CEPI

Call for proposals (CfP3ii)
Topic: Human vaccine development against Rift Valley Fever

Reference number: CEPI-CfP-003ii

CEPI is pleased to announce the second phase of its third call for proposals (CfP3ii) for the development of human vaccines against Rift Valley Fever (RVF), which is co-funded by the European Union. This document describes the scope, requirements, and processes for proposal submission, review, and selection for funding. Further details can be found at www.cepi.net.

CEPI envisions a world in which epidemics are no longer a threat to humanity. CEPI is working to achieve this vision by accelerating development of vaccines against emerging infectious diseases with a view to the ultimate licensure of these products and use in an emergency. Central to all of this is enabling equitable access of these vaccines for populations who need them during outbreaks.

CEPI invites applicants (i.e. relevant vaccine development organizations 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 and criteria for success, and an assessment of risks and proposed mitigation measures to ensure their resolution.

CfP3ii is the second phase of a two-step process in which CEPI is seeking to fund human vaccine development against RVF. The first funding opportunity was in 2019 (CfP3i). We are now proud to announce a second open call in 2022 (CfP3ii), which will make additional funding, for later stage vaccine development, available to successful candidates. Importantly, a successful application for funding in CfP3i (first call) is not a precondition for applying for funding in CfP3ii (second call).

The budget of CfP3ii is USD 50 million and is expected to fund 2 to 3 awards. Applicants who are able to provide co-funding, complementary funding, or in-kind support will be considered favourably.

CfP3ii projects must be completed within 3-4 years from January 2023 and should have made significant progress in the 12 to 15 months after the signing of a CEPI funding agreement.

If you are planning to submit, please let us know by the 14th of October 2022. By this date, you must send a request to receive instructions on how to submit your application. The submission deadline for this call for proposals is Tuesday, the 15th of November 2022, 17:00 CET.

1. Introduction

1.1. The Coalition for Epidemic Preparedness Innovations (CEPI)

Epidemics of emerging infectious diseases (EIDs), particularly those prioritised by the WHO in its "R&D Blueprint for Action to Prevent Epidemics", are a significant threat to global health security. In a

world with increased urbanisation, mobility, and ecological change, their potential for disruptive impact is increasing.

At CEPI, we envision a world in which epidemics are no longer a threat to humanity. Our contribution to this goal is to accelerate the development of vaccines against EIDs whilst enabling equitable access to these vaccines for populations who need them during outbreaks.

CEPI is an international non-profit association established to develop vaccines to prevent and respond to future epidemics and to secure access to such products for the populations who need them. CEPI will advance safe, effective and affordable vaccines that can help to contain outbreaks at the earliest possible stage.

CEPI was launched in January 2017 by the governments of Norway, India, the Bill & Melinda Gates Foundation, the Wellcome Trust and the World Economic Forum. CEPI has further secured financial support from Australia, Austria, Belgium, the Bill & Melinda Gates Foundation, Canada, Denmark, the European Union, Ethiopia, Finland, Germany, Greece, Hungary, Iceland, Indonesia, Italy, Japan, Kuwait, Lithuania, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Portugal, Romania, Saudi Arabia, Serbia, Singapore, Switzerland, The Republic of Korea, United Kingdom, USAID, and Wellcome.

To accomplish our mission, CEPI will:

- Directly fund and coordinate vaccine development, advocate for regulatory innovation and harmonisation, and fund associated costs for meeting regulatory requirements;
- Support the development of vaccine technologies and manufacturing capabilities that can be deployed rapidly against outbreaks of known and recently emerging pathogens;
- Take a role alongside other organisations—including other funders—in support of sustainable manufacturing and in the maintenance and release of investigational vaccine stockpiles (free of charge where funded by CEPI) when an outbreak occurs;
- Together with awardees of CEPI funding and relevant stakeholders, facilitate and coordinate resource mobilisation for Phase III trials to be conducted during outbreaks for the purpose of licensure;
- Take all possible actions at each stage of product development and manufacturing to maximise the achievement of equitable access to our vaccines.

