Call for Proposals:
RNA vaccine platform technologies and vaccine library development against emerging and select endemic infectious diseases

CEPI is pleased to announce a new funding opportunity for the development of RNA vaccine platform technologies and vaccine library development against emerging and select endemic infectious diseases. This document describes the scope, requirements and processes for submission, review, and selection for funding. Further details can be found at https://cepi.net/get_involved/cfps/.

This Call for Proposal (CfP) asks for the submission of an Expression of Interest (EOI) for RNA platform technologies used for the development of vaccine candidates against a specified list of known pathogens and the development of vaccine libraries against high priority virus families with the potential for Disease X emergence. The CfP is divided into two Focus Areas.

Focus Area 1 seeks advanced mRNA vaccine platform technologies that use either (1) N1-methylpseudouridine (or equivalent isomerization) nucleoside-modified non-replicating mRNA formulated with ionizable lipid-based nanoparticle (LNP) at any stage of development, OR (2) other non-replicating or replicating mRNA technological approach that has demonstrated clinical proof-of-concept (PoC). The proposed project should include vaccine development plans for (a) one vaccine candidate from preclinical studies through late-stage clinical trials including licensure to expand the development and regulatory experience with the platform, AND (b) another vaccine candidate from preclinical studies to Phase I/II trials to serve as an exemplar for creation of a vaccine library against high priority virus families for Disease X emergence.

Focus Area 2 seeks novel RNA platform technologies based on potentially high-impact innovations offering substantial advantages over existing mRNA technologies. These advantages may involve attributes such as multivalency, immunogenicity/reactogenicity balance, storage and stability, productivity, response time, and cost-of-goods (COGs). Focus Area 2 provides seed funding for activities including discovery research, preclinical proof-of-concept studies, and limited early clinical proof-of-concept studies.

The CfP for Focus Area 1 is open from January 17,2022 to February 28, 2022. EOIs for Focus Area 1 will be reviewed after the end of the open period. The CfP for Focus Area 2 is open from January 17, 2022 to December 31,2022. EOIs for Focus Area 2 may be submitted at any time during the open period, but will be reviewed approximately on a quarterly basis. The open dates for both Focus Areas may be extended or amended depending on programmatic need. The CfP for both Focus Areas may be re-opened after initial closure depending on programmatic need.

CEPI reviews and evaluates proposals on their merits and in the context of stated eligibility criteria and CEPI's overall project portfolio. Regardless of eligibility at any stage of the funding call, CEPI reserves the right to consider and decline proposals in its sole discretion.

1. Introduction

The COVID-19 pandemic has caused enormous sickness, death and economic hardship throughout the world. However, by necessity, the pandemic has accelerated the development of new technologies, perhaps most notably the mRNA technology platforms that serve as the basis for two of the most widely introduced vaccines against SARS-CoV-2. With their success during the current crisis, mRNA-based technologies hold tremendous promise for the prevention and control of future epidemics and pandemics.

The Coalition for Epidemic Preparedness Innovations (CEPI) is an international coalition of governments, academic, philanthropic, private, public, and intergovernmental institutions whose vision is to create a world in which epidemics and pandemics are no longer a threat to humanity. Our mission is to accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats so they can be accessible to all people in need. CEPI operates under the laws of Norway as a non-profit international association and has offices in Oslo (HQ), London, and Washington, DC. More details about CEPI and our mission can be found on our website: www.cepi.net.

CEPI has played a central role in the global response to COVID-19, creating the world's largest portfolio of COVID-19 vaccines, and co-leading COVAX which aims to equitably deliver COVID-19 vaccines to participating countries worldwide. CEPI aims to build on the success of mRNA technologies against SARS-CoV-2, by strengthening, accelerating and expanding the ability of mRNA vaccine platform technologies to respond rapidly to current and future infectious disease threats in accordance with equitable access principles.

In line with this aim, the current Call for Proposal (CfP) asks for submission of an Expression of Interest (EOI) for the development of RNA vaccine platform technologies against emerging and select endemic infectious diseases to advance them as rapid response platforms. The CfP is divided into two Focus Areas: **Focus Area 1** seeks advanced mRNA vaccine platform technologies based on approaches supported by clinical trial data; **Focus Area 2** seeks novel RNA vaccine platform technologies based on potentially high-impact innovations.

