CEPI

Innovations to Prepare for Future Epidemics and Pandemics

Call for Proposals

Focus Area 3: Innovative manufacturing technologies to improve vaccine scalability and equitable access

1 Introduction

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.

Following the outbreak of COVID-19, which caused significant morbidity, mortality, and disruption of normal life around the world, CEPI has set out a 100-Days Mission to make vaccines and other biologic countermeasures available more rapidly in response to an outbreak of a new pathogen, referred to as Disease X. The aim is to have vaccines ready for initial authorisation and manufacturing at scale within 100 days of recognition of a pandemic pathogen, when justified by the severity of the situation. Coupled with improved surveillance, and swift use of non-pharmaceutical interventions, a vaccine or other biologic countermeasure developed in 100 days could defuse the threat of a new pathogen with pandemic potential.

Achieving the 100-Days Mission will require transformative innovations in vaccine platform and manufacturing technologies, development of vaccines as well as monoclonal antibodies (mAbs) and other biologics against high-risk viruses, and the creation of a global vaccine library, including vaccine prototypes against high-risk viral families, to give a head-start on novel threats (Disease X). It will also require equitable access to these technologies and vaccines so that they are available to all who need them.

2 Objectives for Focus Area 3

This Focus Area aims to advance technologies and innovations that contribute to the goals of:

- Manufacturing at commercial scale within 100 days of recognition of a pandemic pathogen.
- Equitable access especially in the Global South, by significantly lowering the cost of goods of vaccines, and by facilitating distribution and delivery.

3 Scope of Focus Area 3

Three sub focus areas have been defined, related to scale, costs of goods, and distribution and delivery:

- **Focus Area 3a:** Technologies and innovations that accelerate and support scale-up, scale-out and technology transfer, to make vaccines available at the right commercial scale in response to an outbreak, e.g.
    - Standardized, optimized, well understood platform processes (drug substance and drug product), ready for scale-up/-out and tech transfer, using the Quality by Design (QbD) approach.
    - Modular / flexible / continuous manufacturing solutions.
    - Characterization methods to support technology transfer and comparability.
    - Scale-down models, digital twins, artificial intelligence, methods to predict scalability.
    - High-yielding expression systems.
- **Focus Area 3b:** Technologies and innovations that can reduce cost of goods, e.g.
    - Alternatives for raw materials and consumables that substantially contribute to costs of goods and/or limit supply.
    - Technologies that increase yield or reduce dose.
    - Process changes or simplifications to reduce cost of goods and/or facilitate technology transfer.
- **Focus Area 3c**: Technologies and innovations that facilitate equitable access, distribution and delivery in all regions, especially the Global South, e.g.
    - Presentations for easy (self-)administration (e.g. oral, nasal, patches) and single-dose vaccines.
    - Improved thermostability, including easy stability prediction, temperature monitoring and cold-chain distribution.

  Technologies must be applicable to one or more clinically proven vaccine platforms (e.g. nucleic acid, protein subunit [including adjuvants], viral vector, virus like particle, live-attenuated or inactivated virus). Technologies should be able to benefit multiple vaccine candidates including future development against disease X.

  When preclinical and/or clinical comparability studies are necessary to demonstrate that a new technology/innovation aimed at improving scalability or access does not affect the safety or efficacy of a vaccine candidate, we suggest targeting a virus for which there is an already licensed human vaccine and/or generally accepted correlates of protection, to facilitate implementation (Table 1), or a CEPI priority pathogen. In case another target is preferred, please contact CEPI prior to application via **innovations.cfp@cepi.net**.

Table 1: Eligible Viruses for Focus Area 3

Virus	Virus family	Note
SARS-CoV-2	*Coronaviridae*	Licensed human vaccines; generally accepted CoP to prevent infection
RSV	*Pneumoviridae*	Licensed (non-maternal) human vaccine; immunogenicity data available associated with protection from lower respiratory trat infection in adults
Rabies	*Rhabdoviridae*	Licensed human vaccine; generally accepted CoP
Yellow Fever	*Flaviviridae*	Licensed human vaccine; generally accepted CoP
Chikungunya	*Togaviridae*	No licensed vaccine; no generally accepted CoP; biomarker closely associated with protection; CEPI priority pathogen
Japanese Encephalitis	*Flaviviridae*	Licensed human vaccine; generally accepted CoP
Hepatitis B	*Hepadnaviridae*	Licensed human vaccines; accepted CoP
Influenza	*Orthomyxoviridae*	Licensed human vaccines; generally accepted CoP
Measles	*Paramyxoviridae*	Licensed human vaccines; generally accepted CoP
Other virus - with CEPI consent	*To be determined*	Clear path to licensure

Activities in scope:

- CMC development related to the development, optimization, characterization and scale-up of the platform process, analytical methods, and/or formulation.
- Comparability or comparison between the new technology and the established process, method and/or formulation (using analytical methods and/or preclinical studies) to demonstrate that a new technology/innovation aimed at improving scalability or access does not affect the safety, immunogenicity, and/or efficacy of a vaccine candidate.
- CMC-related Phase 1 readiness activities for the vaccine candidate.

