Call for Proposals:
Development of Broadly Protective Filovirus Vaccines

CEPI is pleased to announce its call for proposals (CfP-FILOVAX) for the development of human vaccines that will protect against a range of Filoviruses, with co-funding from the European Union. This document describes the scope, requirements, and processes for the submission of proposals, the process for review, and selection for funding. Further details can be found on our website here.
CfP-FILOVAX aims to support the development of broadly protective Filovirus vaccines with a focus on preventive use. This will be achieved through two focused areas of work: (1) the development of multivalent vaccines comprising several antigens covering filoviruses known to be responsible for human disease outbreaks, and (2) the development of a more systematic approach for the state-of-the-art immunogen design and testing of virus-specific or more broadly reactive immunogens for members of the Filovirus family (contributing to a "vaccine library"). The output of the work under CfP-FILOVAX will be (1) multivalent vaccines with phase II clinical data to support a pathway to licensure, or (2) exemplar vaccine candidates based on immunogen designs from the Filovirus family vaccine library with phase I clinical data.

CEPI invites applicants (i.e. relevant vaccine development organisations and/or consortia) to submit proposals for funding. Applicants should submit detailed plans for product development, manufacturing, and related activities as described in this document, including a clear development plan that describes milestones, timelines, criteria for success, and an assessment of risks and proposed mitigation measures to ensure their resolution. Emphasis on plans to achieve equitable access to the vaccine(s) by providing affordable and timely vaccine availability in low-resource settings consistent with CEPI's mission is a requirement for this CfP.

The budget of CfP-FILOVAX is EUR 50 million and is expected to fund 3 to 5 awards. Please note, those applicants who can provide co-funding, complementary funding, or in-kind support to extend the impact of CEPI's funding will be considered favourably. CfP-FILOVAX projects must be completed within 3-4 years from signature and should have achieved significant progress by 12 to 15 months after the signing of a CEPI funding agreement.

The CfP-FILOVAX is open until 04 August 2024. These dates may be extended or amended depending on programmatic need and at CEPI's discretion.

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 the funding call, CEPI reserves the right to consider and 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 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 -see our 100 Days Mission. 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.

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 vaccine library, including exemplar vaccine candidates against prototype viruses from 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. Toward these ends, CEPI is particularly interested in technology innovations and vaccine candidates that can address the following needs:

- Speed: Development of a vaccine and other biologic countermeasures within 100 days of an outbreak.
- Safety/Efficacy: Acceptable safety/reactogenicity profile, reduction of viral transmission, prevention of disease, protection against potential variants and related viruses, rapid onset of protection, and long duration of protection
- Accessibility: Single-dose, low cost of goods, thermostability, and rapidly scalable manufacturing.

In line with its Mission, CEPI is aiming to develop human vaccines that will protect against a range of Filoviruses. Within this viral family, Ebola viruses and Marburg virus are endemic to West and Central Africa and cause frequent unpredictable outbreaks of varying size and duration. These outbreaks have significant health and societal impacts on populations in the endemic regions. To better prepare for future outbreaks of filoviruses, it is necessary to develop tools to preventively vaccinate at risk populations, such as health-care workers, in endemic regions. While there are two licenced Ebola Zaire vaccines, the impact of such preventive vaccinations would be greatest if the vaccines protected against a broad range of Filoviruses that emerge in those regions.

In line with this purpose, this CfP asks for submission of applications either for (1) the development of multivalent vaccines including phase II clinical data to support a pathway to licensure, or (2) the development of exemplar vaccine candidates based on state-of-the-art immunogen designs covering a larger number of Filoviruses (contributing to a Filovirus vaccine library) up to phase I clinical trials.

2. Objectives

2.1 Development of multivalent Filovirus vaccines

CEPI intends to support the development of broadly reactive Filovirus vaccines that are based on multiple valences. These vaccines should be suitable for the preventive use in at-risk populations in regions where one or multiple Filovirus outbreaks can occur, and therefore be able to contribute to epidemic preparedness.

2.2 Creation and evaluation of a vaccine library for a range of Filoviruses with outbreak potential, from human or animal origin.

