

Coalition for Epidemic Preparedness Innovations (CEPI)

Call for proposals (CfP)

Topic: Platform technologies to enable rapid vaccine development for epidemic prone infections

Reference number: CEPI-CfP-002-platforms

CEPI is pleased to announce its second funding opportunity for the development of vaccines against epidemic infectious diseases. This document describes the scope, requirements and processes for proposal submission, review, and selection for funding. Further details can be found at <http://cepi.net/calls>.

The call seeking to achieve CEPI's strategic objective on rapid response and has been shaped through consultations with the Scientific Advisory Committee (SAC) of CEPI. The call text, review, and eligibility criteria have been informed by a request for information on rapid response platform technologies undertaken in collaboration with the Bill & Melinda Gates Foundation (BMGF).

In this two-step call, CEPI asks for submission of proposals for vaccine platform technologies that enable rapid vaccine development, rapid scale up, and quick time to immunity for reactive use in outbreaks of novel or previously unrecognised viruses. Proposals can include new platforms with the potential for rapidly making a vaccine using materials generally regarded as safe (GRAS), or those compressing the time of an existing (proven) platform to make it more responsive in an unknown threat situation. During the proposed project period, we encourage developers to target the following timelines:

1. Target a 16-week timeframe from identification of antigen to product release for clinical trials
2. Target a 6-week timeframe from administration of first dose to achievement of clinical benefit (i.e. immune response likely to result in clinical benefit)
3. Produce 100,000 vaccine doses within 8 weeks to impact an emerging outbreak (i.e. from Go-decision to scale-up to production, fill, finish, and release)

All applications should show data from a vaccine candidate on the proposed vaccine platform that demonstrate immunogenicity using a relevant animal model. These data could be based on studies with the pathogens targeted in this call, or on another pathogen (ideally an outbreak-prone virus). In addition, all proposed activities through completion of Phase I trials demonstrating safety and immunological proof-of-principle should fall within 3 years.

The deadline for submission of step 1 proposals is **4 p.m. CEST 17 October 2017**

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1. Introduction

Role of vaccine development in epidemic preparedness

Epidemics of emerging infectious diseases (EIDs), such as those listed in the World Health Organization (WHO) "[R&D Blueprint for Action to Prevent Epidemics](#)," are a significant and growing threat to individual life, societies, and general prosperity. There is currently no reliable means of predicting which microbes will emerge as pathogenic threats to humans with the capability of causing local outbreaks or widespread regional or global epidemics. It is therefore important to be prepared in a broader sense, and due to the low predictability of the causative organisms, be focused on activities to accelerate R&D and manufacturing preparedness for EID events that could have a large impact. Previous experience with vaccine development against emerging infectious diseases shows that development of a vaccine appropriate for clinical evaluation usually lags behind the outbreak cases, decreasing the potential to show efficacy in human trials unless the disease becomes endemic. To enable a vaccine to prevent or reverse an ongoing epidemic, decisions need to be made early during an outbreak, and anticipatory investments should be made into systems and technologies that enable rapid response vaccine development and production. This call aims to invest in particular in developing vaccine platform technologies that can easily be adapted to novel antigens and are likely to be safe and provide protection in humans, and can be manufactured quickly and in large quantities.

Rationale for CEPI to invest in vaccine platform technologies

CEPI funding facilitates the development of vaccines against those EIDs for which the usual commercial incentives for development are inadequate. A strategic objective of CEPI is to advance development of vaccine technology platforms that enable a rapid response to immunize at-risk populations against EIDs. CEPI is investing in vaccine platform technologies to support the reduction of the total response time from recognition of a pathogen to the achievement of protective immunity in susceptible populations. Especially in emergencies, rapid vaccine development and immunization of the at-risk population is essential. CEPI believes that this investment can result in great public health impact by rapidly limiting or ending outbreaks. A long term objective of CEPI is to transform a selection of the platforms funded in this call into a sustainable toolbox of platform technologies active and could be ready for response.

