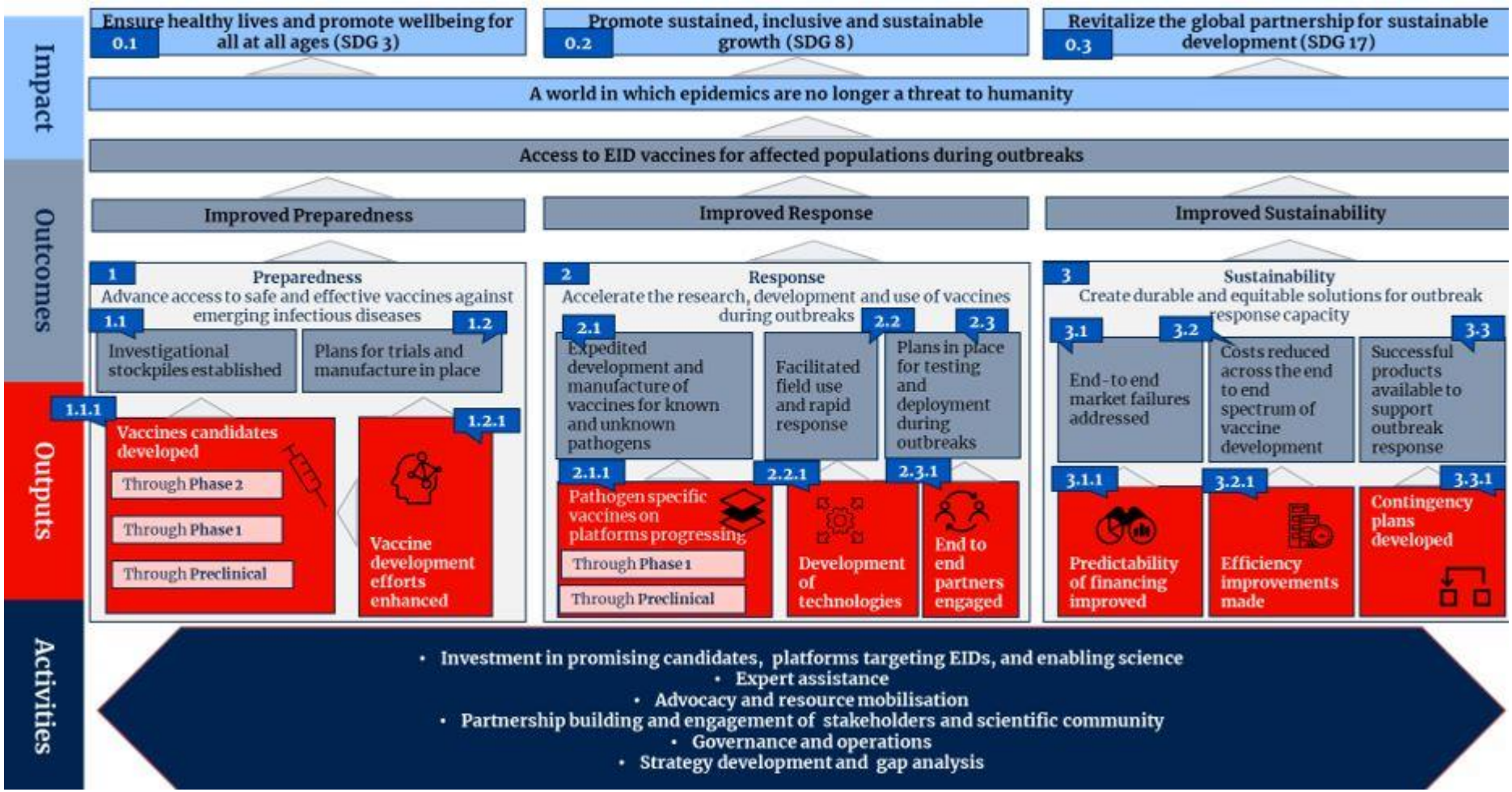
Additionally, the Theory of Change is supported by a Results Framework (Annex B) and a Risk Register (Annex C). The Results Framework provides a more clear-cut and hierarchical approach in order to highlight how given outputs may lead to individual outcomes in a measurable manner, and compare expected achievements to baselines[5]. The Framework depicts a closer relationship between the different levels of results than what will be seen in the real world, and must thus be read in conjunction with the Theory of Change. The issues listed in the Risk Register, covered in more detail in Chapter 5, can also be understood as the inverse of *assumptions* that need to be in place for CEPI to move from activities and all the way up to the impact level[6]. For ease of reading, all necessary assumptions are therefore not listed in the narrative but can be found in greater detail in Annex C. Through monitoring and reporting on key activities through the Results Framework and the Risk Registry, CEPI will thus be able to make adjustments based on lessons learned and to mitigate risks. Further, it will also provide communication on achievements throughout the Business Plan cycle.

The differentiation between activities, outputs, outcomes and impacts might not be as clear cut as depicted in Figure 8. The outputs and the outcomes in the Theory of Change depart from a definition of the 3 major components within each strategic objective. These components contain elements of both outputs and outcome, and the next sub-sections are therefore structured by Strategic Objective for the output and outcome level.

The farther up one moves in the hierarchy, the less control CEPI has over the outcomes, since this also relies on awardee activities and external third parties. On the impact section, for example, there are arguments as to why CEPI can contribute to the overarching global objectives of "ensuring healthy lives and promote wellbeing for all at all ages", cognizant of CEPI being far from the sole contributor to reaching this objective. The different numbers in the figure serve as guidance to the reader when going through the supporting narrative.

[5] It is underscored that the links presented do not necessarily reflect causal relationships.
[6] I.e. the risk higher than expected attrition rates can also be understood as the assumption that attrition rates will follow industry standards.

Figure 8: Theory of Change



5.2 Activities

Starting at the bottom of the hierarchy, the Secretariat is implementing and executing the activities that drive the processes towards CEPI's overarching objectives. The activities listed here are not time limited, but necessary components throughout all of CEPI's operations in order to achieve the intended impacts; both as a gap-filler through its funding scope, and as a facilitator in the end-to-end scope of vaccine development. Appropriate organizational plans and standard operating procedures will be developed to ensure that these activities are directed towards overarching outcomes.

- **Strategy development and gap analysis:** with continuous developments in CEPI's portfolio and the broader vaccines R&D field, this is a necessary component for assessing the most targeted and effective approach. This includes defining the direction and scope of CEPI's operations based on modelling, science and coordination.
- **Governance and operations:** all activities under this heading supports CEPI in being a diligent, effective and decisive organisation with prudent management of the funds we've been entrusted. This includes managing and implementing our governance structure and putting in place policies and procedures and the associated compliance.
- **Partnership building and engagement of stakeholders and scientific community:** In the broad space of vaccine development and global health as such, CEPI remains a relatively small actor. CEPI is therefore dependent on engaging with a wide range of stakeholders to continously inform the organization as to how it can be effective and aligned with priorities of other actors.
- **Advocacy and resource mobilisation:** advocacy is an integral part of making CEPI succesful, to demonstrate achievements and the importance of its mission. Likewise, funding is a necessity to support vaccine research and development and CEPI's day-to-day activities and resource mobilization efforts will thus be integral to CEPI's operations.
- **Expert assistance:** The types of organisations that CEPI is funding suggests that CEPI has to take an active role in managing the projects to ensure speed and scientific excellence. To do this, CEPI has in-house scientific expertise that can address challenges that both single projects and our portfolio at large meet in their development pathways.
- **Investment in promising candidates, platforms targeting EIDs and enabling science:** To reach successful outcomes, CEPI invests in the most promising vaccine candidates and platforms through calls for proposals. Departing from its prioritiy diseases, there may also be a need for investing in scientific challenges that enable expedited advancement. Such enabling investments may include standardisation of assays and epidemiological studies.

5.2.1 Strategic objective 1: Preparedness (box 1)

"Advance access to safe and effective vaccines against emerging infectious diseases"

To support preparedness against emerging infectious diseases, CEPI

1. Invests in promising candidates targeting emerging infectious diseases to drive development of vaccines where markets incentives are insufficient
2. Facilitates the establishment and maintenance of investigational stockpiles and development of robust plans to allow for trials and eventual deployment of vaccines during outbreaks
3. Provides expert assistance and funds enabling science and technologies to enhance vaccine development efforts.

Invests in promising candidates targeting EIDs to drive development of vaccines where markets incentives are insufficient (output 1.1.1).

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.

Having invested in the most promising candidates, 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, and Middle East Respiratory Syndrome (MERS) 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.

Related indicators from Results Framework

- ***Nr 8:*** *Number of vaccine candidates advanced*

This indicator tracks the progress of CEPI's portfolio through the different development stages; preclinical, phase 1 and phase 2 trials. Progress is tracked for each of our priority pathogens, with set targets for how many candidates will have reached what milestone when.

Facilitates the establishment and maintenance of investigational stockpiles and develops 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 (Outcome, box 1.1). 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 (Outcome, box 1.2). 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.

Related indicators from Results Framework

- ***Nr 5, TOC 1.1:*** *Number of vaccine candidates in investigational stockpile for outbreak situations and ready for efficacy studies and emergency use*
- ***Nr 6, TOC 1.2:*** *Percent of vaccine Partnership Agreements that have manufacturing plans in place to enable vaccine production in response to an outbreak.*
- ***Nr 7, TOC 1.****2: Percent of vaccine development partners agreeing to terms that are fully consistent with CEPIs Equitable Access Policy and implementation guidance*

The set of priorities highlighted in this section primarily relate to outcomes achieved, implying that progress may not manifest itself until outyears leading up to 2022. Since stockpiles are considered a key component of ability to respond quickly, indicator 5 will provide a good measurement of CEPI's overall success. Indicator 6 is important in that a stockpile may need to be replenished quickly, and associated plans must therefore be put in place beforehand to avoid undue delay. Indicator 7 will be reported on annually, and reflects CEPI's commitment to implementation of its access policy that guides compliance of our awardees in fulfilling their obligations wrt making the vaccine available – including in the context of an outbreak.

