Call for Proposals:

Vaccine manufacturability focused on speed.

CEPI is pleased to announce a new funding opportunity for the development of manufacturability-related innovations and technologies that can improve the speed of manufacturing vaccines, in response to a new pathogen outbreak. 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) process consists of the submission of a proposal that meets the eligibility criteria of the call, followed by peer review and due diligence. Funding will be awarded to successful applicants to generate results and deliver the project work. The budget for vaccine manufacturability focused on speed is estimated at US$25M over up to 3 years.

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.

CEPI asks for submissions of proposals for manufacturability-related innovations and technologies that can improve the speed of manufacturing vaccines. These can be innovations that can optimise process unit operations in vaccine manufacturing platforms (e.g., mRNA, viral vectors, proteins, or novel platforms) and technologies that can be applied to multiple vaccine products and projects (e.g., rapid analytical technologies such as batch release assays, potency assays, identity tests or reagents) to speed up manufacture. Innovations that can accelerate cell-based manufacturing steps (such as cell-free manufacturing and synthetic approaches) and any other manufacturing-related innovations that can accelerate clinical trial material availability are invited.

This call is open from 04 May 2023 to 15 December 2023, and a proposal may be submitted at any time between these dates. Submitted proposals will be reviewed in two rounds:

- First round – application period from 04 May to 31 July 2023, review from mid-Aug.
- Second round – application period from 01 August to 15 December 2023, review from January 2024

The call may be extended or amended, depending on the programme's needs.

CEPI reviews and evaluates proposals on their merit and in 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 Coalition for Epidemic Preparedness Innovations (CEPI) is an international coalition of governments, academic, philanthropic, private, public, and inter-governmental institutions (launched in 2017). CEPI aims to accelerate the development of vaccines against emerging infectious diseases and to enable equitable access to such vaccines to all populations in the event of an outbreak.

Following the outbreak of COVID-19 which caused significant ill-health, death, and disruption to normal life across the world, it took 326 days for the first emergency vaccine (the Oxford-AstraZeneca COVID-19 vaccine) to be authorised for use, from the day of release of the SARS-CoV-2 genetic sequence. CEPI launched a new strategy in 2021 (CEPI 2.0) for which a key objective is to prepare for epidemic and pandemic threats through (i) developing vaccines and promising biologics against the most prominent threats, and (ii) by building on COVID-19 achievements and the CEPI 1.0 strategy. CEPI has set out a 100-day mission aspiration[1] to make vaccines available for first-in-human emergency use, following the release of the genetic sequence of a new pathogen (referred to as Disease X).

CEPI is supporting innovations that will improve the speed and/or scaling of the production of vaccines, and their equitable access through technology transfer, to low- and medium- income country (LMIC) settings. Extensive critical path analysis of traditional vaccines manufacture compared to the COVID-19 vaccine development timelines showed Chemistry, Manufacturing and Controls (CMC) to be on the critical path to first-in-human vaccines availability. To meet the 100-day mission aspiration, there is a need to support and invest in novel technological approaches that would significantly reduce the time taken to make new vaccines (using current vaccine manufacturing platforms as a benchmark). This in turn will reduce the impact of a new disease outbreak on the global society.

In-line with the 100-day mission aspiration, CEPI is launching this Call for Proposals (CfP) and asks for submission of proposals for vaccine manufacturability focused on speed. Innovative technologies to be introduced by applicants must be applicable to a vaccine manufacturing platform (such as messenger ribonucleic acid/mRNA, viral vectors, protein production) and should significantly reduce the overall processing time for clinical trial material (CTM) generation by 20%.

2 Objectives

Our main objective is to identify manufacturability opportunities that could accelerate the manufacture of clinical trial material, in response to a new outbreak, and can be rapidly adopted for commercial manufacturing and rapid deployment, to achieve the 100-day mission aspiration. A critical path analysis of different vaccine manufacturing platforms at CEPI (unpublished) identified three areas that can improve the development and manufacture of a new vaccine for first-in-human trials.

I. Platform optimization (making multiple vaccine platforms rapidly adaptable to new pathogens).
II. using synthetic biology approaches for cell free manufacturing of DNA template, proteins and viruses or transient transfection of cell lines at scale for proteins.
III. Rapid analytical testing of drug substance/product, which can reduce hold times between vaccine manufacture and release. This can be achieved through accelerated release testing (especially sterility, adventitious agents, potency tests), incorporation of Process Analytical Technology (PAT)

[1] CEPI-100-Days-Report-Digital-Version_29-11-22.pdf

and real-time release,) and implementation of existing but ‘yet to be formally validated’ rapid testing methods.

The aim of this call is to identify innovative technological approaches that could speed up vaccine manufacturing.

3 Scope of the call

The CfP is focused on manufacturability-related innovations and technologies that can accelerate the time required to make vaccines rapidly available for first-in-human assessment. Innovations must optimize processing times on the critical path towards the availability of clinical trial material (CTM) for initial emergency use – for any proven vaccine manufacturing platform. Technologies to be introduced should be applicable to multiple vaccine products and projects.