2. Funding opportunity through this call for proposals

2.1. Objective

The objective of this Call for Proposals is to identify and fund proposals for vaccine platform technologies that enable rapid vaccine development, fast scale up, and achieve clinical benefit quickly for reactive use in outbreaks of novel or previously unrecognised viruses. Proposals can include new platforms with the potential for rapidly making a vaccine using generally regarded as safe materials (GRAS); or those compressing the time of an existing (proven) platform to make it more responsive in an unknown threat situation.

To demonstrate the versatility of the platform the proposal should include studies on three pathogens from different families, including one from the WHO priority pathogens list and two well-characterised pathogens from Table 1 (*see section 2.3 for more details*). Proof-of-concept/efficacy should be demonstrated for all three pathogens in relevant animal models and two of the vaccine candidates in the proposal should be evaluated in Phase I clinical trials, with plans for in-depth analyses of immunological mechanisms of actions of the platform. (*Note: Data generated prior to this call are acceptable in partial or complete fulfilment of the demonstration requirements for one or more model pathogen*).

For reactive use in outbreaks, timing is essential and therefore we are requesting that the proposed projects aspire to meet the time goals below. Proposals should describe the current state of technology and the approach in the proposed project to get closer to fulfilling the following goals:

1. Target a 16-week timeframe from identification of antigen to product release for clinical trials
2. Target a 6-week timeframe from administration of first dose to achievement of clinical benefit (i.e. immune response likely to result in clinical benefit)
3. Produce 100,000 vaccine doses within 8 weeks to impact an emerging outbreak (i.e. from Go-decision to scale-up to production, fill, finish, and release)

CEPI reserves the right to negotiate terms and conditions for funding Phase II and III trials outside the scope of this CfP.

2.2. Time horizon & vaccine candidate portfolio management

Support for vaccine platform technology projects will be for no more than **3 years in duration** in the first instance. The year-to-year continuation of projects, as well as any extension beyond three years, will be determined at pre-specified stage gates based on clearly defined “go/no-go” decision criteria. CEPI reserves the right to discontinue funding if a “no-go” decision is made. We encourage structuring proposals so that there are clear milestones, and that further activities are started based on attainment of milestones.

2.3. Disease scope

The vaccine technology platforms supported through this call should demonstrate versatility through proof-concept with three model pathogens during the funded project period:

- One pathogen from the WHO R&D blueprint priority list ([December 2015](#) or [January 2017](#)):
 - Arenaviral hemorrhagic fevers (including Lassa Fever)
 - Crimean Congo Haemorrhagic Fever (CCHF)
 - Filoviral diseases (including Ebola and Marburg)
 - Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (or other highly pathogenic coronaviral diseases, such as SARS)
 - Nipah and related henipaviral diseases
 - Rift Valley Fever (RVF)
 - Severe Fever with Thrombocytopenia Syndrome (SFTS)
 - Zika
 - Chikungunya (although not included in the official WHO priority lists, this pathogen was considered a “runner-up” and is therefore included here)
- Two well-characterized pathogens for which an immune response is defined as a surrogate for clinical benefit and animal models of infection have been utilized/characterized (see Table 1). If the platform has already addressed any of these targets, please include these data in the application.
- The three chosen pathogens should be from different virus families
- Include testing the vaccine candidates for all three pathogens in animal models
- Take two of the vaccine candidates into Phase I clinical trials with plans for in-depth analyses of immunological mechanisms of actions of the platform.