Provides expert assistance and funds enabling science and technologies to enhance vaccine development efforts (Output, box 1.2.1).

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 described. 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 optimize 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 contribute subject-matter expertise in support of partners. CEPI also promotes and funds enabling science. Examples of this enabling science include the validation of animal models required for vaccine proof-of-concept, the development of correlates of protection, 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.

Related indicators from Results Framework

- ***Nr 9, TOC 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*
- ***Nr 10, TOC 1.2.1:*** *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.*

This section relates to a lot of the day-to-day activity that CEPI's scientific team is doing to support our partners in advancing the portfolio. As such, a lot of the issues that relate to this section are activity-based and therefore hard to measure. Two areas have however been identified as particularly important to prioritise; biological standards and regulatory issues. In addition to speeding up the development process itself, these outputs help to lay the grown for an effective response to outbreaks.

5.2.2 Strategic objective 2: Response (box 2)

"Accelerate the research, development and use of vaccines during outbreaks"

To achieve rapid vaccine deployment, every step in the development process must be accelerated—from research, development, and manufacture to distribution of vaccines to affected populations. To support the epidemic response, CEPI

1. Invests in platforms to speed up the development and manufacture of vaccines
2. Supports the development of technologies to facilitate use of vaccines in the field and rapid response to epidemics
3. Engages end-to-end partners to plan for the deployment of vaccines during outbreaks

Invests in platforms to speed the development and manufacture of vaccines

CEPI invests in platform technologies (output, box 2.1.1) that can be rapidly adapted to new and unknown pathogens, to reduce the time required for vaccine development to as little as 16 weeks (outcome, box 2.1). In addition to expediting vaccine development, our platform technologies will be adaptable for use across different viral families.

CEPI invests in vaccine platforms to accumulate data on the performance of these platforms in a variety of settings, to characterize 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.

Related indicators from Results Framework

- ***Nr 11, TOC 2.1:*** *Number of vaccine platform technologies that can be rapidly adapted to develop vaccines against unknown pathogens for use in humans*
- ***Nr 14, TOC 2.1.1:*** *Number CfP2 vaccine candidates progressing through preclinical and P1.*

As with our priority pathogens, assessing advancement of our portfolio of platform technologies at different stage gates will give an idea of whether we're on track towards success on the outcome level. This is reflected under indicator 2.1.1. Whether the platform technologies are effective on an outcome level depends on whether they are successful in what they're set out to do: ability to adapt rapidly to develop a vaccine once the virus is known.

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

Where appropriate, and often in conjunction with other partners, CEPI supports the development of technologies (output, box 2.2.1) that enable speedy testing and delivery of vaccines in the field (outcome, box 2.2). Examples 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.

Related indicators from Results Framework

- ***Nr 15, TOC 2.2.1:*** *Annual analysis of available technologies and the gaps that currently exist*

There is currently no indicator for the outcome level given that we don't know the types of technologies we will be supporting. The area is however a priority, and the specific activities will be clarified through the annual analysis in 2.2.1. This indicator is an important commitment in that CEPI wants to be an agile and innovative organisation that can quickly to new science. When priorities are subsequently made, the results framework will be updated so that these are reflected on the outcome level (2.2). In any case, this outcome level will be reflected in a monitoring and evaluation plan, to be developed by end of 2019.

Engages 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 (output, box 2.3.1).

This means working with partners to design and implement clinical trials, engage relevant regulators and ethics review boards prospectively, ensure the security and reliability of the supply chain (including any needed cold-chain logistics), and prepare 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—composed of normative bodies, regulators, funders, organizations that support stockpiling 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 as needed with other partners to coordinate its response activities (outcome, box 2.3).

Related indicators from Results Framework

- ***Nr 12, TOC 2.3:*** *Percent of vaccine development partners with necessary agreements in place for vaccines to be deployed and tested during an outbreak*
- ***Nr 13, TOC 2.3:*** *Percent of vaccine development partners with plans in place for equitable access fully consistent with CEPI's Equitable Access Policy.*

Since CEPI wants to be a gap-filler and add value to what others are doing rather than duplicate, engaging with other end-to-end partners is arguably one of the most important things we do. Such engagement does however not manifest itself into a single indicator, but is rather an overall approach that CEPI takes to all of its operations in sharing information, conducting meetings and having an inclusive governance model. For the time being, we have therefore only defined indicators for the outcome level, but will reflect this output level in the monitoring and evalution plan. The rationale for

nr 12 is that whilst having vaccine available is a major step, being able and or allowed to use the products requires additional measures. Without these agreements in place prior to an outbreak, the vaccine will not be able to used when an actual outbreak occurs. Although similar to indicator nr 7, nr 13 is different in that the former measures the *intention/obligations* whilst the latter measures actual *compliance* towards one of the most important issues.

5.2.3 Strategic objective 3: Sustainability (box 3)

"Create durable and equitable solutions for outbreak response capacity"

To ensure that CEPI's approach is sustainable, CEPI

1. Improves the predictability of financing for vaccine development to address end-to end market failures
2. Drives efficiencies in vaccine development to reduce costs
3. Develops contingency plans to reduce risk so that successful vaccines are available during outbreaks

Improves 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 (output, box 3.1.1), and establishing long-term mechanisms for the maintenance of stockpiles, we can ensure that successful vaccines can reach affected populations during an outbreak (Outcome, box 3.1).

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 outbreaks 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.

Related indicators from Results Framework

- ***Nr 16, TOC 3.1:*** *Agreements in place with downstream partners on life-cycle financing a of CEPI-funded products, by disease area.*
- ***Nr 17, TOC 3.****1: $1bn raised as multi-year contributions to CEPI*

There are two important ways to aspects of improving the predictability of finance; i) raising funds and ii) clarify roles and responsibilities in financing. Neither of these aspects are binary in terms of achieving either an output or an outcome, but can rather be seen as a continuum in between. We have chosen to reflect both indicator 16 and 17 as outcomes, and rather provide a narrative update[7] on an annual basis to reflect outputs. Moreover, further detail on monitoring and evaluation of will be provided in a separate plan. While indicator 16 gives a reflection of whether other organisations align with CEPI's activities, nr 17 gives a depiction of whether CEPI is sufficiently financially robust to carry out its mission in full.

Drives efficiencies to reduce costs across the end to end spectrum of vaccine development (output 3.2.1 and outcome 3.2)

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

[7] I.e.: with reference to 17, an annual update will be given on total amount of funds raised.

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 emerging infectious diseases 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.

Related indicators from Results Framework

- ***Nr 18, TOC 3.2.1:*** *Percent of priority actions taken to achieve efficiencies*

Vaccine development is associated with a number of steps which can add significantly to costs and timelines. There are numerous areas which have the potential to be undertaken more efficiently, but it may be difficult to identify all up front. The above indicator pushes CEPI to identify areas where it can improve and implement actions to achieve associated efficiencies. When actions are identified and prioritised, the results framework may be amended with additional indicators to better reflect the outcome level of the theory of change.

Develops contingency plans to reduce risk so that successful products are available to support outbreak response. (output 3.3.1 and outcome, 3.3)

CEPI will establish 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" (ie, a vaccine manufacturing partner goes out of business), we have "plan B", which will enable continued vaccine manufacturing and distribution.

Related indicators from Results Framework

- ***Nr 19, TOC 3.3.1:*** *Percent of vaccine Partnership Agreements in place that contain contingency plans for manufacturing*

CEPI enters into each vaccine Partnership Agreement with an expectation that it will work with that partner from beginning to end. That said, in some cases a partner may be acquired by another company with more of a commercial focus. For this reason CEPI aims to have contingency plans in place for all its vaccine development efforts. Further, even after a grant has ended, there must be continued assurance that, in the case of an outbreak, high quality vaccine will be available for use. As such, CEPI needs to make sure there is "plan B" agreed should the original manufacturer be unable – or unwilling – to produce adequate quantity of the vaccine when it is needed. While this indicator covers the output level, we have not identified an appropriate measurement of the outcome level. The main reason for this is it is difficult to define avilability and populations in need up front, especially since CEPI may not be the primary organisation making the final decision on the actual allocation at the time of an outbreak. In the absence of an appropriate indicator, we will commit to reflecting this through a monitoring and evalutinos plan by end of 2019.

5.3 Impacts

By developing medical countermeasures in an equitable manner, CEPI can help to contain and mitigate future outbreaks. In doing so, low- and middle-income countries, and the world more broadly, will have strengthened capacity for reducing the risk of epidemics becoming humanitarian catastrophes, both nationally and globally as we've seen from outbreaks in the past, including the Ebola outbreak (see 2.1 Situation analysis). Through facilitating collaboration between actors in the end-to-end scope of vaccine R&D and global health preparedness, CEPI will work to ensure that its activities are aligned and supportive of the broader challenges of early warning of and response to outbreaks.

As outlined in section 0, the Ebola epidemic resulted in lives lost and negative economic impact. By taking part as both a funder and a facilitator in the areas of vaccine development, risk reduction through the development of rapid response capabilities, regulatory harmonization, national preparedness planning, and capacity building, CEPI's mission can help mitigate health crises and thereby their associated detrimental effects on human lives and economic growth. CEPI's activities thus align most closely with the following sustainable development goals of the United Nations:

- **SDG3:** Ensure healthy lives and promote wellbeing for all at all ages
- **SDG 8:** Promote inclusive and sustainable economic growth
- **SDG 17:** Strengthen the means of implementation and revitalize the global partnership for sustainable development

By helping to strengthen the capacity for reduction and management of national and global health risks, CEPI's mission can help contribute to SDG3. The same goes for SDG8, whereby CEPI's efforts are directed towards stopping outbreaks before they can cause widespread mortality and disruption, thereby mitigating their potential negative effect on economic growth. Our inclusive and collaborative approach to all of our activities, also aligns well with SDG17 in that CEPI "encourage(s) and promote(s) effective public, public-private and civil society partnerships, building on the experience and resourcing strategies of partnerships"[8]

[8] Target 17.7 of SDG 17: https://sustainabledevelopment.un.org/sdg17

6. Access to CEPI products

CEPI remains strongly committed to the bedrock principle of equitable access. To CEPI, "Equitable access to epidemic vaccines in the context of an outbreak means that appropriate vaccines are first available to populations when and where they are needed to end an outbreak or curtail an epidemic, regardless of ability to pay". This is articulated in CEPI's policy on "Equitable access", together with an outline of means to achieve it[9]. Given that the diseases CEPI targets primarily affect low-income countries, ensuring that developers are incentivised to advamce these products are just as important as affordability and delivery.

