Call for Proposals: Innovative technologies to improve vaccine thermostability

CEPI is pleased to announce a new funding opportunity for the development of innovative technologies to improve vaccine thermostability. 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/.

The Call for Proposals (CfP) consists of two parts: Step 1 is an Expression of Interest (EoI, the subject of this announcement) and Step 2 is the submission of a full proposal for funding. After the EoI review process, applicants may be invited to submit full proposals for funding (Step 2). Funding will be awarded to successful applicants to generate results that could form the basis for full development. The total budget for thermostability innovations is $17.5M over a five-year period, with the aim to start funding 3 to 5 projects in 2022.

This CfP is part of the CEPI 2.0 strategic goal of harnessing innovative technologies to improve the speed, scale and access of vaccine development and manufacturing in response to epidemics and pandemics. The call may be extended to include other innovation areas that contribute to this goal.

In Step 1 of this Call for Proposals, CEPI asks for submissions of Expressions of Interest (EoI) for innovative technologies that improve vaccine thermostability for use in outbreaks of known viruses as well as novel or previously unrecognised viruses. These can be novel technologies or adaptations of existing (proven) technologies that show measurable improvements in terms of increased thermostability of any proven vaccine platform (e.g. nucleic acid, protein subunit (including adjuvants), viral vector, virus like particle (VLP), live-attenuated or inactivated virus) to extend vaccine access.

This call is open for EoIs from 31 January 2022 to 31 December 2022. An EoI may be submitted at any time and the review process will start at the end of each quarter for the applications that came in during the preceding months. Application deadlines for inclusion in the respective review rounds are thus 31 March, 30 June, 30 September and 31 December. The call may be extended or amended depending on programmatic need.

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

1. Introduction

The ongoing COVID-19 pandemic has caused immense morbidity, mortality, and disruption of normal life around the globe. While the pandemic has accelerated the development of new vaccine technologies, it has also shown the importance of making these vaccines equitably accessible to the people who need them. One of the factors that complicate the worldwide distribution and administration of COVID-19 vaccines is their need for a cold chain for shipment and storage. Some of the novel mRNA-based vaccines currently require continuous storage at ultra-cold temperatures, which is not feasible in many parts of the world.

The need for thermostable vaccines was already recognized before the COVID-19 pandemic, for example in a study by the Vaccine Innovation Prioritisation Strategy (VIPS), in which the ability to withstand heat exposure was identified as the most desired characteristic for vaccines used in outreach and campaign settings by experienced immunization staff[1]. Lack of vaccine thermostability leads to limited or no access to vaccinations by people living in remote areas or low-resource settings. It also leads to wastage when vaccines must be discarded after they have been (potentially) exposed to heat or freezing, which is a main cost driver[2], adding to the costs of the cold chain itself. There might even be a risk that vaccines with reduced potency are administered, leaving people vulnerable to disease.

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 recognizes that thermostability is a main enabler to achieve equitable access, for COVID-19 and other vaccines for epidemic response.

In line with this purpose, this Call for Proposals (CfP) asks for submission of an Expression of Interest (EoI) for the development of innovative technologies to improve vaccine thermostability. Selected applicants will be invited to submit a full proposal for funding. Technologies must be applicable to current or future vaccines for epidemic response, and for vaccine distribution in low and middle-income countries (LMICs).

Several related Calls for Proposals are currently open or will soon be published. These are focused on vaccine platform technologies for rapid response, or on innovations improving the speed, scale and access of vaccine development and manufacturing in response to epidemics and pandemics. Further details can be found at https://cepi.net/get_involved/cfps/.

2. Objectives

Two objectives have been defined, and a proposal may target one or both focus areas: firstly, to improve the thermostability of vaccine platforms that currently require freezing or lyophilization to a minimum target that allows them to be distributed via the established cold chain; and secondly, to improve thermostability of any vaccine platform to a preferred target that allows the last stage of the supply chain to occur without cold chain equipment.

[1] Mvundura, Mercy, et al. "Vaccine innovation prioritisation strategy: Findings from three country-stakeholder consultations on vaccine product innovations." Vaccine (2021).

[2] Karp, Christopher L., et al. "Evaluating the value proposition for improving vaccine thermostability to increase vaccine impact in low and middle-income countries." Vaccine 33.30 (2015): 3471-3479.