Table 1. Overview of well-characterized pathogens for which an immune response is defined as a surrogate for clinical benefit

Pathogen	Immune mechanism correlating with/ contributing to clinical benefit
Cytomegalovirus	Neutralising antibodies (nAb) + T cells
Dengue virus	nAb
Enterovirus 71	nAb
Hepatitis A virus	antibodies
Hepatitis B virus	antibodies
Hepatitis C virus	nAb + T cells
Hepatitis E virus	antibodies
Herpes simplex virus	antibodies + T cells
Human papillomavirus	antibodies
Influenza	Hemagglutination inhibition
Japanese encephalitis virus	nAb
Measles virus	antibodies
Norovirus	binding Ab
Poliovirus	nAb
Rabies virus	nAb
Respiratory syncytial virus	nAb
Rubella virus	nAb
Tick-borne encephalitis virus	antibodies
Vaccinia virus	nAb + T cells
Varicella virus	antibodies
West Nile virus	nAb
Yellow fever virus	nAb

nAb: neutralising antibodies

2.4. R&D scope

This call for proposals is limited to the development of multi-purpose vaccine platform technologies that can demonstrate rapid response to newly emerging pathogens, including the prioritized diseases listed under section 2.3. Development may include activities from preclinical testing in animal challenge, non-clinical toxicology studies, and immunogenicity models to dose ranging, safety and immunogenicity Phase I studies in healthy volunteers with plans for analyses of immunological mechanisms of actions of the platform. Development may include process development, product analytic assay development, formulation development, stability studies, cGMP production, and lot release, noting that these development activities must be completed during the funding period and contribute directly to the vaccine candidates being tested in the demonstration of versatility. Development should also include a plan to assess the immunological mechanism of action of the vaccine technology and time to protection, which is critical for understanding its utility as a platform.

All organizations with platforms that meet the stipulated goals of this call are encouraged to respond, but CEPI will not provide additional funding through this call for vaccine development projects funded under CfP1 to develop MERS, Nipah and/or Lassa vaccines.

3. Who can apply?

This call for proposals is open worldwide to vaccine relevant R&D entities that bring the relevant expertise and experience to address challenges within the scope of this call. Funding beneficiaries must be legal entities, or consortia of at least two legal entities. Applicant organisations or consortia of partnering organisations should have experience in vaccine development, i.e. a track record of bringing vaccine candidates through to human clinical trials in the last ten years. CEPI may conduct due diligence reviews for feasibility verification, legal, business and financial compliance before awards are made.

This call is open for proposals on vaccine platform technologies that can provide data from a vaccine candidate on the proposed platform that **demonstrate immunogenicity using a relevant animal model**. These data could be based on studies with the pathogens targeted in this call, or on another pathogen, ideally an outbreak-prone virus.

4. Eligibility

4.1. Completeness and registration of submission

For the submissions to be accepted as registered, applications must fulfil the following norms:

- Online submission must be completed before **17 October 2017, 4pm CEST**
- Application package must include **only the requested documents** (*section 5*)
- Project proposal document cannot exceed the maximum **page limit of 10 pages**

Any submission not fulfilling the above norms will not be considered for further review. Applications that fulfil these norms will be registered into the system and screened for eligibility.

4.2. Screening and preliminary review of proposals

Proposals will be eligible for funding only if they are:

1. Aligned with the call objectives described in section 2.1. They need to describe the current state of technology and the approach in the proposed project to get closer to fulfilling CEPIS aspirational goals:
 - a. Target a 16-week timeframe from identification of antigen to product release for clinical trials
 - b. Target a 6-week timeframe from administration of first dose to achievement of clinical benefit (i.e. immune response likely to result in clinical benefit)
 - c. Produce 100,000 vaccine doses within 8 weeks to impact an emerging outbreak (i.e. from Go-decision to scale-up to production, fill, finish, and release)