CEPI seeks to support the generation of antigens for the Filovirus family and their evaluation in preclinical and/or clinical studies. It is expected that computational prediction will be used to create a collection of immunogen designs for multiple selected viruses within the Filovirus family, and if possible, to design cross-protective antigens. These designs should then be evaluated for expression, antigenicity, and stability. Selected immunogen designs should be combined with vaccine platforms to generate exemplar vaccine candidates that can be further tested in *in vitro* and *in-vivo* preclinical experiments. The most promising pre-clinical exemplar vaccine candidates should then be advanced into translational development up to the end of phase I clinical trials.

3. Scope of the Call

3.1 Development of multivalent Filovirus vaccines

In addition to the licenced Ebola Zaire vaccines, there are different other candidate vaccines under development for Ebola viruses and Marburg virus; their combination into multivalent vaccines could provide the desired breadth of protection against the Filoviruses that have caused the majority of outbreaks in humans. The intent is to support the translational and clinical development of multivalent vaccine candidates up to the end of phase II clinical trials and explore pathways to licensure (ideally based on immuno-bridging approaches).
Multivalent vaccines or individual monovalent vaccines on the same platform will ideally have an established preclinical proof-of-concept (PoC) as well as initial clinical safety and immunogenicity data.

3.2 Creation and evaluation of a vaccine library for a range of Filoviruses

The CfP intends to consider and evaluate application proposals for the use of computational methods for immunogen design and to support experimentally based methods (where applicable) for immunogen verification against several members of the Filovirus family.

The desired outcome from this effort is to have the resultant immunogen designs combined with and tested in various vaccine technology platforms, contributing to a Filovirus vaccine library (i.e., consisting of a knowledge-base, working seed materials and reagents, and/or candidate formulations) that are either ready and available to be used in future Filovirus outbreaks or that create a solid base for the rapid generation of new vaccines for emerging Filoviruses. Immunogen designs should be generated through state-of-the-art computational and structural methods, and tested for their ability to present the right epitopes to maximize the adequate immune response, to be properly expressed in the chosen vaccine technology platform, to generate a protective immune response in animal models, and if possible, to be amenable to early clinical proof=of-concept of safety and immunogenicity. Antigens that are broadly protective against multiple filoviruses are preferred. CEPI encourages applications from consortia that can tackle the different aspects of vaccine library development, as well as preclinical and clinical testing.

CEPI has the capability to support development through its centralised laboratory network and animal models network, and/or adjuvant library (that can be screened for optimal adjuvants for a particular candidate) where applicable. Applicants must discuss these opportunities with CEPI staff prior to application submission.

Applicants based in the Global South and/or partnerships that include developers in the Global South are encouraged to apply. Applications by consortia of partners with complementary competences are encouraged.

4. Eligibility criteria

The funding opportunity through this CfP is open worldwide to all types of non-profit research organisations, for-profit companies, international organisations and foundations, joint R&D ventures, government research organisations, and academic institutions. Applicants must be legal entities, or consortia comprised of legal entities. Applicants must own the technology proposed or have the rights to develop and commercialise the vaccine incorporating the proposed technology.

4.1 Development of multivalent Filovirus vaccines

Applicants must meet the following criteria:

- Existing monovalent or multivalent vaccines should have preclinical PoC, identified production process and analytical methods, and ideally phase I clinical safety and immunogenicity data.
- Proposed multivalent vaccines should cover at least two Filoviruses.
- At least one of the partners in the applicant organisations or consortia of partnering organisations should have experience in human vaccine development, clinical development, and manufacturing.

4.2 Creation and evaluation of a vaccine library for a range of Filoviruses

Applicants must meet the following criteria:

- Demonstrated capability for immunogen design using state-of-the-art methodologies.
- Ability to express and characterise *in vitro* vaccine candidates/designs.
- Ability to perform animal studies and relevant assays to confirm vaccine immunogenicity, and efficacy if animal models are available.

Proposals will be eligible for funding under 4.1 or 4.2 only if they are:

- Coherent with the CfP objectives, as described in section 2
- Relevant to the CfP scope, as described in section 3
- Consistent with the CfP timeline and award conditions as described in sections 5 and 8
- Complete in terms of required content in the proposal templates described in section 5.1

5. Applicant guidelines

5.1. Application steps and templates

Step 1:
To respond to this CfP, you may express your intent to submit a proposal duly in advance in order to receive instructions to prepare the application template and instructions for submission well ahead of the submission deadline. The FILOVAX submission template application will be provided along with instructions for submission to CEPI's Portal. We encourage applicants to submit their proposals well in advance of the deadline.