- Focus area 1: Improve thermostability to the minimum target of ≥ 12 months at 2-8°C plus ≥ 3 days at 40°C (controlled temperature chain (CTC)) for vaccine platforms that currently have frozen liquid or lyophilized formulations.
- Focus area 2: Improve thermostability to preferred target of at least 1-2 months at 40°C for any vaccine platform. Long-term storage may be at 2-8°C (3-5 years) or at higher temperatures.

The aim of this call is to advance promising thermostability technologies towards innovation validation and implementation for vaccine products.

3. Scope of the call

The CfP intends to support technologies that improve the thermostability of any proven vaccine platform (e.g. nucleic acid, protein subunit (including adjuvants), viral vector, virus like particle (VLP), live-attenuated or inactivated virus). Focus area 1 is mainly aimed at mRNA vaccines, which currently require frozen storage, but for example live virus vaccines that presently require freezing or lyophilization are also in scope. Any vaccine platform may be used for focus area 2, as long as it is relevant to CEPI's mission of accelerating vaccine development for epidemic response and making these vaccines equitably accessible.

The thermostable formulation could be a liquid product for parenteral administration, or any other dosage form and administration route. The novel technology should not negatively impact other equitable access criteria such as costs, capacity, and ease of use (see eligibility criteria below), which excludes traditional lyophilization, but improvements to lyophilization or dried formulations circumventing these issues are in scope. Such dried formulations may be reconstituted before use, or administered via a non-parenteral route, e.g. as a microarray patch, or as an oral, nasal or sublingual dosage form.

The aim of this CfP is to identify innovative technologies that can be rapidly adapted for use against emerging threats, including Disease X (WHO Research and Development Blueprint for Action to Prevent Epidemics). Proposals that show proof of concept of the technology with a clinically proven vaccine (candidate) are strongly preferred. In case such data is not yet available, a clear pathway towards the application of the technology for a vaccine (candidate) must be presented.

The desired outcome of this effort is the implementation of innovative thermostability technologies for vaccines against epidemic and pandemic threats, thereby making these vaccines more equitably accessible.

4. Eligibility criteria

Applicants (individual organizations or consortia) must provide information in their EoI to show their proposal meets the following eligibility criteria:

- Technology is applicable to one or more proven vaccine platforms (e.g. nucleic acid, protein subunit (including adjuvants), viral vector, virus like particle (VLP), live-attenuated or inactivated virus). For focus area 1, this must be an RNA-based vaccine platform, or another platform that currently requires freezing or lyophilization.
- Thermostability proof of concept data with any vaccine (candidate) or model thereof must be included in the EoI to support the application. The proposed development of the technology should be performed with one or more vaccine candidates targeting CEPI's or WHO's priority pathogens, or other pathogens that may be of interest from an epidemic/pandemic point of view (see section 9).
- Technologies that have a positive impact on one or more attributes such as speed of development, scale of manufacturing, global manufacturing capacity, suitability for

flexible and regional manufacturing, costs per dose, ease of supply/distribution through to administration, immunogenicity and safety are preferred.
- Willingness to allow use of the innovative technology to develop vaccines, either directly or through a jointly agreed third party, against high priority pathogens as part of CEPI's strategy to respond rapidly to future outbreaks.
- Willingness to commit to CEPI´s Equitable Access principles, supported by applicant's plan to enable that equitable access. The plan may include rights to intellectual property for the technology, and access to GMP-grade raw materials, or a clear pathway to achieve such access.
- Willingness to share data, samples, methods, etc. and to use common assays and international reagent standards, under the appropriate confidentiality agreements.
- Willingness to engage with regulatory agencies to discuss the innovative technology.

5. Applicant guidelines and review process

EoIs must include essential evidence as required in the EoI template, and contain sufficient detail for review of the proposed technology development. Any claims made within the proposal must be supported by evidence.