Activities out of scope:

- For projects related to scalability, the actual manufacturing of large-scale GMP batches is out of scope, and scalability should be demonstrated in other ways (e.g. linear scale-up shown at smaller scales, scale-down models, platform data).
- Clinical trials and manufacturing of clinical trial material are out of scope.
- Projects focused on a single vaccine candidate development, where the technology is not applicable to other products, are out of scope.
- Vaccine platforms without clinical safety, immunogenicity and efficacy data are out of scope. **Such platforms with attributes beneficial for speed, scale and access are referred to Focus Area 1.**

4 Eligibility criteria for Focus Area 3

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

- The technology has the potential to substantially improve our ability to manufacture vaccines at the right commercial scale, make them available at lower cost of goods, and/or make them more equitably accessible. Proof of concept data to support this claim must be included in the application.

- The technology can be utilized to develop vaccines against a variety of viral pathogens and antigens, and is applicable to one or more proven vaccine platforms (e.g. nucleic acid, protein subunit (including adjuvants), viral vector, virus like particle, live-attenuated or inactivated virus).
- The application describes a development plan to advance the technology, with a timeline not exceeding 36 months and a budget not exceeding US$5M, though exceptions may be considered on a case-by-case basis.

In addition, the applicant should confirm:

- 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 applicant's plan may include licensing or otherwise disposing of rights to intellectual property for the technology, and access to GMP-grade raw materials, or a clear alternative pathway to achieving 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 Review criteria for Focus Area 3

Applications that have met the eligibility criteria described under Focus Area 3 will be assessed against the review criteria in Table 2.

Table 2: Review Criteria for Focus Area 3

Criterion	Description
Impact	- Focus Area 3a: Extent to which the technology allows rapid and robust scale-up or scale-out to commercial scale. - Focus Area 3b: Extent to which the technology contributes to substantial reduction of the cost of goods. - Focus Area 3c: Extent to which technology facilitates equitable access to vaccines especially in the Global South, through easy distribution via existing cold chain systems, and administration without the need for trained healthcare workers. - Suitability for regional manufacturing, taking into account facilities, equipment, infrastructure, work force and supply chain needs. - Does the technology have a positive impact on all dimensions of speed, scale and access, for the development of novel vaccines in response to an outbreak? - Can the technology be broadly applied to (proven) vaccines or vaccine platforms with minimal impact to established manufacturing conditions?
Innovation	- To what extent does the proposed technology offer a substantial versus an incremental advancement over alternatives that are currently available or in development? - To what extent does this proposal present a new paradigm or solve a critical technical challenge facing the field?

R&D Strategy & Feasibility	- How well do the provided data support the intended use of the proposed technology? - Are there any major problems inherent in the proposed technology that are unlikely to be resolved? - To what extent do the proposed studies demonstrate the feasibility of the technology and advance the technology to the next stage, addressing key data gaps towards implementation? - Is there a strategic path to regulatory approval for use of the technology in clinical trials and for marketed/authorized vaccines?
Personnel & Environment	- How appropriate is the background and experience of key personnel for the successful completion of the proposed project? - How well do the facilities and infrastructure provide the necessary resources for the successful conduct and completion of the project (including collaborative arrangements)?
Budget	- Is the budget appropriate for the proposed project?

6 Applicant Guidelines for Focus Area 3

6.1 Submission and review process

Key Dates: Applications will be accepted beginning on 24 October 2023, with application deadline at 23:59 CET on the date indicated below:

	Application Receipt Period	Application Deadline	Review Period Starts
Innovative Manufacturing Technologies	24 Oct 2023 – 12 Feb 2024	12 Feb 2024	Feb 2024

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

- All communication of information and application documents must be in English.
- All budget amounts must be submitted in US dollars.

6.2 Application Steps and Application Templates

Step 1:

- Applicants should inform CEPI of their intent to apply as soon as possible by email to: **innovations.cfp@cepi.net**.
- In the subject line of the email, applicants should note the Focus Area under which they intend to apply. Applications to the call described in the text above should state **Focus area 3** in the subject line of the email.

- **Applicants intending to apply will receive instructions for uploading their completed template via CEPI's secure online portal.**
- Technical support or clarification on the submission process can be requested by contacting **innovations.cfp@cepi.net**. CEPI staff will address your questions within the shortest time possible.