1.2. About this call for proposals

This new call for proposals builds on CEPI's previous investment in two vaccine candidates for Rift Valley Fever virus (RVFV). This was further informed by a thorough review of progress in November 2021. Initially, in September 2018, the CEPI Scientific Advisory Committee (SAC) advised that CEPI should invest in human vaccine development against RVFV. This advice was based on the feasibility of vaccine development and the potential public health impact of vaccines against this disease. Whilst a human vaccine against the virus appears to be technically feasible, the commercial prospects for such a product are relatively non-existent, hence the need for our intervention. RVF disease was included among the WHO R&D Blueprint list of priority pathogens in 2018.

Landscape analysis suggests that there are some 17 candidate RVFV vaccines in development. To date, only two have been in Phase II where development seems to have stalled. Significant further development was achieved by CEPI's previous funding of two preclinical and early-stage clinical vaccine candidates for RVFV (CfP3i). Now we seek further clinical development in this new call for proposals, henceforth known as CfP3ii. The focus of this call for proposals will be to complete Phase I/II clinical testing in a country endemic for RVFV. Building on developments from CfP3i funding, and/or including the work of others, applicants should have a well- defined manufacturing plan and possess significant existing preclinical data in order to be eligible for the call.

1.3. European Union support

This is the second jointly funded call for proposals resulting from the collaboration between CEPI and the European Union's Horizon programmes[1],[2]. Thanks to generous co-funding from the European Union, CEPI is now able to present this second funding opportunity in 2022 (CfP3ii). This was unfortunately significantly delayed due to the COVID-19 pandemic. Whilst successful CfP3i applicants could be granted further funding through the current CfP3ii call, dependent on the progress of their vaccine development projects, a successful CfP3i application is not a precondition for applying for funding in CfP3ii.

1.4. Funding opportunity

Allocated funding: total funds allocated for CfP3ii is USD 50 million with which it is envisioned that 2-3 projects could be supported. Applicants who can access co-funding, complementary funding, or in-kind support will be considered favourably.

Project duration: Projects of 3-4 years are anticipated which should include production of clinical trial material and at least one clinical trial.

2. Objectives of CfP3ii

Proposals for CfP3ii must present their plans for clinical stage vaccine development of their RVFV candidate. This may, or may not, build on data gathered from a previously CEPI supported project. Previous funding from CEPI is *not* a precondition for support. CEPI aims to achieve the following objectives:

a) Complete Phase I/II clinical testing in an endemic region using a viable vaccine candidate.

b) GMP manufacture and release can be supported, providing established release assays and production processes have been developed. These assays should include the testing of cell and virus banks (where applicable) making them ready for GMP production and release. Technology Transfer to a recognised contract development manufacturing organisation (CDMO) can be supported.

c) Toxicology will be supported but early-stage preclinical development will not. It is an eligibility requirement that significant preclinical proof of concept data are already available.

d) Regulatory interactions, including those with a view to ultimate vaccine licensure and/or emergency use, will be supported.

e) Assuming that the clinical trials are successful, awardees may be asked to prepare a ready-reserve of vaccine which could be deployed in an emergency situation. This may be subject to a separate funding call.

[1] http://ec.europa.eu/research/participants/data/ref/h2020/wp/2018-2020/main/h2020-wp1820-health_en.pdf

[2] https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/wp-call/2021-2022/wp-4-health_horizon-2021-2022_en.pdf

3. Scope and call for proposals structure

3.1. RVFV Phase I/II clinical vaccine development

Disease scope: human vaccines to protect against RVF disease

Indicative work package (WP): funding will be targeted towards WPs that will result in clinical testing of vaccine candidates suitable for prophylactic and/or reactive use in target populations in countries affected by RVF disease, as described in Table 1 below.

Project eligibility criteria:

- *Key criterion:* data demonstrating protective efficacy studies in relevant animal challenge models must exist. These data must be included within the application (either referenced or as an appendix) and will be evaluated for quality.
- *Specific additional criteria:* are provided to give applicants further information in Table 1.