CEPI's current policy was updated in December 2018 following extensive consultations with CEPI's wider coalition partners, including civil society representatives, investors, academia and the pharmaceutical industry. The Board also took an active role in its redrafting, considering the importance of its application. The updated policy clearly articulates what is meant by "equitable access" and outlines pathways to achieve it for all our partners across multiple sectors including industry. It also supports access as a core value and ensure it can be achieved without impeding the ability of industry partners to advance products.

Specifically, CEPI will facilitate equitable access to epidemic vaccines by

1. Funding the development of vaccines and maintaining investigational stockpiles, to be used free of charge when an outbreak occurs
2. Coordinating with others in the global health community to enable licensure of vaccines funded by CEPI, including by securing resources for pivotal clinical trials
3. Collaborating with others in the global health community to ensure the procurement, allocation, deployment and administration of licensed vaccines to protect global health, at a price that does not limit equitable access and is sustainable to the manufacturer

CEPI will also ensure open access to data, results and publications arising from its funding and facilitate access to materials to accelerate vaccine development.
All entities that CEPI awards funds to have to accept and comply with these principles. A detailed description of all access provisions in all partnership agreements has been summarised to the Board and the general public.

Although not expected to, there may be situations where commercial benefits accrue to the awardee as a result of CEPI funding including both from licensed vaccines or from any other foreground IP generated from a CEPI funded project. In such situations CEPI will recoup a share of such commercial benefits or elect an alternate benefit sharing arrangement of equivalence commensurate with CEPI's investment. Any commercial benefits recouped by CEPI will immediately be returned to the funding pool for re-investment in other projects since CEPI is a non-profit organisation.

[9] The following documents provide additional detail on how CEPI works with equitable access: Partnership Template Agreement" and "Access Summary report".

7. Risk assessment and cross-cutting issues

CEPI places great emphasis on risk management. Risks are inherent to the global development and health sector. As it is not possible to avoid all risks, it is necessary to be *aware* of the risks we are exposed to and try to mitigate them to an acceptable level. A top risk register for CEPI's programme is set out in Annex C, which also includes assessments of a selection of cross-cutting issues. Policies and standard operating procedures are also seen as an integral part of giving legal, financial, reputational and operational assurances of CEPI and its subsidiaries taking the appropriate measures to managing risks and achieving outcomes. An overview of policies, procedures and guidance documents that are either signed off or planned is given in Annex D.

In the following, CEPI's risk management approach will first be set out. Secondly, CEPI's four risk categories will be explained. Finally, the risks and cross-cutting issues that are considered most serious in the attached risk framework are scrutinised in depth.

7.1 Risk management approach

CEPI's approach to risk management is set forth in a risk management policy, together with procedures with guiding principles and description of the process for risk management.

Every activity involves some kind of risk. CEPI does not aim to avoid all risks, but rather to make good decisions that enable achievement of the desired results. Effective risk management will protect CEPI assets and people and enable performance of both CEPI and its awardees in compliance with applicable laws and regulations. The CEPI approach to risk management is to deliver benefits for an appropriate level of effort and risk management should be integrated in daily ways of working.

Measures to raise awareness of risks amongst CEPI staff and awardees, as well as establishing a follow-up plan for the risks, will create a platform to mitigate and ensure respect for identified risks and cross-cutting issues. The risk management policy and procedure, include assessment of the risks, in addition to mitigating measures and follow-up plan.

In practical terms, every employee is responsible for assessing and monitoring the risks associated with their daily work, for managing and reducing these risks where reasonable, and for ensuring that the expected benefits of any significant activity outweigh the expected risks. In addition, clear areas of responsibility is set forth in the policy for the CEPI Board, the Audit Committee, the CEO, the Chief Financial Officer, the risk owners, and the Governance Risk and Compliance Manager.

Monitoring and governance will be carried out by the CEPI Board, the CEPI Leadership Team and the Chief Financial Officer, with the support of the risk owners and the Governance, Risk and Compliance Manager. Moreover, there will be conducted annual audits of CEPI accounts, by an external auditor appointed by the Board. The audit will be conducted in relation to International Standards on Auditing (ISA). CEPI is in addition seeking further assurance through its internal audit work, as detailed in the Annual Internal Audit Plan.

Awardees will be obliged to identify key risks to their development projects. These risks will be monitored by both CEPI's project management team and the Joint Monitoring and Advisory Group that will be established for each project, and risks and mitigating measures will be part of each milestone review.

7.2 Risk categories

CEPI has chosen to organise risks into four categories in its preliminary risk register. The categories in the list below include some examples of risks, however, a full overview of all risks can be found in annex C to this Programme Document:

Risk categories	Content explanation
Financial risks	Related to the management and control of CEPI resources.
Legal risk	Related to legal agreements
Operational risks	Related to inadequate or failed internal processes, people and systems
Reputational risk	Related to how CEPI is perceived by the general public

7.3 Assessment of the most serious risks

An important element of CEPI's operations is close collaboration with a diverse set of partners. Maintaining these relationships is key to CEPI's ability to deliver on its financing- as well as on its end-to-end scope. Loss of interest or engagement from key partners – including vaccine developers, investors, civil society or global health institutions – would be highly detrimental to CEPI's function and jeopardize its ability to succeed and therefore must be considered a serious risk. CEPI's broad-based governance structure is set up to mitigate this risk by ensuring the engagement and inclusion of stakeholders across the broad range of CEPI's activities. Amongst others, both the Investors Council and the reconstituted Joint Coordination Group are integral parts in meeting these needs.

Another major risk for CEPI are higher than expected rates of attrition for the vaccines that it is supporting. This entails that even if CEPI delivers all activities, successful vaccines will for some reason not be developed and thus there will not be any positive effect for the beneficiaries. Vaccine development is inherently risky and failure of vaccine candidates due to technical, safety or other reasons cannot be wholly avoided but the risks that lead to such failure can be managed. Since a proportion of CEPI-financed candidates will fail, it must invest in a sufficient number to increase the likelihood of positive outcomes at the end of the 5-year period. This entails that CEPI must i) have the necessary funds available to start the desired number of projects and ii) that CEPI invests in the most promising candidates. Moreover, the technical risk of cost overrun and delay must be dealt with both financially and by putting in place mechanisms to enhance the likelihood of achieving the desired results. These risks will be dealt with through CEPI's approach to establishing partnership agreements. CEPI will only commit to incremental funding based on the satisfactory achievement of defined milestones and will secure the option to stop funding at each major review. Thus, CEPI will maintain the ability to prioritize funding of the most promising projects over time through rigorous portfolio management.

Potential shortfalls in funding presents a serious risk for CEPI. There is much positive momentum from an increased awareness of the necessity of preparing for outbreaks that speak in CEPI's favour of being able to attract more resources. In the absence of the desired funding base, however, it is unlikely that CEPI will be able to achieve fully the strategic objectives. CEPI has therefore made considerable investments in developing a resource mobilization strategy that is closely aligned with its communications and advocacy efforts. CEPI will work closely with its investors to identify additional funders and to maximize the value of its investments. Additionally, CEPI is working closely with partners such as the EC and World Bank to coordinate funding of related capacity building activities in a way that supports CEPI goals so as to maximize CEPI's ability to concentrate its investments on vaccine development efforts. By design, CEPI's investment strategy allows CEPI to operate in a flexible manner to allow for fluctuations in resource availability and unanticipated requirements and will allow CEPI to divert resources to the areas of greatest need or perceived value.

In supporting vaccine research and development, challenges around vaccine access and intellectual property naturally arise and thereby pose as an inherent risk. If vaccines are developed before

epidemics occur, the global health community can potentially prevent outbreaks from becoming epidemics or pandemics, contain loss of life, limit social and economic disruption, and protect against future epidemics. The principle of equitable access is therefore core to CEPI's objectives and crucial to prevent epidemics. As a measure to ensure equitable access, CEPI has developed policies around intellectual property so that research and development material will be shared in situations when needed. Thus, the preferred approach of CEPI is not to take ownership of the intellectual property but to ensure access to the relevant information and vaccines, as described in CEPI's policies on equitable access, shared risks/shared benefits and management of intellectual property. Mutually agreed approaches to implementing these policies will be negotiated with CEPI's partners as elements of the partnership agreements, thereby giving CEPI the legal assurance that the products it seeks to develop are accessible by the populations in need. Furthermore, progress in implementing these three policies will be reported to investors.

Likewise, the principle of equitable access also reflects the risk of discrimination and gender inequality arising from CEPI operations. CEPI will therefore work to ensure non-discrimination and gender equality through reflecting the goals of the WHO and the OHCHR for health programmes and services to be available, acceptable, accessible, and of good quality, as set out in the UN Human-Rights Based Approach to Health.

Misconduct, anti-corruption and transparency will also be given particular focus in risk assessments and reporting. CEPI's standpoint regarding anti-corruption, transparency and conflict of interest have been set forth in policies, attached to this Programme Document, that guide all operations. In addition, CEPI has established internal standard operating procedures, including procurement and financial management procedures.