Points a. and b. above should be completed within the funding period, while plans for point c. should be outlined carefully as this is subject to results from the Phase I trial.
2. Relevant to the Cfp's disease and R&D scope focus, as described in section 2.3 and 2.4. This means that the application needs to:
 - a. Show data from a vaccine candidate on the proposed vaccine platform that **demonstrate immunogenicity using a relevant animal model**. These data could be based on studies with the pathogens targeted in this call, or on another pathogen, ideally an outbreak-prone virus.
 - b. Include **a total of three target pathogens**; according to requirements i, ii and iii below:
 - i. One of the following pathogens (WHO priority list): Arenaviral hemorrhagic fevers (including Lassa Fever), Chikungunya, Crimean Congo Haemorrhagic Fever (CCHF), Filoviral diseases (including Ebola and Marburg), Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and other highly pathogenic coronaviral diseases, Nipah and related henipaviral diseases, Rift Valley Fever (RVF), Severe Fever with Thrombocytopenia Syndrome (SFTS), Zika

- ii. Target two well-characterised pathogens (see section 2.3, table 1).
 - iii. The three chosen pathogens should be from different virus families
 - c. Test proof of concept/efficacy for all **three vaccine candidates in animal models**
 - d. Take **two of the vaccine candidates into Phase I clinical trials**
 - i. Include a plan to assess the immunological mechanism of action of the platform technology in humans in the Phase I trials.
- 3. Consistent with the CfP timeline and award conditions as described in sections 2.2 and 9:
 - a. All funded activities must occur within the given timeframe of three years post-award
 - b. Willing to work with CEPI to bring project into compliance with CEPI policies on equitable access policy, including data sharing, shared risks/shared benefits policy, clinical trials conduct, management of intellectual property (IP), and comply with the BMGF Open access program for clinical data and secure commitment to publish results in a given timeframe
- 4. Complete in terms of required content in the proposal templates and additional files as described in section 5
 - a. Provide all requested details in project description template
 - b. Provide all requested details in milestone plan
 - c. Provide all requested details in budget plan
 - d. Provide the excel files of the milestone and budget plans via cfp@cepi.net

The CEPI Secretariat will screen the eligibility of the proposals according to the criteria described above. Applications that are missing critical eligibility criteria will be excluded from further review.

5. Applicant guidelines

All communication of information and documents related to this call must be conducted in English. No costs incurred by the applicants will be covered for the development and submission of proposals or for contractual negotiations, if applicants are selected for funding.

CEPI uses the online application system of the Research Council of Norway (RCN) for the submission of proposals under this call for proposals. Only proposal forms and related documents submitted through this system by the submission deadline will be considered.

In case of questions in relation to the electronic submission system, access to proposal form templates, or any other issue related to this call for proposals, please contact cfp@cepi.net. The CEPI secretariat will address your questions within the shortest possible timeframe. Any question submitted, along with answers, may be made public. [Instructions for applicants](#) as well as a summary of [frequently asked questions and answers](#) (FAQs) will be uploaded to the CEPI website.

5.1. Proposal submission

Entities that want to respond to this call for proposals must submit their Step 1 proposal to CEPI via the [online application system](#) of the Research Council of Norway before **4 p.m. CEST¹ on 17 October 2017**. All documents must be uploaded as pdf files. Applicants are requested to complete the online application form and only submit the following attachments:

- A completed project description form (**max 10 pages**)

¹ Please be aware that the given deadline is absolute. Potential applicants are recommended to complete and submit the proposal well ahead of the deadline. Please refer to the "Check-Page" function frequently during creation of the electronic application.

- A milestone plan (for each target pathogen), showing the key activities and events on a relevant timescale (**which should also be sent to cfp@cepi.net in Excel format**)
- A completed budget plan (**which should also be sent to cfp@cepi.net in Excel format**)
- Short bio sketches of project leader/principal investigator (**max 1 page per sketch**), including up to five co-investigators/key staff. In the case of consortia of partnering organisations, co-applicants must provide electronic copies of signed letters of intent, confirming their agreement to participate in the proposed projects and agreeing with the content of the proposals.

Templates and guidelines for the required attachments are accessible via [the CEPI](#) and [RCN website](#). Submissions that exceed the page limits given above will be excluded for consideration. No additional documents should be submitted.