Table 1: RVFV vaccine development WPs and additional eligibility criteria

Work packages	*Specific additional eligibility criteria*
Clinical: Carry out Phase I/II studies in an endemic region for RVFV. Multiple vaccine modalities will be considered and platform technologies are of particular interest. In particular, vaccine technologies that align with CEPI's 100-day challenge are particularly encouraged to apply. All proposed vaccine candidates must be able to show preclinical evidence of protection from viral challenge. Whilst the current call is limited to Phase I/II clinical trials, applicants will be expected to develop a regulatory plan for not only the proposed trial but also later stage development towards emergency use and/or licensure.	Applicants must propose a clinical development plan, including testing in countries with documented burden of RVF disease in humans, which outlines development of the vaccine to clinical proof of concept stage. Applicants are further advised to evaluate the feasibility of late-stage clinical studies (currently outside the scope of this call) with assessment based on epidemiology/modelling to inform the regulatory pathway and any post-approval commitments.
Clinical development: Sites chosen for the phase 1/2 clinical trial should be able to demonstrate that RVFV has been detected within their region and previous experience of involvement in vaccine development would be beneficial. Applicants are encouraged to develop a One Health[3] approach, taking into account environmental, human and veterinary variables, to predict where and when outbreaks are likely to occur. Studies that could inform the determination of a correlate of protection are eligible for funding. These	Applicants should be able to demonstrate that they have suitable pre-existing data on animal challenge studies or human survivor studies/clinical trials that could inform the development of a correlate of protection. Data are expected to be shared in relation to correlates of protection using open access resources.

[3] https://www.who.int/news/item/01-12-2021-tripartite-and-unep-support-ohhlep-s-definition-of-one-health#:~:text=Joint%20Tripartite%20(FAO%2C%20OIE%2C%20WHO)%20and%20UNEP%20Statement&text=One%20Health%20is%20an%20integrated,of%20people%2C%20animals%20and%20ecosystems

data should contribute to the identification, testing, evaluation and prioritization of surrogate-endpoints of protection in RVF disease (e.g. immunobridging between human survivor studies and/or testing of clinical trial samples.)	
Regulatory Affairs: An engagement plan with regulatory authorities/agencies to seek relevant input/scientific advice in connection with the proposed Ph I/II clinical trials is requested. An initial draft regulatory plan considering further product and clinical development should be prepared. This could include the preparation of a Phase IIb stockpile on a pathway to full licensure/ emergency use approval. All plans will be considered but applicants should be aware that the current funding opportunity will only cover Phase I/II clinical development. The plan should clearly describe any activity/interaction held with regulators in the past as part of the project development.	Applicants are strongly encouraged to develop and present an engagement plan to interact with authorities involved in the conduct of the proposed clinical studies in endemic regions. Such interactions might be with local regulators responsible for clinical trial application review and approval and/or with regulatory authorities that are not directly involved in the approval of the clinical trial application. Applicants are suggested to provide a draft regulatory plan that describes pathway to licensure/emergency use, considering the overall project development plan.
Chemistry, Manufacturing and Control (CMC): Applicants will be expected to deliver a preliminary production process that will deliver the vaccine with desired quality at reasonable yield/cost. The process should have identified preliminary process control parameters, raw materials/consumables, and appropriate in-process analytical methods. The process should be suitable for rapid adaption into a Contract Manufacturing Operation (CMO) to produce GMP Phase I/II clinical materials. The production process should also be amenable for future scale-up to support future Phase III and commercial production requirements. The final product of the process (DS) should have established quality attributes and analytical methods required to measure those attributes identified. Validated stability indicating assays should also be provided. Production of a ready-reserve of Phase IIb product and late-stage development are currently *out of scope* but applicants are requested to provide an outline plan of how a stockpile could be produced and an estimate of how large it may need to be. It is envisaged that future funding opportunities may arise which will seek to develop a ready reserve of vaccine for outbreak control. Batch release with stage appropriate analytics and some initial formulation studies should be included. Programs that would assist WHO prequalification should consider (i) thermostability studies including extended controlled temperature conditions (ii)	Demonstrated experience in developing a vaccine process that has gone forward to licensure through stringent regulatory agency. Applicants must provide the evidence of partnership with experienced CMC human vaccine manufacturing providers or in-house capacity such that GMP material suitable for clinical study can be produced. Manufacturing plans suitable for technology transfer to LMICs are particularly encouraged.