The speed CEPI is moving at, the heavy workload of continuing building the organisation, and staffing shortages, create risks which CEPI has developed mitigation steps against. Making permanent appointments has been prioritised, with all director level positions filled as of January 2018, new resourcing plan approved in the October 2018 Board meeting; and professional consultants have been appointed on an interim basis. An associated risk has been potential conflicts of interest, particularly recognizing the commercially sensitive nature of vaccine development, and the high number of consultants and advisors who support CEPI's work. A robust policy has been developed to mitigate against this risk; and more broadly protocols, checklists, and software put in place to prevent leakage or unwanted accessing of sensitive information due to human error or IT risks. CEPI has launched work streams to further strengthen the management of information and mitigate potential cyber risks of the organization.

8. Financial affairs

8.1 Budget

There has currently been committed funds to CEPI totalling MUSD 647 (at exchange rates per 28.01.19), and close to MUSD 750 counting an anticipated co-funding from the EC of MEUR90 . These commitments have come from sovereigns and philanthropies, and are in broad long-term commitments (see table 1). CEPI needs to be able to demonstrate results, value for investments and its financing needs to Investors. As such, the exact allocation of the committed amounts over the 5-year period, as depicted in Annex A, might be revisited depending on the budgetary flexibility of the Investor in question and the expected cash-flow requirements of CEPI in a given year. CEPI is now actively in the process of broadening its funding base, and specifically reach the $1bn target identified in CEPI's Preliminary Business Plan.

Table 2: Overview of current investors (per 28.01.2019)

Investor	
Germany	EUR 90 mill
Japan	USD 125 mill
Norway	NOK 1,6 bn
Gates Foundation	USD 100 mill
Wellcome Trust	USD 100 mill
Canada	CAD 14 mill
Australia	AUD 2 mill
Belgium	EUR 500 k
United Kingdom	GBP 10 mill

Annex A gives an excerpt of the 2017 & 2018 actuals, 2019 budget and CEPI's 5 year plan as presented to the Board in October 2019. The budget for the 2 out years of the (2020-21) was only shared for information to the CEPI Board, which recognized that there will be changes as funding requirements and timing of investor contributions is clarified. It should be noted that the budget is not fixed and that it will be updated in accordance with CEPI's planning cycle. Annual budgets for subsequent budget cycles will be presented to the Board for approval in the last quarter of the preceding year.

The main cost drivers of the budget are the Calls for Proposals as described in section 2. These directly answer to achievement of CEPI's strategic objectives of developing vaccines for both known and unknown emerging infectious diseases. The contracts that CEPI enters into with awardees will contain provisions that gives CEPI necessary flexibility in the event of or poor scientific results, funding constraints or strategic re-prioritization. CEPI's finance team will work in close collaboration with CEPI's portfolio team to ensure that changes in financial and R&D projections with awardees are accounted for in CEPI's financial management.

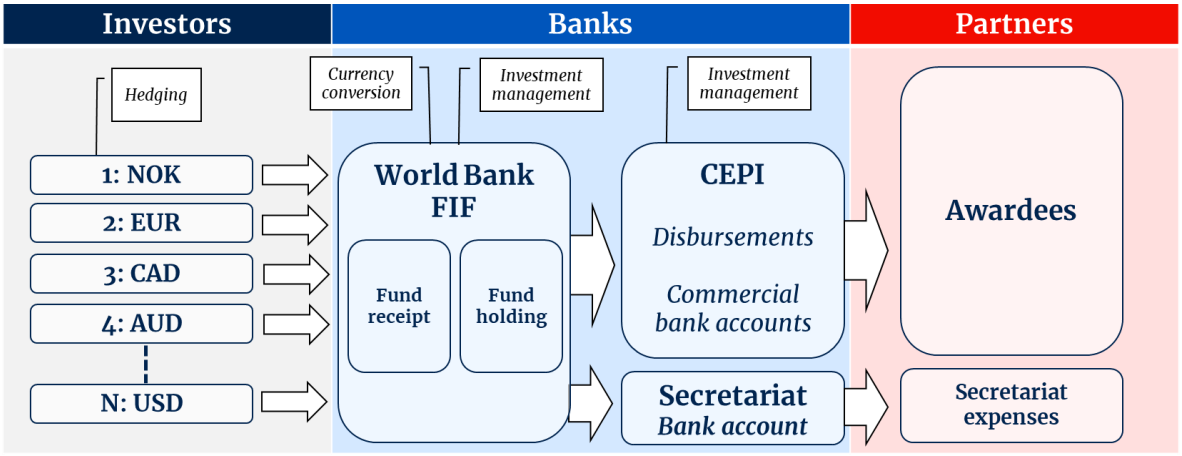
The Secretariat has been instructed by the Board to maintain a small and nimble organization. The planned resources within the current budget are understood as the minimal level of staff necessary to maintain an effective organization that can give an added value to the projects it funds. The Secretariat is being built in a way that allows it to manage considerably larger funds than is currently committed, acknowledging the economies of scale for the scope of investments that are planned. As CEPI does not view its function merely as that of funder, CEPI will work actively with awardees, regulatory agencies, multilateral organizations and vaccines developers to ensure a predictable and effective development pipeline. To achieve this, a diverse and highly skilled group of employees and consultants will be needed to fulfil CEPI's mission and CEPI will need to compete for these individuals on the open market, providing salaries for key positions that are competitive with the private sector.

CEPI will have annual financial reporting supported by reporting on the Fund's financial status from the World Bank, and has an external auditor to audit the annual accounts.

8.2 Fundholder arrangements

The World Bank has been established as CEPI's principal fundholder, and DNB as CEPI's operational banking partner. As depicted in Figure 9**Error! Reference source not found.** below, these arrangements serve to facilitate the financial flows between Investors and Partners, with CEPI as the intermediary.

Figure 9: CEPI flows and financing



Starting from the left, CEPI will receive funds from investors in a multitude of currencies. To mitigate risks of fluctuations, CEPI is constantly reviewing the currency exposure to avoid negative impacts on its budget, which is denominated in USD. The World Bank is the fundholder of CEPI funds through a Financial Intermediary Fund (FIF). The FIF will hold funds for as long as deemed necessary by CEPI, and disburse funds to commercial bank accounts upon the request by the CEPI Secretariat. Subsequently, funds will be transferred from the commercial bank accounts to awardees of CEPI projects according to individual project plans. The Secretariat will also have a separate account for operational expenses incurred in either of the CEPI Secretariat offices. Both the FIF and the commercial accounts will invest the positive balance at any given point in time under the CEPI requirements of liquidity and cash preservation. Hedging of currencies will take place in commercial banks[10], and supplemented by spot conversions in the FIF as needed.

Table 3 below provides an overview of services established and sought from the World Bank and commercial banks respectively.

[10] See Hedging Policy in Chapter 11 under the attachments

Table 3: overview of services provided by World Bank and Commercial banks respectively

Services	World Bank	Commercial banks
Hedging		☑
Investment management	☑	☑
Short term credit		☑
Currency conversion*	☑	☑
Fundholding	☑	☑
Operating bank accounts (NOR/UK/US)		☑
Awardee disbursements		☑

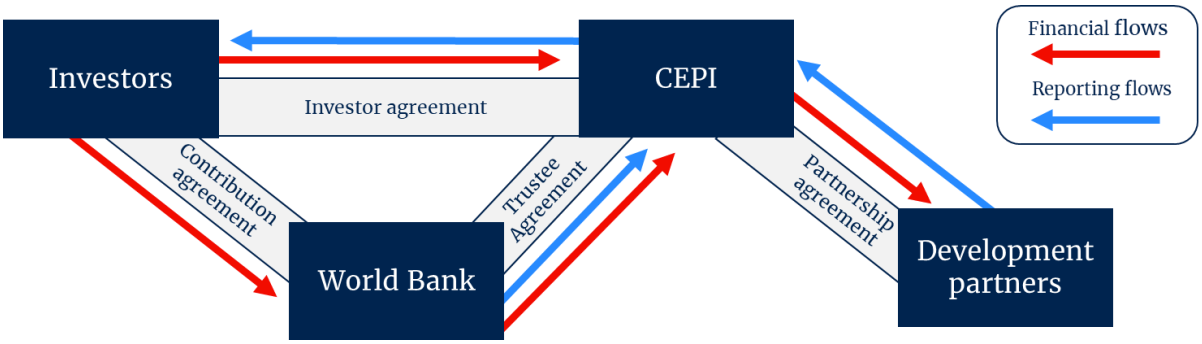
* Some, not all.

** The World Bank can execute spot currency conversions of received contribution payments

8.3 Reporting and financials

There are four types of entities involved in financial transactions for CEPI operations; i) Investors contributing funds, ii) the World Bank holding (most of) CEPI funds, iii) CEPI Secretariat – including its operational bank account and iv) the development partners CEPI awards funds to. The relationship between these entities are regulated by separate agreements, of which reporting to the grant-making entity is often the trigger for release of funds. An illustrative depiction is given in the figure below.