The EoI template is 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 innovations.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 4 (applicant eligibility criteria) met
- Communication of information and documents conducted in English
- Budget figures submitted in US Dollars
- EoI should not exceed 5 pages (references excluded)

Submissions that fail to meet the above criteria will not 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 Call for EoIs, please contact innovations.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 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 (section 4), and evaluate the potential of the technology to meet the targets and to have an impact for equitable access of epidemic response vaccines. EoIs not meeting eligibility criteria will not be further reviewed for funding. CEPI staff and external experts will then evaluate the eligible EoIs against the review criteria outlined in section 6.

After the EoI review process (Step 1), applicants may be invited to submit full proposals for funding (Step 2). The CEPI call core team will provide notice to the applicant either that submission of a full proposal for funding is invited, or that the application was unsuccessful. CEPI may also redirect applications to other open calls that are deemed more appropriate for the project. Applicants without a vaccine candidate (second point in section 4) may be supported by facilitating synergies with vaccine developers.

CEPI staff and external experts will evaluate the full proposals against the review criteria outlined in section 6, and the most promising proposals will be invited to proceed to due diligence and negotiations.

6. Review criteria

EoIs that have met the eligibility criteria described under section 4 will be assessed against the following criteria.

Criterion	Definition
Thermostability improvement	• Extent to which technology reduces the thermostability bottleneck for mRNA vaccines / other vaccines that currently have to be stored frozen or lyophilized. • Extent to which technology removes the need for cold chain equipment during the stages of the vaccine supply chain. • Improvement of thermostability as evidenced by moving a vaccine (platform) to a more stable VVM category.
Innovativeness	• Extent to which the technology is innovative and transformative, causing a true change in the way in which vaccines can be delivered, rather than an incremental improvement. • Impact on all stability aspects, including stability at the intended storage condition, during temperature excursions, freeze/thaw, transport, and light exposure.
Route to implementation	• Extent to which the technology has been proven with relevant vaccine drug products. • Extent to which the project proposal includes relevant vaccine drug products. • Strategic path to regulatory approval for use of the technology in clinical trials and for marketed/authorized vaccines.
Scalability and speed	• Speed of development for novel pathogens. • Extent to which the technology is suitable for large scale, flexible, geo-diversified manufacturing, especially in LMICs. • Extent to which the technology can be applied to (proven) vaccines or vaccine platforms with minimal impact to established manufacturing conditions. • Cost per dose added by the formulation. • Ease of supply/delivery through to administration. • Ability to predict long-term stability based on limited data.
Access/ route to patient	• Extent to which platform is likely to enable simplified delivery of vaccine product for epidemic or pandemic response and be affordable and accessible particularly for LMICs. • Temperature monitoring system planned or implemented, with cumulative heat exposure and/or threshold indicator as applicable.
Partnership	• Capabilities, capacity and experience of the applicant / consortium to meet the above criteria. • Willingness to make the technology available for vaccines against high priority pathogens as part of CEPI's strategy to respond rapidly to future outbreaks.

7. 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 respond to this CfP.

8. Technical and administrative questions

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

9. List of pathogens

The proposed development of the thermostability technology should preferably be performed with one or more vaccine candidates targeting a pathogen from the below table.

Virus / viral disease	Family	CEPI priority disease	WHO priority diseases	PAVM priority disease	Well characterized pathogen	Prototype virus (for the family)
Lassa Fever	Arenaviridae	x	x	x		x
Middle East Respiratory Syndrome Coronavirus (MERS-CoV)	Coronaviridae	x	x			x
Nipah	Paramyxoviridae	x	x			x
Rift Valley Fever (RVF)	Bunyaviridae	x	x	x		x
Chikungunya	Togaviridae	x		x		
COVID-19	Coronaviridae	x	x	x		
Ebola Viral Disease	Filoviridae	x	x	x		x
Disease X		x	x	x		
Crimean-Congo Hemorrhagic Fever	Bunyaviridae		x			
Zika Disease	Flaviviridae		x			
Influenza (pandemic response, not seasonal)	Orthomyxoviridae			x	x	x
HIV	Retroviridae			x		x
Rotavirus	Reoviridaea			x		x
Yellow fever virus	Flaviviridae			x	x	x
Hepatitis B virus	Hepadnaviridae			x	x	x
Measles virus	Paramyxoviridae			x	x	x
Rabies virus	Rhabdoviridae				x	x
Japanese encephalitis virus	Flaviviridae				x	x
Other viral or bacterial indication as agreed with CEPI						