The project description form should address the following aspects:

- Evidence on proof-of-concept of the platform and supporting technologies, specifying existing preclinical and clinical data for the platform
- Evidence/rationale on application to a relevant pathogen and how it allows evaluation of feasibility and performance
- Evidence/rationale on how the proposed platform can enable rapid vaccine development and response to epidemics
- A description of planned non-clinical and clinical studies
- A description of planned Chemistry, Manufacturing and Control (CMC) data to be generated
- Thorough analysis of risks and mitigation measures where failures are likely to occur, including mitigation measures applicants plan to take
- Experience and track record of applicants, including management of vaccine development under the auspices of third party funding (e.g. government or private foundation)

6. Review criteria

Step 1 proposals for funding that have met the administrative and eligibility criteria described under section 6 will be assessed against the following criteria:

CRITERION	DEFINITION
Feasibility	This criterion gives an indication of whether the project is feasible in terms of successfully advancing the proposed vaccine candidates through end of Phase I. Feasibility will be assessed based on: <ul style="list-style-type: none"> - Scientific rationale and current development status of the proposed vaccine platform technology, considering evidence of proof-of-concept of the platform based on existing data for the platform - Soundness of the non-clinical development approach - Rigor of the clinical development approach up through Phase I
Anticipated potential use	This criterion gives an indication of the extent to which the proposed vaccine candidate is suitable for use in outbreak settings. This will be assessed based on: <ul style="list-style-type: none"> - Suitability of the technology platform to address multiple pathogens, especially novel emerging pathogens - Suitability of the technology platform for use in outbreak settings - Time to product release for clinical trial after identification of antigen - Time to achievement of clinical benefit after administration of first dose - Time to production of 10,000/ 100,000 / 500,000 / 1,000,000 vaccine doses - In Step 2 a target product profile (TPP) for vaccine platform technologies will be available and adherence to this TPP will be assessed

CRITERION	DEFINITION
Manufacturing scalability	<p>This criterion gives an indication of whether the proposed vaccine platform technology is suitable for scalable and rapid manufacturing for clinical testing and emergency use. This will be based on:</p> <ul style="list-style-type: none"> - Existing data on the platform technology being produced at cGMP standards - Anticipated manufacturing capacity and yield - Time to manufacture a dose equivalent vaccine product for clinical testing in an emergency response for 10,000/ 100,000 / 500,000 / 1,000,000 dose equivalents of bulk and vaccine product - Suitability of candidate vaccine/technology platform control strategy
Experience and track record	<p>This criterion gives an indication of the extent to which the applicant organization or consortium is seen as being capable of performing the proposed activities of the project. This will be assessed based on:</p> <ul style="list-style-type: none"> - Competency/expertise of key personnel in the project, based on provided bio sketches and documented vaccine development achievements and research results - Experience of applicant organization or consortium in Phase I/II clinical vaccine trials including in developing countries - Experience of applicant organization or consortium and their staff in advancing vaccines through regulatory reviews by functional National Regulatory Authorities (NRAs) over the past 10 years - Infrastructure and facilities in-house, or alternatively contract manufacturing partnerships for clinical lot and scale-up production and release in quantities specified above - Quality and content of a summary Integrated Product Development Plan (IPDP) - Project management expertise as demonstrated by proposed organisation, submitted product development and implementation plans
Cost	<p>This criterion gives an indication of the extent to which the proposed costs for the project are based on valid and realistic assumptions, reflect an understanding of the technical milestones and objectives, and are consistent with the applicant's proposed activities. In Step 2 applicants will be asked to provide a detailed cost plan (for more information see the template used in Step 2 of CfP on MERS, Lassa and Nipah to get an idea of the level of detail that will be required). Costs must be based on "Fair Market Value" in the territory where activities are performed.</p>
Time to completion	<p>This criterion gives an indication of the extent to which the proposed timeframes for the completion of the project (i.e. advancing the proposed vaccine candidate through end Phase I within 3 years) are based on valid and realistic assumptions, reflect an understanding of the technical milestones and objectives, and are generally consistent with the applicant's proposed activities.</p>

The **level** and **quality** of the information made available by applicants to CEPI against the above criteria will help determine the expected performance of their proposals for funding and will inform subsequent investment decisions by CEPI. Information requirements to address the above criteria are provided in the document 'Project description'.