***Figure 10:** Relationship between entities involved in financial flows*



Annex A: Budget (as presented to the CEPI Board March 2019)

MUSD	Budget 2017	Budget 2018	Budget 2019	Plan 2020	Plan 2021	Plan 2022-25	Aggregate
Revenue	**82,2**	**113,3**	**187,6**	**173,6**	**197,9**	**0,0**	**754,6**
Norway (MNOK 1600)	11,9	17,1	93,8	30,0	45,0	0,0	197,8
Wellcome (MUSD 100,4)	1,7	20,0	0,2	27,3	51,2	0,0	100,4
BMGF (MUSD 100)	22,0	20,0	20,0	20,0	18,0	0,0	100,0
Germany (MEUR 90)	18,7	16,3	22,4	22,4	22,4	0,0	102,2
Japan (MUSD 125)	25,0	25,0	25,0	25,0	25,0	0,0	125,0
Australia (MAUD 6.5)	0,0	1,4	1,1	1,1	1,1	0,0	4,9
Belgium (MEUR 0,5)	0,0	0,6	0,0	0,0	0,0	0,0	0,6
Canada (MCAD 14)	2,8	0,3	6,7	0,8	0,0	0,0	10,7
UK (GBP 10)	0,0	12,6	0,0	0,0	0,0	0,0	12,6
EC CfP3i/ii (MEUR 90)	0,0	0,0	18,4	47,0	35,1	0,0	100,5
Investments	**0,0**	**34,7**	**149,4**	**183,6**	**197,9**	**169,1**	**745,9**
CFP1	$0,0	34,2	81,6	68,4	78,7	81,2	344,0
CFP2	$0,0	0,0	19,8	36,8	37,0	26,5	120,0
CFP3		0,0	16,0	36,0	48,5	43,2	143,7
Ebola	$0,0	0,0	10,1	20,4	18,2	16,2	65,0
Enabling Science	$0,0	0,5	21,9	22,0	15,5	2,1	62,0
EDCTP		0,0	3,7	3,7	3,7	0,0	11,2
Operating costs	**9,3**	**17,9**	**24,9**	**26,1**	**26,9**	**27,7**	**132,9**
Salary & Social	2,8	6,5	10,5	12,1	12,5	12,8	57,2
Consultants	4,4	8,0	8,8	8,3	8,6	8,8	46,9
Infrastructure	1,1	0,8	1,0	1,1	1,1	1,1	6,1
Travel	1,0	2,1	3,1	3,2	3,3	3,4	16,0
Service Providers/Other	0,1	0,6	1,4	1,5	1,5	1,6	6,6
Financial costs	**0,2**	**-3,5**	**5,0**	**-1,0**	**-1,0**	**-1,0**	**-1,3**
Cash Balance	**72,6**	**64,3**	**8,3**	**-35,1**	**-26,0**	**-195,8**	**-122,8**
Accumulated cash balance	**72,6**	**137,0**	**145,3**	**110,2**	**84,2**	**-111,6**	

Annex B: Results Framework

CEPI RESULTS FRAMEWORK - INDICATORS
Prepared by the CEPI Secretariat

Introduction

This Results Framework has been developed October 2018 and presented to the Investors Council. As CEPI continues to evolve, additional indicators may be added and existing reviewed, following consultation with our Investors.

Of note, while CEPI aims to contribute to achievement of these outputs and outcomes, success or failure cannot be attributed slely to CEPI as it is only one of many actors working in the field and part of a complex ecosystem of vaccine R&D. While for impact and outcomes, the indicators focus on the broader ecosystem changes required for CEPI to achieve success, for outputs, to the extent possible, the indicators aim to capture progress in the main areas of CEPI investments through its calls for proposals and other activities. Measurement of outputs aims, to the extent possible, to link with grantee reporting such that grantee performance links to CEPI's assessment of its overall performance. Also, while results related to outputs should be achievable within the next 5 years, results related to outcomes and impact are purposefully ambitious within this time period. Under the "Output and Outcome" level, the number of the "TOC level" corresponds with the boxes in the figure 7 in chapter 5.1.

Updated April 2019

Indicator number	TOC number	Indiactors	Baseline Y0	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 CEPIs 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 P1 trials	Lassa: 0	Progress towards targets reported	Lassa: 2	Lassa: 3	Lassa: 3	
8	1,1,1 b	Number of vaccine candidates advanced through P1 trials	Nipah: 0	Progress towards targets reported	Nipah: 0	Nipah: 3	Nipah: 3	
8	1,1,1 b	Number of vaccine candidates advanced through P1 trials	MERS: 0	Progress towards targets reported	MERS: 1	MERS: 2	MERS: 3	
8	1,1,1 c	Number of vaccine candidates advanced through P2 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 P2 trials	Nipah: 0	Progress towards targets reported	Progress towards targets reported	Nipah: 0	Nipah:1	Nipah:3
8	1,1,1 c	Number of vaccine candidates advanced through P2 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 P1 100%	Subject to successful completion of P1 100%	Subject to successful completion of P1 100%	Subject to successful completion of P1 100%	Subject to successful completion of P1 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 P2 100%	Subject to successful completion of P2 100%	Subject to successful completion of P2 100%	Subject to successful completion of P2 100%	Subject to successful completion of P2 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 products through preclinical		
14	2,1,1 b	Number CfP2 vaccine candidates progressing through P1	0	Progress towards targets reported	Progress towards targets reported	Progress towards targets reported	6 products progressed through Phase I	
15	2,2,1	Annual analysis of available technologies and the gaps that currently exist	N/A	Annual update	Annual update	Annual update	Annual update	Annual update
	2.2	The outcome level on "Facilitated field use and rapid response" does currently not have an indicator. The reason for this is that without having defined which technologies CEPI will support under this priority, it is difficult to define an indicator that accurately reflects the associated outcome. When priority areas here are identified, CEPI will amend its results framework to capture this.						
	2,3,1	The Secretariat did not find a telling indicator for the output level. Engaging end-to-end partners could arguably be defined as an indicator, but the framing here suggests that it could also be an output. An indicator on meetings held etc was considered, but not deemed as helpful in this context						
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
	3,2	The difficulty with defining this indicator up-front relates to the multitude of areas that can potentially be a source of reductions in costs or timelines. As is reflected in the section "5.***Error! Reference source not found.*** ", CEPI was able to drive reduction in both timelines and costs as part of its CFP process in 2018. 2019 however will likely not see efficiencies in the same areas as the portfolio will be established. As such, CEPI will – for the time being – consider from time to time which areas make sense to report on. The process for this will be						

		further detailed in a monitoring and evaluation plan. As part of this exercise CEPI may also be able to identify appropriate indicators for this outcome level.						
	3,3	Availability of products is supported by a multitude of activities and the associated complexity was difficult to depict in a theory of change. Moreover, availability will ultimately depend on other actors than just CEPI, who will deliver the vaccine in the field and help define target populations.						
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%

Impact level

The following indicators under this sub-heading have been developed by the UN. The Secretariat has chosen to monitor these, as they relate to CEPI's strategic objectives. Some of the indicators have not been finalized by the UN, and the Secretariat will thus update the below definitions as changes are made. All indicators have been collected from the UN site for the Sustainable Development Goals.

SDG 3: Ensure healthy lives and promote well-being for all at all ages. (TOC LEVEL 0.1)

3.B.2 Development assistance to medical research & basic healthcare

Definition: Indicator 3.B.2 is the total net official development assistance (ODA) to medical research and basic health sectors.
Goal: By 2030 Support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries, providing access to affordable essential medicines and vaccines for all.

3.D.1 Health emergency preparedness

Definition: Indicator 3.D.1 is the International Health Regulations (IHR) capacity and health emergency preparedness.
The IHR Core capacity index is measured as the percentage of attributes of 13 core capacities that have been attained at a specific point in time. The 13 core capacities are: (1) National legislation, policy and financing; (2) Coordination and National Focal Point communications; (3) Surveillance; (4) Response; (5) Preparedness; (6) Risk communication; (7) Human resources; (8) Laboratory; (9) Points of entry; (10) Zoonotic events; (11) Food safety; (12) Chemical events; (13) Radionuclear emergencies.
Goal: By 2030 Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks.

SDG 8: Promote sustained, inclusive and sustainable economic growth (TOC LEVEL 0.2)

8.1.1 GDP per capita growth rate

Definition: Indicator 8.1.1 is annual growth rate of real GDP per capita.
This is measured as the annual percentage growth in gross domestic product (GDP) per capita based on constant local currency.
Goal: Sustain per capita economic growth in accordance with national circumstances and, in particular, at least 7 per cent gross domestic product growth per annum in the least developed countries through 2030.

SDG 17: Revitalize the global partnership for sustainable development (TOC LEVEL 0.2)

17.6.1 Science and technology cooperation

Definition: Indicator 17.6.1 is the number of science and/or technology cooperation agreements and programmes between countries.
Goal: Enhance North-South, South-South and triangular regional and international cooperation on and access to science, technology and innovation by 2030.

Facilitates the establishment and maintenance of investigational stockpiles and development of robust plans to allow for trials and eventual deployment of vaccines during outbreaks	
Indicator 5 **TOC level 1.1**	Number of vaccine candidates in investigational stockpile for outbreak situations and ready for efficacy studies and emergency use
Definition	Readiness is defined as meeting criteria for Good Manufacturing Practice (GMP) released stockpile of at least 100,000 doses.
Rationale for use	GMP enables stockpiling for efficacy testing and outbreak use.
How it is measured	"Readiness" will be measured as a binary indicator.
Baseline and Target(s)	Baseline: 0 Target (2022): At least 4 candidates for at least 2 priority diseases (Lassa, MERS, and/or Nipah).
Data source and reporting frequency	Awardee milestone reporting and documentation from Stage Gate review.11 Progress reported annually with deliverable due end 2022.
Limitations	This indicator will likely only show progress (or not) at the end of the 5-year period and thus it is not adequately sensitive to show annual progress or inform year-to-year decision-making. Also, some of CEPI's investments will not result in viable candidates developed. As such, success cannot be guaranteed for this indicator in this time period for each of the disease areas. However, number of candidates having passed go/no-go criteria according to contracted milestone plans can be monitored annually. Finally, while ability to test vaccines in the initial stages of an epidemic is critical, it does not guarantee capacity or ability to sustainably manufacture or stockpile sufficient supply.

Facilitates the establishment and maintenance of investigational stockpiles and development of robust plans to allow for trials and eventual deployment of vaccines during outbreaks	
Indicator 6, **TOC level 1.2**	Percent of vaccine Partnership Agreements that have manufacturing plans in place to enable vaccine production in response to an outbreak.
Definition	"In place" means defined and documented through Partner Agreements (concluded agreements between CEPI and awardees) for manufacture of an investigational stockpile of vaccine or commitment to production in response to an emergency, following achievement of appropriate development milestone.
Rationale for use	Deployment of an investigational vaccine in a trial or under an emergency use setting requires that grantees have articulated and agreed manufacturing development plans and are ready to manufacture upon request from CEPI.
How it is measured	Manufacturing development plans are one of the conditions of a CEPI award and included in the basic contracts with grantees. "In place" is defined as binary variable (yes/no) measured by submission of plan for an investigational stockpile and all related partner agreements to CEPI Secretariat. The nominator for this indicator is the candidates for which

[11] Stage Gate review for CEPI investments will include CEPI staff and SAC members

	plans are specified in Partnership Agreements with CEPI. The denominator is awards have entered phase II development (or beyond).
Baseline and Target(s)	**Baseline**: n/a **Target:** 100%
Data source and reporting frequency	Awardee contracts as verified by CEPI secretariat; reported annually.
Limitations	This indicator is only relevant for projects conducting reached phase II clinical trials or beyond. As noted above, while an agreement around stockpiling is necessary to enable deployment, it is not sufficient. There are any other aspects that must be addressed both on the "supply" (e.g. volume, times length of maintenance) and "demand" (e.g. stockpiling financing and operation). Also, while obligations are broadly defined in the standard award agreement, details will likely evolve over time including through development of operating procedures or other documents. Finally**,** Whilst having vaccine available is a major step, being able and or **allowed to use** the products requires additional measures.