Step 2:

All application documents must be uploaded in the file formats specified below:

- **Completed Focus Area 3 application template.**.
- A list of **relevant publications** in the last 5 years (Section 8 in the application template)
- A maximum of **8 CVs or biosketches** (max. 2 pages per CV/biosketch) for applicants, partners, and key experts. (Section 9 in the application template).

Step 3:

All applicants that advance to the due diligence stage may be requested to submit the additional documents specified below:

- **Project plan**
- **Detailed budget** template with budget narrative
- Signed **letters of support for all partners** confirming their agreement to participate in the proposed projects and agreeing with the content of the proposal (PDF file)

It is the responsibility of the applicant to ensure that all requested documents are submitted and to contact CEPI in advance of the submission deadline in case there are any issues regarding the application submission process.

Any costs incurred by applicants in the development and submission of proposals to this call for proposals will not be reimbursed by CEPI.

Data protection

- All applications will be stored in a restricted access repository.
- Personal data included in applications will be handled according to CEPI's Privacy Notice www.cepi.net/terms/.
- All project materials will be considered confidential and proprietary.

7 Award conditions for Focus Area 3

Funding must reflect the proposed activities and agreed conditions of the award decision made by CEPI. CEPI reserves the right to terminate agreements according to mutually agreed "go/no-go" decision criteria.

CEPI's commitment to enabling equitable access through all CEPI-supported programmes is a cornerstone of its mission. Specifically, for awards made under this announcement, equitable access outcomes will be focused around the goals of the particular Focus Area. These may include but are not limited to:

	Equitable Access Outcomes
Focus Area 3	• Open access publication of results • Data available to inform global and regional decision and policymakers • Data shared with CEPI • Funded technology available to progress adjacent CEPI vaccine projects in an affordable manner • Enable the wider community to access tools to accelerate innovation • Willing to engage with regulatory agencies to discuss the funded technology

Through its role as a funder of R&D for pandemic preparedness, CEPI will work with key stakeholders, including the awardee, to enable equitable access to a reserve of investigational vaccines ready for use in a clinical trial setting during an outbreak using an unbiased allocation and distribution process, in accordance with CEPI's Equitable Access Policy and CEPI's principles for maintenance and use of a clinical trial ready reserve.

If you have specific questions regarding the equitable access policy, please contact CEPI at **innovations.cfp@cepi.net**.

CEPI maintains the following research-related policies to provide further guidance to its research partners on:

- Animal research
- Clinical trials (including transparency requirements)
- Equitable access policy
- Scientific integrity/open access policy

Other policies/guidance designed to support CEPI partners on general administrative issues and ensure investor requirements and industry best practices include:

- Anti-corruption
- International sanctions
- Managing conflict of interest
- Procurement
- Travel
- Transparency and confidentiality
- Cost guidance
- European Union regulatory bodies rights of review and audit plus acknowledgement of EU funding.

8 Animal Welfare and Well-Being

The National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) is collaborating with CEPI to embed the 3Rs into CEPI funded projects. The collaboration focuses on reviewing proposals to ensure that animal welfare standards are genuinely high and exceed the legal minima, local issues relating to poor practice are addressed, and overseas work is conducted to standards equivalent to those in the UK (https://www.nc3rs.org.uk/integrating-3rs-publicly-funded-research).

In this Call for Proposals, the NC3Rs will only evaluate **proposals entering due diligence/contracting processes** and that include projects involving the use of animals highlighted by NC3R (i.e., non-human

primates (NHPs), cattle, dogs, cats, pigs, and equines). Based on the review, the NC3Rs will provide recommendations to CEPI, including advice on opportunities to implement the 3Rs, raise specific animal welfare concerns, highlight where good practice is not being adopted, and monitor the implementation of specific policies and guidance. This advice will be used during decisions on funding and when drafting the terms and conditions of grant awards.

To prepare your proposal for this review process, please consider the following guidelines:

- NC3Rs Guidelines: Non-human primate accommodation, care, and use
- Responsibility in the Use of Animals in Bioscience Research, which applies to use of any vertebrate species.
- ARRIVE Guidelines on the reporting of *in vivo* studies.

Implementation of the principles in these guidelines is a condition of receiving funds from CEPI.

Other information that will be considered during the review can be found on the NC3Rs website:

- Directive 2010/63/EU
- Scientific literature on applying the 3Rs in drug development.
- NC3Rs resources on best practice – including those on improving non-human primate welfare (such as the Macaque Website)

In addition, the NC3Rs has produced a PDF presentation to remind applicants of the required animal welfare standards and to provide advice on choosing appropriate contractors. Applicants contracting out animal research or collaborating with other laboratories (regardless of species) are advised to view the presentation well in advance of submitting their application.

9 Technical and administrative questions

Technical and administrative questions about this Call for Proposals should be directed to **innovations.cfp@cepi.net**.