First, the applicant will need to be set up as a Portal User. This will give the applicant the option to submit a full application, follow the status of the proposal, and check in on project data if receiving funding from CEPI.

Once CEPI has granted access to submit a full application, the applicant will receive a confirmation email from CEPI, with guidance on how to use the new CEPI Portal and how to submit the application. A separate auto-generated email will be sent with a link to log on and create a password.

The submission should be uploaded in PDF format. No additional documentation other than those specified in the template should be submitted.

Additional needs for technical support/clarification must be requested via the Portal.

The CEPI Secretariat will address any questions within the shortest possible timeframe. Any questions submitted, along with answers, will be anonymised and made public if relevant to the preparation of this application. Summary of frequently asked questions (FAQ) will be uploaded to the CEPI website.

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

CEPI will not cover any costs incurred for the development and submission of the application. Furthermore, CEPI will not provide funding retrospectively for activities carried out prior to an award.

Step 2:

Entities that have notified CEPI of intent to apply, must submit their completed proposal to the CEPI Portal by 04 August 2024, 17:00 CET. All associated documents must be uploaded in the file formats specified below:

- Completed application template including a product development plan (in English, PDF format, 30 pages)
- Project plan/GANTT (MS-Project format)
- Completed budget and narrative templates.
- A maximum of 10 CVs or bio sketches (max. 2 pages per CV/bio sketch for applicants, partners, and key experts) (PDF format). Personal data included in proposals will be handled according to CEPI's Privacy Notice.
- Signed letters of support for all partners confirming their agreement to participate in the proposed projects and agreeing with the content of the proposals (PDF format).

5.2. Submission overview

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

- Submission of applications must be completed by 04 August 2024 17:00 CET
- All communication of information and documents must be conducted/translated in English
- All budget proposals should be submitted in US Dollars

5.3 Timeline overview

- Call publication date: 04 June 2024
- Applicants are encouraged to apply well in advance of the submission deadline in order to receive the application template with secure link and instructions for submission.
- Final Submission deadline for applications: 17:00hrs CET, 04 August 2024*
- Peer review and selection: August/September 2024*
- Target dates for due diligence, contract signatures, project launch: December 2024*
- CEPI Grant duration: 66 months

*NOTE: CEPI reserves the right to modify open Call for Proposal timelines in accordance with European Commission funding requirements for CfPs published on the EC Horizon Cascade Funding Calls Applicant guidelines and review process.

6. Review criteria

Proposals will be assessed against the criteria listed in Tables below. Performance of proposals will be evaluated through the evidence provided on all aspects listed under each criterion. Therefore, the quality of the information provided by applicants is crucial to CEPI's funding decision. The basis for selecting proposals for funding will be technical performance, the total costs, and timeframes for completing the projects, and the realism and reasonableness of the proposed project plans. Information requirements to address the criteria are provided in the documents listed in section 5.1.

Applications that have met the eligibility criteria described under section 4 will be assessed against the review criteria in Tables below.

Table 1: Review criteria for the development of multivalent Filovirus vaccines

Categories	Description
Impact	- How well is the vaccine candidate anticipated to protect at-risk populations against multiple filoviruses? - How suitable is the proposed vaccine candidate for preventive vaccination in limited resource settings (number of vaccinations, thermostability, route of administration) - To what extent is the applicant well-positioned to make the proposed vaccine available and affordable in the Global South?
Innovation	- To what extent does the proposed vaccine offer a substantial versus an incremental advancement over alternatives that are currently available or in development (in terms of breadth of coverage, durability of immune response, for example)?
R&D Strategy & Feasibility	- How well do the provided data support the proposed scope of work? - Are there any intrinsic limitations in the proposed vaccine candidate? How well are potential problems identified and alternative methods or approaches addressed? - Is the proposed vaccine development plan, including immunogenicity and safety studies, CMC development, and regulatory pathway, feasible and rigorous based on the information provided?
Personnel & Environment	- How appropriate is the background, experience and availability 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)? - Are applicants in the Global South included in the proposal?
Budget	- Is the budget appropriate for the proposed project?