Facilitates the establishment and maintenance of investigational stockpiles and develops robust plans to allow for trials and eventual deployment of vaccines during outbreaks.	
Indicator 7 **TOC level 1.2**	Percent of vaccine development partners agreeing to terms that are fully consistent with CEPIs Equitable Access Policy and implementation guidance
Definition	Agreement defined as having terms and conditions in CEPI partnership agreements that are fully in alignment with CEPI's Equitable Access Policy and implementation guidance
Rationale for use	CEPI's equitable access policy and associated implementation guidance describes the terms to be included in CEPI Partnering Agreements to ensure the output and outcome of the funded projects meet CEPI's mission.
How it is measured	Numerator is development partners that have agreed to CEPI's access policy; denominator is total number of partners (including those actively receiving funding and ever having received funding). If a partner has more than one award it must agree to the access policy for all awards.
Baseline and Target(s)	Baseline: 0 Target: 100%
Data source and reporting frequency	CEPI partner agreements. Reporting upon signing of agreement and subsequently depending on results of Access Advisory Group.
Limitations	The current access policy is now under revision thus partners who already have grants from CEPI many not agree to the revised policy. Further, CEPI is establishing an independent Access Advisory Group to offer advice as to whether CEPI partner agreements are consistent with CEPI's Equitable Access Policy. That advice may reveal that one or more CEPI partnership agreements are not, in fact, consistent with CEPI's Equitable Access Policy.

Invests in promising candidates targeting EIDs to drive development of vaccines where markets incentives are insufficient.	
Indicator 8, **TOC level 1.1.1**	Number of vaccine candidates – for each priority disease – advanced through preclinical, phase I and phase 2a clinical trials

<table>
<tr><td>Definition</td><td>“Advancement” defined as having met project reporting milestones and undergone Stage Gate review for “go” decision to the next phase of clinical development.</td></tr>
<tr><td>Rationale for use</td><td>This measure captures the extent projects are progressing and allows CEPI to evaluate the overall success of its portfolio approach.</td></tr>
<tr><td>How it is measured</td><td>Number of funded candidates that have received a “go” decision at the Stage Gate review.</td></tr>
<tr><td>Baseline and Target(s)</td><td>Baseline: 0 for all, except for Nipah and MERS (1 for preclinical)
Target:
<table>
<tr><th></th><th>2018</th><th>2019</th><th>2020</th><th>2021</th><th>2022</th></tr>
<tr><td>Preclinical</td><td>Lassa: 1
Nipah: 1
MERS: 1</td><td>Lassa: 3
Nipah: 3
MERS: 2</td><td>Lassa: 4
Nipah: 4
MERS: 3</td><td>Lassa: 4
Nipah: 4
MERS: 4</td><td></td></tr>
<tr><td>P1</td><td></td><td>Lassa: 2
Nipah: 0
MERS: 1</td><td>Lassa: 3
Nipah: 3
MERS: 2</td><td>Lassa: 3
Nipah: 3
MERS: 3</td><td></td></tr>
<tr><td>P2</td><td></td><td>Progress towards targets reported</td><td>Lassa: 0
Nipah: 0
MERS: 1</td><td>Lassa: 2
Nipah:1
MERS: 1</td><td>Lassa: 3
Nipah:3
MERS: 3</td></tr>
</table></td></tr>
<tr><td>Data source and reporting frequency</td><td>Awardee milestone reporting and documentation from Stage Gate review. Progress reported annual with deliverable due end 2022.</td></tr>
<tr><td>Limitations</td><td>The definition of “advancement” is relative to the initial stage of investment and does not in itself imply readiness for stockpiling. Further, the number of candidates advanced will depend on the success of particular investment. Taking a portfolio approach to investments, in order to move four to six candidates to proof of concept for example, CEPI has estimated that it would need to invest in 14 candidates (at different stages of clinical or preclinical investments). This assumption may be incorrect and subject to a diverse set of risks. Furthermore, while estimated timelines are specified by awardees in project Gantt charts submitted to CEPI, product development timelines are subject to multiple risks and delays, making it difficult to guarantee that the given estimates will be met within a particular time period. Timelines will be added and updated following contract negotiations for CFP1.</td></tr>
</table>

Provides expert assistance and funds enabling science and technologies to enhance vaccine development efforts	
Indicator 9 **TOC level 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
Definition	**Biological standards** include sera, antibodies, antigens, pseudo-virus and virus-strains for use in various assays, and challenge models to be used by all awardees as reference in measurements and immunological evaluation of vaccine immune responses of various vaccine formulations. **Biological Assays** for measuring immune responses following vaccination come in many forms and variations. From a simple ELISA measuring the total antibody response against a vaccine specific antigen to various neutralization assays (e.g. Plaque Reduction Neutralization Test (PRNT) for quantitation of the amount of virus neutralizing antibody in a serum). These are biological assays and the inherent and inevitable nature of such assays can lead to substantial variation in the results obtained. Efforts to

	harmonize the results of these tests through internal calibration using a common antibody standard are of therefore of the utmost importance. "Availability" for "Biological Standards" means available for use by awardees as well as non-CEPI vaccine developers. **Validation** of an assay means to assure and document that the assay performs as expected regarding specificity, sensitivity and reproducibility. Inter- and intra-laboratory variability of results is also often studied and reported. Internationally acknowledged Biostandards are most often developed under the auspices of WHO's Expert Committee on Biological Standardization (ECBS). Proposed projects for standard development are first presented to the ECBS (meets once a year in October) where they are discussed and, if the ECBS is positive about the proposal, endorsed. The development of an International Reference Preparation (IRP) usually takes more than 18 months and involves testing in a number of different laboratories worldwide. The result of the inter laboratory study is finally submitted to the ECBS and the outcome published in the WHO Technical Report Series. If the data are satisfactory, the ECBS establishes the defined candidate material as an IRP.
Rationale for use	By using the same standards and harmonized assays it will be possible to compare the performance of the different vaccine candidates.
How it is measured	Availability measured as binary value (yes/no)
Baseline and Target(s)	Baseline: 0 Targets: • by 2020 the necessary Biological Standards for evaluation of immune responses against Lassa fever, Nipah and MERS-CoV will be developed; • by 2022 at least one validated assays for each of the three prioritized diseases will be used for evaluation and comparative measurements of the CEPI supported vaccine projects
Data source and reporting frequency	Reports from disease-specific Task Forces within CEPI's Working Group on Standards, Assays and Animal Models (WG-S&A). Progress reported annually with deliverables due end 2020 and end 2022.
Limitations	It is always a challenge to harmonize the assay and measurement activities performed by all vaccine developers in the field. However, if common standards and suggested assays are provided early in the development project it will increase the chance of more universal use of these important reference materials. CEPI's WG-S&A and its respective Task Forces give advice on priorities in this area. The WG-S&A is co-Chaired by WHO, and the members come from key international normative organizations. CEPI support to the development of standards is organized and performed in such a way that it is compatible with WHO International Reference Preparations (IRP) and aims to be acknowledged by the WHO Expert Committee on Biological Standardization (ECBS). While CEPI does not have as its mission developing and establishing IRPs, nor does it have direct control over the decisions of this group, the intent is that the CEPI efforts would end up as IRPs, presented in WHO Technical Report Series. Note that it is only the Antibody Standards that CEPI can promise to provide for all. Antigens might be more difficult and limited).

Provides expert assistance and funds enabling science and technologies to enhance vaccine development efforts	
Indicator 10 **TOC level 1.2.1**	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
Definition	"Relevant engagement" defined as submission of the following documentation to SRAs and NRAs in affected countries, by stage, as follows End preclinical/move to phase I (Stage Gate 1): Scientific advice for CTA/Pre-IND package. End phase I/move to phase II (Stage Gate 2): End of phase I, type C meeting/scientific advice, CTA for phase II, submission of CTA to NRAs in affected countries. Emergency use options discussed with key unaffected NRAs and relevant affected NRAs (i.e. AVAREF or similar regional WHO body).
Rationale for use	Decision on use of vaccine requires agreement between regulatory agencies and applicants. Achieving this in a timely and efficient manner to enable use in an emergency and eventual licensure requires regular and on-going dialogue on a project by project, stage by stage basis.
How it is measured	The numerator is the number of projects with adequate documentation of submission per milestones specified in project Gantt charts. The denominator is the number of active projects. Projects stopped will be excluded from consideration.
Baseline and Target(s)	Baseline: N/A Target for each of the three diseases in every stage: 100 percent
Data source and reporting frequency	Copies to CEPI of awardee CTA/IND submissions and responses obtained from regulatory submissions and scientific advice with regulatory authorities; reported annually.
Limitations	As part of the reporting, awardees will be contractually required to submit the actual documentations submitted to the regulator and responses and minutes received in return. Regulatory requirements differ by regulatory jurisdiction, so submissions may not always be fully comparable. Of the current projected investments, 14 awardees will require (CTA/pre IND) scientific advice for moving between preclinical and clinical. Numbers will depend on how many of the projects are successful. Given uncertainty and likelihood that some projects will not be assessed as "go", the indicator has been defined as percent of projects that remain funded (e.g. have passed go/no go decision making) rather than percent of total projects ever funded.