2. Objectives

Focus Area 1:

- To expand the development and regulatory experience of advanced mRNA vaccine platforms (advanced platforms defined as technological approaches that have received licensure in humans or have generated promising clinical proof-of-concept data) by supporting vaccine development against known pathogen indications to licensure.
- To facilitate rapid response to future unknown pathogens of epidemic and pandemic threat by supporting the creation of vaccine libraries against high priority virus families for Disease X emergence, with vaccine development against Lassa virus and/or Nipah virus serving as exemplars of such vaccine library generation.
- To increase access to advanced mRNA vaccine platforms for diverse populations and geographies.
- To promote technical improvements in these mRNA vaccine platforms where possible.

Focus Area 2:

- To accelerate the early development of novel RNA vaccine platform technologies based on potentially high-impact innovations that could facilitate rapid response to future pathogens of epidemic and pandemic threat, and/or increase access for diverse populations and geographies.

3. Scope of the Call

Focus Area 1:

The CfP for Focus Area 1 intends to support advanced mRNA platform technologies for the development of two vaccine candidates per Awardee. Advanced mRNA platform technologies can fall into two categories: (i) N1-methylpseudouridine (or equivalent isomerization) nucleoside-modified non-replicating mRNA formulated with ionizable lipid-based nanoparticle at any stage of development, or (ii) other non-replicating or replicating mRNA technological approach that has demonstrated clinical proof-of-concept as a preventive vaccine candidate.

Of the two vaccine candidates to be supported per Awardee:

(a) One vaccine candidate is intended to expand the development and regulatory experience with the platform. This vaccine candidate would be supported (with some cost share by the Awardee) to licensure, targeting a known pathogen selected from Table 1, and should have commercial viability and relevance for vaccination in low- and middle-income countries (LMICs). Table 1 reflects well-defined vaccine preventable diseases, with generally accepted correlate of protection (CoP) or biomarker closely associated with protection, that provides a pathway to market authorization for vaccine candidates using the mRNA platform technology in the absence of an outbreak.

(b) One vaccine candidate is intended to serve as an exemplar for the creation of a vaccine library for a particular high priority virus family. The selected exemplar vaccine candidate would be supported to Phase I/II, targeting a pathogen from Table 2. Table 2 currently contains Lassa virus (representative of *Arenaviridae*) and Nipah virus (representative of *Paramyxoviridae*) and reflects less well-defined diseases caused by pathogens that have been designated by CEPI as priority pathogens for vaccine development. Vaccine libraries are collections of vaccine materials (e.g., DNA plasmids with research constructs evaluated *in vitro* and/or *in vivo*, seed materials, GMP materials) designed against approximately 10-15 viral pathogens per virus family, representative of virus families and their genera, that may pose a significant risk to public health, that can then be available for rapid response vaccine development and deployment. The collections within the library can be used in one of three ways: (i) against a matched pathogen using a monovalent vaccine formulation, (ii) against a closely matched pathogen using a monovalent or multivalent formation, or (iii) as a prototype to accelerate the development of a new homologous vaccine construct. To select and develop the exemplar vaccine candidate from Table 2, the Awardee would be expected to collaborate as needed with jointly approved third parties for immunogen design and vaccine library generation. The Awardee would also be expected to allow a jointly approved third party (e.g., academic organization) to generate, develop and store vaccine materials for vaccine libraries for *Arenaviridae*, *Paramyxoviridae* and other high priority virus families.

Table 1: List of known pathogens for Focus Area 1(a) and Focus Area 2; this list may be amended depending on CEPI requirements and the global public health situation

Pathogen indication	Virus family	Note
Rabies	*Rhabdoviridae*	Licensed human vaccine; generally accepted CoP
Rotavirus	*Reoviridae*	Licensed human vaccine; *no generally accepted CoP (but biomarker closely associated with protection)
Yellow Fever	*Flaviviridae*	Licensed human vaccine; generally accepted CoP
Chikungunya	*Togaviridae*	No licensed vaccine; *no generally accepted CoP (but biomarker closely associated with protection); CEPI priority pathogen