The four focus areas for this CfP are:

- **Focus Area 1**: Platform process development in batch or continuous manufacturing mode, process optimization, standardization, and acceleration (such as mRNA, viral vectors, proteins, or other novel platforms are considered).
- **Focus Area 2**: Analytical technologies that can accelerate drug substance/product batch release and availability of master cell bank (MCB)/ master viral stock (MVS). Rapid technologies for batch release assays exist and new analytical technologies (e.g., identity / potency tests or reagents) will need to be established. These technologies require implementation as part of product licensing.
- **Focus Area 3**: Innovations to accelerate cell-based manufacturing steps, including synthetic approaches (such as the use of synthetic DNA for mRNA manufacture). Implementation of cell-free manufacturing innovations (such as cell lysate for protein production) can improve vaccine production.
- **Focus Area 4**: Any other manufacturing-related innovations that can accelerate CTM availability**.** The use of Artificial Intelligence (AI) in developing and controlling the manufacturing process can aid in post-approval rapid vaccine deployment.

The focus areas above were determined following a critical path analysis of key manufacturing platforms (mRNA, protein, and viral vectors) where the time taken to produce CTM (from the release of the pathogen’s genetic sequence) was performed. Some key assumptions were made to facilitate the critical path analysis (which are not provided as part of this CfP).

Proposals that show proof of concept for manufacturability-related innovations and technologies with a clinically proven vaccine (candidate) or model thereof, demonstrating its feasibility are strongly preferred. Where such data are not available, a clear pathway towards the technology application must be presented.

4 Eligibility criteria

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

- Technology should significantly accelerate one or more steps on the critical path towards clinical trial material availability, for one or more proven vaccine platforms; a 20% reduction in processing time for an existing manufacturing platform is anticipated.

- Vaccine platform technologies should be suitable for rapid vaccine manufacturing and deployment in response to an outbreak.
- Material generated from process acceleration innovations should be comparable to that from the current process, and preferably demonstrated by appropriate analytical (characterization) methods.
- Proof of Concept (PoC) data (e.g., process scale) with a vaccine (candidate) or model thereof, demonstrating feasibility of the innovative technology.
- Development plan to advance the innovation towards implementation.
- Technology/innovation should have a positive impact on manufacturing scale and equitable access attributes (such as technology transfer plan and materials availability).
- Willingness to commit to CEPI´s Equitable Access principles.
- Willingness to share data, samples, and methods.
- Willingness to engage with regulatory authorities.

5 Application guidelines and review process

The proposal must include essential evidence required in the template and sufficient detail to review the proposed innovations or technologies that can accelerate time required to make vaccines rapidly available for first-in-human assessment. Any claims made within the proposal must be supported by evidence.

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

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

- Requirements in section 4 (applicant eligibility criteria) are met.
- Communication of information and documents are conducted in English.
- Budget figures are submitted in US Dollars
- Proposals should not exceed five pages (references excluded)

Submissions that fail to meet the above criteria will not be considered for further review.

For any questions relating to the submission system, access to the proposal template, or any other issue related to this call, please contact innovations.cfp@cepi.net. The CEPI Secretariat will address your questions within the shortest possible time.

No costs incurred by the applicants for the development and submission of proposals will be covered by CEPI. Furthermore, CEPI will not provide funding retroactively for activities conducted 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 or innovation to meet the targets and to have an impact for accelerated development of epidemic response vaccines. Proposals not meeting the eligibility criteria will not be further reviewed for funding. CEPI staff and external experts will then evaluate the eligible proposals against the review criteria outlined in section 6.

Following the submission of a proposal and its subsequent review, the CEPI call core team will provide notice to the applicant either that their application has been progressed to the next stage, 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 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

Eligibility of entries will be assessed as per section 4, against the following objectives:

Objectives	Criteria
Improvement related to speed	• Extent to which the innovative approach transforms vaccine manufacturing and enables quicker availability of CTM, thereby contributing to CEPI's 100-day mission aspirations. • Extent to which significant reductions in processing time (from sequence identification to CTM availability) can be demonstrated. • Extent to which rapid analytical testing can accelerate critical path items and how the test compares to current methods.
Robustness	• Analytic technologies must be robust, accurate and as sensitive as the approved equivalent, to reduce the risk of deviations and waiting time. They should be of low complexity and have a reliable supply chain for distribution and components. • Processes should be understood, capable and compliant. Standardization and low variability are preferred to reduce the risks of deviations and waiting times. • As far as possible the procedure should be able to detect the moieties of interest in its native state without processing so that it could be used in PAT.
Route to implementation	• Acceleration results in comparable product to current process. • Extent to which the speed-related manufacturability improvement can be achieved. • Extent to which the technology has been proven with a relevant vaccine project. • Strategic path to regulatory approval for use of the technology in clinical trials and for marketed/authorized vaccines.
Scale and access	• Extent to which the technology is suitable for large scale, flexible, geo-diversified manufacturing. • Complexity of process and the total time required for the manufacturing process. • Scalability of the technology, while maintaining comparability of the product.

Objectives	Criteria
	• Extent to which the technology can be applied to (proven) vaccines or vaccine platforms with minimal impact to established manufacturing conditions. • Extent to which the technology can be deployed to produce vaccines in response to an outbreak at a low but sustainable cost per dose.
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 including possible out-licensing of vaccine or technology offering low but sustainable pricing for LMIC use.

7 Award conditions

Prior to submitting a proposal, applicants should take note of two award conditions.

- Each awardee adheres to CEPI's policies, which can be found on CEPI's website.
- 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 (https://cepi.net/wp-content/uploads/2019/01/Equitable-Access-Policy.pdf) to all CEPI-supported programmes including vaccines, innovations, platforms, data, results, and materials. Specifically, equitable access to vaccines (including combination with innovations) 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).