Invests in platforms to speed the development and manufacture of vaccines	
Indicator 11, **TOC level 2.1**	Number of vaccine platform technologies that can be rapidly adapted to develop vaccines against unknown pathogens for use in humans
Definition	"Unknown pathogen" refers to an as yet unspecified emerging or re-emerging viral pathogen for which no licensed vaccines exist. "Rapidly" is defined as "characterized" with the ability to be ready for clinic in 4 to 6 months after the antigen sequence is identified. "Characterized" is defined as having met a series of technical criteria (see below).
Rationale for use	Platforms can accelerate R&D, manufacturing, and clinical evaluation. For a platform to be useful in the case of an outbreak, it must be both versatile (i.e., able to be used against multiple pathogens) and well-characterized in terms of safety and immunogenicity, so that it exhibits reasonably predictable behavior characteristics when adapted to a new antigen (i.e. safety, immunogenicity and manufacturability). This indicator aims to measure the extent to which platforms themselves are being characterized.
How it is measured	Platform is characterized if it meets <u>all</u> the following criteria:

	• At least two vaccine candidates (targeting viruses from different families) should be tested in phase I clinical trials on the given platform. • Associated with a predictable and acceptable safety profile in humans. • Induces a predictable set of robust immune responses in humans. • Adaptable to new antigens within a specified time frame (as defined by CEPI on a platform by platform basis). • Platform owner has a manufacturing plan for production of materials during outbreak response. Platform can be rapidly adapted if it: • Demonstrate ability to be ready for the clinic in 4 to 6 months from the time of antigen identification.
Baseline and Target(s)	Baseline: 0 Target (2022): 2 or greater, including at least one novel (innovative) platform, i.e., that has no prototyped licensed vaccine.
Data source and reporting frequency	Awardee milestone reporting and documentation from assessment during Stage Gate reviews. Progress reported annually and upon completion.
Limitations	As with other outcome indicators, this indicator will likely only show progress (or not) at the end of the 5-year period and thus it is not adequately sensitive to show annual progress or inform year-to-year decision-making. Also, some of CEPI's investments will not result in viable platforms developed. As such, success cannot be guaranteed in this time period. However, number of platforms having passed go/no-go criteria according to contracted milestone plans can be monitored annually. This includes preclinical immunogenicity studies, preclinical efficacy studies, and Phase I clinical studies, which will involve detailed immune monitoring.

Engages end-to end partners to plan for the deployment of vaccines during outbreaks	
Indicator 12, **TOC level 2.3**	Percent of vaccine development partners with necessary agreements in place for vaccines to be deployed and tested during an outbreak
Definition	"Development partner" denotes an entity receiving funding from CEPI for vaccine development. "Necessary agreements" are defined as agreements related to a) stockpiling, b) manufacture, and c) clinical protocols. "In place" means defined and documented through Partner Agreement
Rationale for use	Whilst having vaccine available is a major step, being able and or **allowed to use** the products requires additional measures. Without these agreements in place prior to an outbreak, the vaccine will not be able to used when an actual outbreak occurs.
How it is measured	"In place" is measured as binary variable (yes/no). The nominator for this indicator is awardees that have agreements in place for all the areas listed above (a, b, c). The denominator is all concluded agreements.
Baseline and Target(s)	Baseline: N/A Target: 100%
Data source and reporting frequency	Awardee contracts as verified by CEPI secretariat (Director of Vaccine Development); reported annually.
Limitations	This indicator is only meaningful if the vaccine development process has advanced sufficiently such that there is a vaccine to deploy and test during an outbreak. Also, deployment will require resolution of other key issues such as product liability. While obligations are broadly defined in the standard award agreement, details will likely evolve over time including through development of operating procedures or other documents. Further while having an

	agreement to act is necessary first step, it does not guarantee appropriate implementation (e.g. timeliness, quality).

Engages end-to end partners to plan for the deployment of vaccines during outbreaks	
Indicator 13, TOC level 2.3	Percent of vaccine development partners with plans in place for equitable access fully consistent with CEPI's Equitable Access Policy.
Definition	"Plans in place" are defined as submitted to CEPI as part of annual reporting following stage gate review of progression from Phase 1 to Phase 2 trials. "Fully consistent" means consistent with the implementation guidance associated with the equitable access policy.
Rationale for use	While creating an effective vaccine is a critical milestone, there is no guarantee that once a vaccines has been developed it will reach those who need it most. By requiring an access plan, CEPI is requiring developer to plan in advance how the vaccine will be priced to promote equitable access once it has passed regulatory and other requirements.
How it is measured	Following contract is signed or stage gate passed need to put forward plan for access.
Baseline and Target(s)	Baseline: N/A Target: 100% of projects which have passed stage gate review for progression from Phase I to Phase II trials.
Data source and reporting frequency	CEPI development partner reporting as reviewed and confirmed by the Access Advisory Group
Limitations	Vaccine development must be undertaken with the end-user in mind. Waiting for stage gate review following Stage 1 may be late for development of access given the complexity of delivering a vaccine to end users. As such it is important to have an access commitment from the developer also at the initial signing of the agreement with CEPI.

Invests in platforms to speed the development and manufacture of vaccines	
Indicator 14, TOC level 2.1.1	Number CfP2 vaccine candidates progressing through preclinical and P1
Definition	CfP2 candidates defined as those that address diseases listed in the CFP2 call text and that have passed through either preclinical or phase I development using a CEPI funded platform.
Rationale for use	While the development of platforms is the ultimate goal, the development of pathogen specific vaccines are also an important activity that has value in itself in addition to being a "means to an end." As such, this indicator measures a different aspect of success – the number of individual pathogen specific vaccines that are progressing as assessed at each Stage Gate review.
How it is measured	# of funded candidates assessed at each Stage Gate review.
Baseline and Target(s)	Baseline: 0 Target: 8 products through preclinical and 6 products progressed through Phase I.
Data source	Awardee milestone reporting and documentation from Stage Gate review.
Limitations	While it is not CEPI's aim to develop products against other priority diseases and there is risk of failure in this area, it is also important to

	capture success as a reflects a positive externality of CEPI's work. Also, while progress through Phase I would represent a significant contribution to both science and public health, CEPI has may not have a mandate to take forward products which do not address its priority disease areas. There is some reputational risk to measuring this as output as it may suggest some responsibility or obligation to further development or engagement. Timelines will be added and updated following contract negotations for CFP2.

Supports the development of technologies to facilitates field use and rapid response	
Indicator 15, **TOC level 2.2.1**	Annual analysis of available technologies and the gaps that currently exist
Definition	"Gaps" defined as those technologies requiring action or investment.
Rationale for use	In order to enable timely response, it critical to understand gaps based on up-to-date knowledge.
How it is measured	Binary (published/not published) on annual basis.
Baseline and Target(s)	Baseline: n/a Target: annual update from 2019 onward.
Data source and reporting frequency	The analysis will be based on published sources, grey literature, and expert knowledge and will be updated every year.
Limitations	Data required can be extensive and requires manufacturer willingness to share publicly status of portfolio and funding needs. Also estimates of funding needs for different stages of clinical development can differ and thus the methodology will need to be peer reviewed and agreed prior to publication of first report.

Improves the predictability of financing to address end-to end market failures	
Indicator 16, **TOC level 3.1**	Agreements with downstream financing partners in place for each of CEPI's priority diseases.
Definition	"Financing agreement" defined as agreement to purchase and roll out the vaccines if developed and approved for use. "In place" means public commitment to fund. "Downstream financing partner" means multilateral institutions, NGOs, government agencies, public-private partnerships and others whose missions include financing vaccine procurement, delivery or development not covered by CEPI's funding scope.
Rationale for use	*In order for a vaccine to be accessible once it has passed clinical and regulatory requirements, there must be adequate financing including for manufacturing, stockpiling and delivery.*
How it is measured	Public commitment is measured signed agreement, publicly announced board or senior management decision
Baseline and Target(s)	Baseline: 0 Target: 3 (1 for each disease - Lassa, Nipah and MERS)
Data source and reporting frequency	Public documents by funders committing uptake of vaccine if and when developed and approved for use.
Limitations	The decision for financing by a downstream partner is not within direct control of CEPI. Also, a decision to prioritize funding does not necessarily mean funding or appropriate distribution systems will be available at time of outbreak.

Improves the predictability of financing to address end-to end market failures	
Indicator 17, **TOC level 3.1**	$1bn raised as multi-year contributions to CEPI
Definition	"Raised" defined as existence of legally binding commitments by donors to CEPI.
Rationale for use	$1B reflects preliminary CEPI 5-year modelling that estimated for costs to advance 4-to 6 candidates against 2 to 3 disease to the end of clinical phase IIa development. Multi-year funding serves as an indicator of financial predictability, which a key variable for incentivizing vaccine developer participation.
How it is measured	Measured in US dollars at time of commitment. Legally binding means signed agreement in place between donor and CEPI.
Baseline and Target(s)	Baseline: $630M Target (2019): $1BN
Data source and reporting frequency	Signed donor agreements; progress reported annually.
Limitations	This modelled estimate of financing may not be sufficient to cover the investment requires over the 5-year period.

Drives efficiencies to reduce costs across the end to end spectrum of vaccine development	
Indicator 18 **TOC level 3.2.1**	Percent of priority actions taken to achieve efficiencies
Definition	"Priority" defined as on those actions on critical path to achieve efficiency. These will be identified and prioritized during an annual scoping and analysis exercise to be initiated in 2019. "Efficiencies" refers to a reduction in development costs, timelines and/or cost of delivery with the aim of speeding development and sustaining access.
Rationale for use	Vaccine development and associated regulatory processes have a number of steps which can add significantly to cost and timelines and in numerous areas there are potential for efficiency (eg. joint clinical application reviews in case of an emergency; data master files). Similarly, there are steps which can be taken during vaccine development to ultimately reduced costs including of manufacturing and vaccine delivery, which if achieved, could reduce the EID funding gap.
How it is measured	Denominator will be priority areas identified each year. Numerator will be number of areas where CEPI actions are intended to address issues identified and which has resulted in a reduction of development timeline and/or cost of production and vaccine delivery % refers to percent of identified actions taken.
Baseline and Target(s)	Bassline: n/a Target: 2018 (N/A): 2019 (50%); 2020 (50%); 2021 (50%); 2022 (50%)
Data source and reporting frequency	CEPI internal reports as validated by SAC; reported annually.
Limitations	It is difficult to determine in advance opportunities for efficiency and associated trade-offs. Also, the priority identified and the extent to which it has been addressed will be determined by CEPI and thus in some cases may lack external validation or verification.