7. Review of applications

7.1. Confidentiality

All internal and external experts that will be participating in the review process will be evaluated for any potential conflicts of interest and will need to sign confidentiality agreements.

7.2. Review of proposals

As a screen and preliminary review, proposals will be evaluated against the eligibility criteria (section 4.2) by a minimum of two technical staff members. Applicants who do not fully meet the given criteria will not be considered further and will therefore be excluded from the review process.

The review process will be performed by a small group of experts, consisting of CEPI and BMGF technical experts and potentially external consultants, covering the broader field of vaccine development. This review team will evaluate the proposals according to the review criteria described in section 6. Each proposal that fully meets all of the eligibility criteria will be discussed and the team will decide whether the applicant is invited to submit a full proposal for Step 2.

7.3. Step 2 process

After the review process of Step 1, all applicants will receive a notification of the outcome of the review process. Shortlisted applicants will be invited to submit a full proposal and will be provided with feedback and the documents needed for Step 2. In addition, a teleconference may be set up when it is felt it may be beneficial to ensure that any outstanding questions are resolved prior to submission of the full proposal.

The Step 2 review process will be similar to the Step 1 review process. Additional consultants might be asked to contribute to the evaluation of the proposal, if deemed necessary. The recommendations from the review process will be presented to the CEPI Scientific Advisory Committee (SAC) for their considerations. The SAC will provide their funding recommendation and the CEPI Board Investment group will make final investment decisions, building on SAC recommendations, business and strategic considerations.

The CEPI Secretariat will support the SAC and the Board Investment group in assessing cost/risk/benefit profiles of shortlisted proposals and in concluding the business case for investment on each of these proposals to the CEPI Investment group.

8. When will applicants be notified of the award decision?

The CEPI Secretariat will publicly announce each award when the relevant negotiations are complete and a partnership agreement has been signed. Applicants whose proposals will not advance to negotiations will be notified confidentially of the outcome of the process in a timely fashion.

9. Award conditions from funders

The project activities and associated budgets should fall within the specified three year time period. Funding must reflect the proposed activities and agreed conditions of the award decision made by the CEPI Investment group. 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.

The National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health may provide in-kind pre-clinical services, support for proof-of-concept clinical trials, and other technical expertise to highly meritorious projects supported by CEPI to rapidly advance vaccine platform concepts to the clinic. NIAID also may support product-independent activities such as required animal model development and refinement, generic assay development, and standardization and procurement of reference agents. The type and level of in-kind support will be determined during the negotiation of awards to ensure the most appropriate commitment of resources.

More details on award conditions are available online in [CEPI policies](#) on:

- Equitable access policy, including data sharing
- Shared risks/shared benefits policy
- Management of intellectual property (IP)
- Clinical trial policy
- Cost guidance document (*updated version will be available in the week of September 4th*)

10. Technical and administrative questions

Technical and administrative questions about this call should be directed to CEPI Secretariat (cfp@cepi.net). Questions and answers will be posted online. Deadlines for the first and second round of questions are 15 Sept and 29 Sept, respectively.

11. Estimated CfP-2 platform Timeline

Date	Action
1 Sept 2017	Launch Call for Proposals - Platforms
15 Sept 2017	First deadline for questions submitted to cfp@cepi.net
29 Sept 2017	Second deadline for questions submitted to cfp@cepi.net
17 Oct 2017	Deadline for submission of pre-proposals (Step 1)
Dec 2017	Notifications outcome Step 1 review
February 2018	Deadline for submission of full proposals (Step 2)
May 2018	Contract negotiations