Japanese Encephalitis	*Flaviviridae*	Licensed human vaccine; generally accepted CoP
Hepatitis B	*Hepadnaviridae*	Licensed human vaccine; generally accepted CoP
Influenza	*Orthomyxoviridae*	Licensed human vaccine; generally accepted CoP
Measles	*Paramyxoviridae*	Licensed human vaccine; generally accepted CoP
Other viral or bacterial indication as agreed with CEPI	*To be determined*	Clear path to licensure

*Discussions with regulatory authorities would be required to determine the design of pivotal trials and route to licensure

Table 2: List of pathogens for Focus Area 1(b); this list may be amended depending on CEPI requirements and the global public health situation

Lassa	*Arenaviridae*	No licensed vaccine; no CoP; CEPI priority pathogen
Nipah	*Paramyxoviridae*	No licensed vaccine; no CoP; CEPI priority pathogen
Other viral indication as agreed with CEPI	*To be determined*	Within priority virus family

Selected applicants will proceed with partnering agreements in two steps. Under a Step 1 agreement, project activities for both vaccine candidates per Awardee (i.e., from Table 1 and 2) will proceed through Phase I/II. Then, at CEPI's discretion, a Step 2 agreement would be executed (presuming successful progression of the project through Step 1, and depending on CEPI resource availability) for project activities for the vaccine candidate from Table 1 to proceed through licensure.

The desired outcome from this effort is to have advanced mRNA vaccine platforms, ready and available against future epidemics and pandemics.

Applicants (individual organizations or consortia) must provide information in their EOI that meets the following **eligibility criteria**:

- mRNA platform technology using N1-methylpseudouridine (or equivalent isomerization) nucleoside-modified non-replicating mRNA formulated with ionizable lipid-based nanoparticle at any stage of development (i.e., mRNA platform similar to currently authorized COVID-19 mRNA vaccines), OR using other non-replicating or replicating technological approach but having demonstrated clinical proof-of-concept as a preventive vaccine candidate against an infectious disease indication (clinical proof-of-concept defined as robust binding and neutralizing antibody, and cellular immune responses in the clinic, along with acceptable safety and reactogenicity at doses eliciting such robust immune responses).
- Product development plan for two vaccine candidates.
  a) One vaccine candidate for development to licensure, to expand the development and regulatory experience with the platform.
     - Pathogen indication selected from Table 1.
     - Development plan includes all necessary preclinical, clinical, CMC and regulatory activities to licensure.
     - Timeline to initiation of Phase I preferably within 6-12 months of project initiation (although faster timelines would be advantageous), and licensure within 5 years of project initiation.
  b) One vaccine candidate for development to Phase I/II, to serve as an exemplar for the creation of a vaccine library for a particular high priority virus family.
     - Pathogen indication selected from Table 2.

        - Development plan includes all necessary preclinical, clinical, CMC and regulatory activities to Phase I/II trials.
        - Timeline to initiation of Phase I preferably within 12-18 months of project initiation (although faster timelines would be advantageous).
        - To select and develop the exemplar vaccine candidate, the Awardee would be expected to collaborate as needed with jointly approved third parties for immunogen design and vaccine library generation.
- Sufficient capabilities, capacity, and experience, either internally or through current or future partnerships, in end-to-end vaccine development, including execution of late-stage clinical trials, large-scale commercial manufacturing, regulatory interactions with stringent regulatory authorities, vaccine licensure, and vaccine supply.
- Sufficient production capacity, either internally or through current or future partnerships, to deliver at least several hundred million doses per year.
- Preferably having evidence or plans for other potentially advantageous characteristics such as (but not limited to) multivalency, thermostability at or above 2-8°C, and low anticipated cost-of-goods.
- Rights to background and foreground intellectual property or license for all key technologies that comprise the formulated mRNA vaccine candidate, or a clear pathway to such rights within 6 months of project initiation.
- Willingness to technology transfer of drug substance and drug product of the formulated mRNA vaccine candidate to developing country vaccine manufacturer(s) using a non-exclusive license.
- Willingness to engage with stringent regulatory agencies, developing country regulatory agencies and WHO to discuss the mRNA platform technology and any potential areas where development might be accelerated.
- Commitment to data sharing and use of common assays and international reagent standards.
- Willingness to use CEPI's Centralized Laboratory Network (if relevant).
- Willingness to allow use of the mRNA technology platform to develop additional vaccine materials and candidates for vaccine libraries against *Arenaviridae*, *Paramyxoviridae*, and other high priority virus families, either directly or through jointly approved third parties, as part of CEPI's strategy to respond rapidly to future outbreaks.
    - CEPI would support the development of these additional vaccine materials and candidates for vaccine libraries through additional separate projects, some proceeding to preclinical stage and others to Phase I/II.
    - Capability, either directly or through jointly approved third parties, to create GMP DNA plasmids for vaccine libraries, and potentially utilize the plasmids to produce tens-of-thousands of GMP grade vaccine doses.
    - Storage capability and quality control for vaccine libraries, either directly or through jointly approved third parties.
    - Willingness to in-license immunogen designs from a jointly approved third party (e.g., academic organization) to generate vaccine materials and candidates.
    - Willingness to out-license and share material with a jointly approved third party (e.g., academic organization) to generate and develop vaccine materials and candidates for vaccine libraries.