Develops contingency plans to reduce risk so that successful products are available to support outbreak response	
Indicator 19, **TOC level 3.3.1**	Percent of vaccine Partnership Agreements in place that contain contingency plans for manufacturing
Definition	"Contingency plans" are defined plans so that the vaccine can manufactured in perpetuity, including if the original developer is unable or unwilling to continue the program. "In place" means defined and documented through Partner agreements (concluded agreements between CEPI and awardees).
Rationale for use	CEPI enters into each vaccine Partnership Agreement with an expectation that it will work with that partner from beginning to end. That said, in some cases a partner may be acquired by another company with more of a commercial focus. For this reason CEPI aims to have contingency plans in place for all its vaccines development efforts. Further, even after a grant has ended, there must be continued assurance that, in the case of an outbreak, high quality vaccine will be available for use. As such, CEPI needs to make sure there is "plan B" agreed should the original manufacturer be unable – or unwilling – to produce adequate quantity of the vaccine when it is needed.
How it is measured	Manufacturing contingency plans are one of the conditions of a CEPI award and included in the basic contracts with grantees. "In place" is defined as binary variable (yes/no) measured by submission of plan and all related partner agreements to CEPI Secretariat. The nominator for this indicator is candidates for which plans are in place. The denominator is all vaccine awards (active and past).
Baseline and Target(s)	**Baseline**: n/a **Target:** 100%
Data source and reporting frequency	Awardee contracts as verified by CEPI secretariat; reported annually.
Limitations	While a contingency plan for manufacturing mitigates some of the risk related to manufacturing, it will also carry its own associated risks. Having a plan does not mean it will be successful enacted, when required. Also, in addition to manufacturing, there are other critical areas that will require contingency planning, including around stockpiling, regulatory pathways, and eventual distribution. Finally, while this indicator represents a commitment, the success of the contingency plan can only be evaluated if and when required in the case of an outbreak.

Annex C: Risk register

TOP RISKS CEPI									
	Category	Risk description	Probability	Consequence	Risk prior to mitigating	Mitigating measures	Risk after mitigation	Risk Owner	progress on Status mitigating measures
1	Reputational, Financial, Legal, Operational risk	CEPI not developing safe and effective vaccines five years after launch	M	H	H	1. Ensure partner contracts are agreed in a timely manner. Procure suitable insurance coverage for legal risks related to use of vaccines. 2. Rigorous assessment of funded projects by Secretariat, SAC and independent expert reviewers in advance of start 3. Close follow up of projects through JMAG, milestones and stage gate reviews. Since the selected CEPI partners are small biotech companies in consortia with academic partners and CROs, this requires significant staff increase to allow close follow up of all projects. 4. Balancing portfolio of development projects 5. Project failure hedged against through investment strategy and portfolio review 6. Ensure clarity about what CEPI is responsible for and where there are dependencies on others	M	CEO	1. The first partner contracts are signed. Legal risk related to future vaccine use considered and will be insured against in due time. Insurance needs currently under review. 2. CfP1 and CfP2 processes have been very thorough on technical assessment. Financial and integrity due diligence performed on all awardees. CfP3 due diligence planned. 3. Principles agreed in partner contracts and need for additional staff estimated based on realistic number of projects. October 2018 Board approved staff increase, recruitment process ongoing, expected completed Q4 2019. 42 of 66 hired pr Feb 2019. 4. Assessment of re-opening/rolling calls initiated, to be raised at the March Board meeting. 5. Investment strategy signed off by Board, portfolio review principles under development. First annual potfolio review planned Q3-Q4 2019. 6. Continuous alignment with CEPI stakeholders, complexities included in business plans and contingency arrangements. Note: risk stays red until staff increase is in place, may then be downgraded to orange.

2	Operational risks	Understaffing in Secretariat leading to too high workload, reduced quality, delays and	H	H	H	1. Hire leaders with clear roles and responsibilities2. Organisational and operational planning. Avoid people working unreasonable hours over a long time and make sure that people take vacations 3. Hiring of necessary/planned staff, including external help temporarily. Avoid loss of institutional memory by relying too much on consultants.4. Input/assistance from hosting organisations and partners to the Coalition to learn from experience and best practices5. Strengthen forecasting of HR needs to match planned workload and get Board approval for proposed increase in staff6. Tracking of staff engagement	M	Deputy CEO	1. Completed. Close follow up of employees from line managers to avoid burnout.2. Organisational plan for 2019 planned finalised Feb 2019, individual key priorities defined for 2019. Clear messages on importance of taking vacations have been communicated.3. Ongoing. Staff increase will reduce need for external consultants.4. Ongoing5. Staff increase approved by the Board October 2018, recruitment ongoing.6. Staff survey performed January 2019, ongoing follow-up.
3	Financial risks	Loss of political interest and willingness to fund	M	H	H	1. Diversification of funding base and implementation of innovative financing mechanisms 2. Reporting and communication of achievements and progress 3. Establish MoU and contract requirements for investors to inform about future funding in a timely manner 4. Ensure good governance to build trust 5. Revision of business plan 6. Replenishment from investors	M	Director Advocacy, Comms and Resource Mobilisation	1. Ongoing, resource mobilisation strategy developed - under implementation. 2. Signing of partner contracts have been communicated. Proactive communication in media. Standardised investor reporting in process. 3. Agreements in place, frontloading of MUSD from Norad work in progress. 4. Ongoing, continuous work with stakeholders and governments on global health security. 5. Board approved for 2019. 6. Preparatory considerations started.

4	Operational risks	Insufficient collaboration with central partners (e.g., WHO, GAVI) leading to lack of	M	H	H	1. Mapping and prioritising key partners and to formalise collaboration, including through MOUs 2. Partner participation in development of strategies, including through representation in Board and JCG 3. Task team collaboration. Dedicated staff in place working on stakeholder engagement and management4. Internal coordination of external relations	M	Deputy CEO	1. Mapping and prioritisation in process. MOUs signed with a number of critical partners, with many reps serving on JCG or SAC. Considering update to WHO MOU.2. Funders and key partners included in Board, Investors forum and JCG3. Task teams/WGs (e.g. JCG WG) have representation from key partners, including WHO (including regional offices), Gavi, UNICEF. Interlocutor at strategic level with WHO and other central partners. Discussions with GAVI around investment strategy and criteria for epidemic diseases. Resource Mobilisation strategy developed, under implementation. 4. Continuous collaboration between CEPI departments to have coordinated approach to partners. Developing internal coordination mechanisms with "key account managers"(e.g. for WHO). Recruitment ongoing to employ policy manager and investor relations resource.
5	Operational risks	Leakage of sensitive information	H	H	H	1. Increase awareness and anchor best practice on handling of sensitive information within the secretariat2. Develop standard operating procedures (SOPs) for handling sensitive information and responding to leakages. 3. Refrain where possible from sharing documents and rather use links4. Non-Disclosure Agreements (NDA) to be signed by all CEPI awardees 5. Have external assessment of IT security and implement mitigating measures, including through having insecure email network with sensitive information to be moved to safe area 6. Establish and monitor a SharePoint with access control to be used for sensitive information	M	Director Finance and Operations + General Counsel	1. Information on how to handle sensitive information shared by mail. IT security training completed for all employees in June 2018. Includes training on protection of personal data and update on GDPR regulations. Cyber risk review/audit planned for 2019 focusing on both insider risk and external threats.2. In process. Information Security Policy approved Feb 2019. Procedures under development and to be implemented as a part of Information Management Project.3. Communicated, mandatory training performed of all staff.4. Included in partner contracts5. Completed. Audit verifying that all specifications given Intility have been implemented initiate and planned finalised Q1 2019. 6. Completed CEPI Intranet site with access control. Ongoing work to further strengthen access control (ref Information Security Policy)

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6	Reputational risk	Abuse of power, misuse of public funds	M	H	H	1. Best practice Governance, prevent and control activities.a. Tone from the top: CEPI valuesb. Code of Conductc. Policiesd. Procedurese. Training and awarenessf. Control activitiesg. Establish channels for report of concerns (whistleblowing)	M	CEO	a. CEPI values defined and communicated, needs to be repeated continuouslyb. Code of Conduct implemented. Summarises the existing policies which have been approved by the CEPI Board. c. Policies completed and approved by the CEPI Board. d. Most procedures completed, some in final review and targeted to be signed off in Q1 2019. e. Mandatory IT security and GDPR training completed in June 2018. Mandatory anti-corruption, whistleblowing and conflict of interest training performed. New employees to be trained during Q1 2019, then continuously refresh work.f. Project control routines - ongoing work. Internal Audit plan 2019 approved. g. Whistleblowing policy approved by the CEPI Board. Whistleblowing procedure approved. External whistleblowing channel implemented Dec 2018.

Annex D: List of Policies, procedures and guidance documents*

Policies
Animals in Research Policy
Anti-Corruption Policy
Clinical Trials Policy
Delegation of Authority
Equitable Access Policy
Expenses Policy
External Complaints
Gifts and Hospitality policy
Hedging policy
Human Resources Policy
Information Security Policy
International Sanctions Policy
Investment and Treasury Policy
IT and Communications Policy
Managing Conflict of Interest Policy
Organizational Policy Creation and Management Policy
Procurement Policy
Protection of Personal Data Policy
Risk Management Policy
Scientific Integrity Policy
Transparency and Confidentiality Policy
Travel Policy
Whistleblowing Policy