Table 2: Creation and evaluation of a vaccine library for a range of Filoviruses

Criterion	Description
Impact	- Are the proposed methods for prediction of antigen structure likely to enable rapid and durable immune responses providing protection/ clinical benefit? - Does the proposed work lead to increased understanding of factors affecting expression, stability and antigenicity of potential vaccine antigens for a broad range of Filoviruses? - Will the work lead to a better understanding of potential for cross-reactivity or wide applicability of immunogen design within the Filovirus family? - Is the work likely to lead to the development of tools (e.g., antibodies, assays, animal models) for a broad range of Filoviruses?
Innovation	- To what extent does the proposed strategy offer a substantial versus an incremental advancement over alternatives that are currently available or in development? - Do the applicants use state of the art or advanced methodologies for antigen design and characterization? (e.g., IA/ML, cryoEM or crystallography, high-throughput assays, etc)
R&D Strategy & Feasibility	- To which extent is the proposed work likely to predict, generate and evaluate antigens with the desired characteristics of expression, conformation, protective epitope presentation? - Do the applicants have a track record in structural biology, antigen discovery, early vaccine development, as shown by publication in peer-reviewed journals, execution of pre-clinical or clinical studies, reports, etc. ? - Have the proposed methods been shown through structural biology approaches and other studies to yield immunogens that provide useful immune responses and protection from other viruses? - Do the applicants have the ability to conduct in vitro and in vivo experiments to confirm antigen structure, antigenicity, immunogenicity and efficacy? - Is the proposed vaccine development plan, including immunogenicity and safety studies, CMC development, and regulatory pathway (up to phase I), feasible and rigorous based on the information provided? - To what extent do the proposed studies demonstrate the feasibility of the vaccine and address key data gaps? - How well are potential problems identified and alternative methods or approaches addressed?
Personnel & Environment	- How appropriate is the background, experience and availability 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)?

Criterion	Description
	- If necessary, has the applicant formed a consortium to cover the various steps involved in antigen discovery, early vaccine development (including a proposed technology platform), assay development, animal models and studies, phase 1 clinical trial? - Are applicants based in the Global South and/or does the partnership include applicants in the Global South?
Budget	- Is the budget appropriate for the proposed project?

7. Review and due diligence process timeline

The Secretariat will assess whether received applications fulfil the published eligibility criteria of the call and may send the eligible proposals to internal and independent external experts for peer review. All reviewers who participate in the review process will be evaluated for any potential conflicts of interest and will be required to sign non-disclosure agreements.
Applicants may be invited to clarify any outstanding questions, further details prior to concluding the full review. Proposals and budgets will be subject to a cost challenge undertaken in the context of the applicant's projects and CEPI's policies and cost guidance.
Contract arrangements will be initiated along with technical, financial and integrity due diligence and pursued with recommendations for funding to the Board. For the candidates not proceeding to due diligence the Secretariat will seek to communicate this as early as possible.
The CEPI Secretariat will publicly announce each award when the partnering agreement has been signed. Applicants whose proposals do not advance to contract will be notified confidentially of the outcome of the process.
NOTE: CEPI reserves the right to modify timelines subject to programmatic and review requirements.

8. Technical and administrative questions

Technical and administrative questions about CfP-FILOVAX should be directed via the CEPI Portal. A summary of frequently asked questions and answers (FAQs) may be posted on CEPI's website.

9. Funder Award conditions

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 is committed to achieving equitable access to all CEPI-supported programmes including vaccines, platforms, data, results, and materials. Specifically, equitable access to epidemic vaccines in the context of an outbreak means that appropriate vaccines are first available to populations when and where they are needed to end an outbreak or curtail an epidemic, 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. If you have specific questions regarding the equitable access policy (https://cepi.net/equitable-access), please contact CEPI using the CEPI Portal.

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

- Animal research policy
- Clinical trials policy (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:

- Third-Party code of conduct
- Anti-corruption policy
- International sanctions
- Managing conflict of interest policy
- Procurement policy
- Travel policy
- Transparency and confidentiality policy
- Data protection and privacy policy
- Cost guidance
- European Union regulatory bodies rights of review and audit plus acknowledgement of EU funding Award conditions

10. Animal Welfare and Well-being

The National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs https://nc3rs.org.uk/) 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 CEPI's call for vaccine development, the NC3Rs will only evaluate proposals entering due diligence/negotiation 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.