An EOI that does not meet all eligibility criteria may still be considered if other aspects of the mRNA technology platform are deemed to be exceptionally advantageous over other criteria. Occasionally, solely based on CEPI's peer review process and any required secretariat recommendations, proposals with novel approaches, but with shortcomings against certain criteria or with short term results of interest, may be awarded seed funding to enable the generation of additional supportive data. Typical seed funding would be for a period of less than two years.

Focus Area 2:

The CfP for Focus Area 2 intends to support novel RNA platform technologies (e.g., circular RNA-based platforms) for early development of vaccine candidates that use potentially high-impact innovations which offer substantial advantages over existing mRNA technologies, with a pathogen indication selected from Table 1. Potential advantages may include (but are not limited to) multivalency, improved immunogenicity/ reactogenicity balance, improved storage and stability, increased productivity, faster manufacturing response time, and lower COGs.

The desired outcome from this effort is to have RNA vaccine platforms with substantially improved attributes, ready and available in the long-term, against future epidemics and pandemics.

Applicants (individual organizations or consortia) must provide information in their EOI that meets the following **eligibility criteria**:

- Novel RNA platform with technological innovations (e.g., circular RNA-based platforms) that offer substantial potential advantages over existing advanced RNA platform technologies. Examples of such attributes and aspirational targets are listed in Table 3 but may include other advantages. Innovations can be in RNA design, delivery systems, formulation, manufacturing or other areas.
- Existing discovery and/or preclinical data support the specified potential advantages.
- Project plan details the relevant preclinical, clinical, CMC and regulatory activities to generate preclinical and/or limited early clinical proof-of-concept data to support the specified potential advantages, specifies the criteria for successful proof-of-concept, and indicates next steps in the event of successful proof-of-concept.
- Pathogen indication for vaccine development selected from Table 1.
- Timeline to completion of preclinical (or limited early clinical proof-of-concept studies if applicable) preferably within 12 to 18 months of project initiation.
- Sufficient capabilities and experience, either internally or through partners, in preclinical development, clinical development (if relevant) and cGMP manufacturing (if relevant).
- Rights to background and foreground intellectual property or license for all key technologies that comprise the formulated RNA vaccine candidate, or a clear pathway to such rights.
- Willingness to commit to technology transfer of drug substance and drug product of the formulated RNA vaccine candidate to developing country vaccine manufacturer(s).
- Commitment to data sharing and use of common assays and international reagent standards.
- Willingness to use CEPI's Centralized Laboratory Network (if relevant).

Table 3: Aspirational target attributes

Attribute	Aspirational target
Multivalency	10+
Immunogenicity/ reactogenicity balance	Immunogenicity comparable to current licensed mRNA vaccines/ reactogenicity comparable to typical licensed vaccines (e.g., inactivated flu vaccine); reactogenicity profile suitable for vulnerable populations
Dose schedule	Single primary dose
Thermostability	Stable at ≥2-8°C for ≥12 mos
Productivity/ Response time	>100M doses in <100 days
COGs	<$2 USD per dose

An EOI that does not meet all eligibility criteria may still be considered if other aspects of the RNA technology platform are deemed to be exceptionally advantageous over the other criteria.

4. Applicant guidelines and review process

Applicant should apply to either Focus Area 1 or Focus Area 2, and the EOI should indicate which Focus Area is the target of the submission. CEPI may occasionally redirect the application to a different Focus

Area if deemed appropriate, with the applicant's concurrence. EOIs must include essential evidence as required in the EOI templates, meet the presented timeline requirements, and contain sufficient detail for review of the proposed product development process. Any claims made within the proposal must be supported by evidence.

The EOI templates are accessible via https://cepi.net/get_involved/cfps/. To respond to this CfP, entities must submit their EOI to CEPI via a secure portal. Please send an email to rna.cfp@cepi.net to be provided with a secure link to upload your EOI to the secure portal. The EOI should be uploaded in pdf format. No additional documents should be submitted. Personal data included in proposals will be handled according to CEPI's Privacy Notice on www.cepi.net/terms/.

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

- Requirements in section 3 (applicant eligibility criteria) met
- Communication of information and documents conducted in English
- Budget figures submitted in US Dollars
- EOI should not exceed 10 pages (references excluded)

Submissions that exceed the specified page limits outlined in the EOI template or that fail to meet the above criteria will not generally be considered for further review.

In case of questions in relation to the submission system, access to the EOI template, or any other issue related to this CfP, please contact rna.cfp@cepi.net. The CEPI Secretariat will address your questions within the shortest possible timeframe. No costs incurred by the applicants for the development and submission of EOIs will be covered by CEPI. Furthermore, CEPI will generally not provide funding retroactively for activities carried out prior to an award.

A review team composed of CEPI staff will assess compliance with the eligibility criteria in Section 3. CEPI staff and external experts will then evaluate the eligible EOIs against the review criteria outlined in Section 5. CEPI CfP core team will provide notice to the applicant of either an invitation to proceed to Due Diligence and negotiations, or that the application was unsuccessful.

5. Review criteria

EOIs that have met the eligibility criteria described under Section 3 will be assessed against the following criteria:

Criterion	Assessment levels	Definition
1. Immunogenicity/ efficacy potential	1.1. Non-clinical 1.2. Clinical	• Extent to which platform is likely to enable rapid and durable immune responses providing protection/ clinical benefit against emerging infectious diseases, as supported by *in vitro*, animal and human studies (as applicable)
2. Safety/ reactogenicity potential	2.1. Non-clinical 2.2. Clinical	• Extend to which platform is likely to be safe and tolerable at immunogenic dose levels, as supported by animal and human studies (as applicable)
3. Technical/ manufacturing scalability and speed	3.1. Quality 3.2. Formulation	• Extent to which platform is likely to enable rapid development and production in sufficient

Criterion	Assessment levels	Definition
	3.3. Speed and scale of production	volumes to respond to epidemics or pandemics, including multivalent approaches (as applicable)
4. Access/ route to patient	4.1. Regulatory pathway 4.2. Delivery 4.3. Supply (only applicable to Focus Area 1) 4.4. Equitable access 4.5. Vaccine library use	• Extent to which platform is likely to enable uncomplicated delivery of vaccine product for epidemic or pandemic response under extreme conditions including high temperatures, and be affordable and accessible, including willingness for technology transfer to developing country vaccine manufacturer • Extent to which platform is likely to be useful and available to enable responses to novel emerging pathogens, including multivalent approaches (as applicable)
5. Partnership	5.1. Capabilities, capacity and experience 5.2. Quality of product development plan 5.3. Legal, intellectual property and reputational issues 5.4. Strategic and business obstacles	• Extent to which applicant, partnerships, plans and procedures are viable and of sufficient quality to deliver on proposed activities

6. Award conditions

Before submitting an EOI, applicants should take note of two Award conditions. The first is that each Awardee adheres to CEPI's policies, which can be found on CEPI's website. The second is that any funding is dependent on the signing of an Award Agreement, which provides the terms and conditions under which the Award will be made, in line with CEPI's Third Party Code, which can be found on CEPI's website.

CEPI is committed to achieving equitable access to all CEPI-supported programmes including vaccines, platforms, data, results, and materials. Specifically, equitable access to vaccines in the context of an outbreak, epidemic or pandemic means that appropriate products are first available to populations when and where they are needed, regardless of ability to pay. To ensure that CEPI delivers on its commitment to equitable access, CEPI must include access considerations as a component of any agreement with an Awardee.

Applicants unable or unwilling to meet these requirements should not submit to this CfP.

7. Technical and administrative questions

Technical and administrative questions about this Call should be directed to the CEPI Secretariat (rna.cfp@cepi.net).