determination of appropriate vaccine vial monitoring (iii) defining supply chain strategy, e.g. packaging and presentation, cold-chain footprint and multidose vial presentation.	
Toxicology: Whilst early-stage preclinical development will be out of scope (this should have been completed), preclinical toxicology studies required for clinical trial application(s) will be eligible. **Applicants may also want to consider DART and neonatal studies to support vaccine deployment in vulnerable populations, although this is not considered mandatory for Phase I/II.**	Study design and conduct must be in compliance with national and international guidelines.
Enabling Science: All assays should be validated, where possible, such that they will facilitate vaccine licensure and/or emergency use. Use of appropriate international standards is encouraged.	CEPI has an established programme of serological standard development for RVFV and applicants are encouraged to engage with this as, and when, it becomes available. Applicants who promote capacity building with the performance of assays in-country are particularly encouraged. There is an expectation to share assay protocols, standards, and animal models with any other developers irrespective of CEPI funding. Developers should also be prepared to allow centralised laboratory testing of clinical samples should CEPI make such a facility available during the course of the project.

4. Applicant 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. At least one of the partners in the applicant organisations or consortia of partnering organisations should have experience in **human vaccine development** and have a track record of bringing vaccine candidates through to human clinical trials in the past 10 years. Applicants unable to demonstrate this experience will not be eligible for funding.

Proposals will be eligible for funding only if they are:

- **Coherent** with the CfP3ii objectives described in section 2
- **Relevant** to the CfP3ii's disease scope, as described in section 3
- **Consistent** with the CfP3ii timeline and award conditions as described in sections 1.4 and 8
- **Complete** in terms of required content in the proposal templates described in section 5.1.

5. Applicant guidelines

Proposals must include essential evidence as described in the "Proposal and templates" section below, meet the presented timeline requirements for completion, contain sufficient detail for review of the proposed product development process, and any claims made within the proposal must be supported by evidence. Adherence to CEPIs policies is a condition for receiving funding (see section 8).

All applications must use the CEPI portal, which is an online interface allowing applicants to interact with us. To apply, you need will need to become a portal user so please send an e-mail to CfP-311-RVF@cepi.net to receive your user information and guidelines. You will receive a confirmation from CEPI and then an autogenerated e-mail with a link to log on and create your password.

CEPI recommends only 2-3 people from your organization request a portal user and that they are responsible for filling in the proposal and uploading attachments. CEPI will provide step by step user guide to all applicants, and if you need technical support during the application please contact: CfP-311-RVF@cepi.net.

To apply go to the portal and select CfP3ii (https://cepivaccines.force.com/portal/s/opencfps)

Please read the Introduction to the CEPI portal for applicants for more information.

5.1. Proposal and templates

Entities that want to respond to this call for proposals must submit their proposal to CEPI via the dedicated secure platform by the **November 15, 2022 (17.00 CET)**. All associated documents must be uploaded in the file formats specified below:

- **Product development plan** (pdf file)
- **Project plan** (MS-Project format)
- A maximum of 10 **CVs or bio sketches** *(max. 2 pages per CV/bio sketch for applicants, partners and key experts)* (pdf file)
- 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 file)

No additional documents should be submitted.

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

Personal data included in proposals will be handled according to CEPI's Privacy Notice on www.cepi.net.

5.2. Submission overview

If you are planning on submitting, please let us know by the **14th October 2022** in order for CEPI to best plan for the subsequent review process.

To ensure a secure submission process, you must request instructions on how to submit your application by emailing CfP-311-RVF@cepi.net **by the 14th of October 15:00 CET**. We encourage you to submit your proposal well in advance of the deadline.

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

- Submission must be completed by **15th of November 2022 17:00 CET**
- Requirements in section 5.1 must be completed

- All communication of information and documents related to this call must be conducted in English
- All budget proposals should be submitted in US Dollars

In case of questions in relation to the submission system, access to proposal form templates, or any other issue related to this call for proposals, please contact CfP-311-RVF@cepi.net. The CEPI secretariat will address your questions within the shortest possible timeframe. Any questions submitted, along with answers, may be made public if having relevance to inform preparation of the application. Instructions for applicants as well as a summary of frequently asked questions and answers (FAQs) will be uploaded to the CEPI website.

It is the responsibility of the applicant to ensure that all requested documents are submitted within the deadline, and to contact CEPI in advance of the submission deadline in case there are any issues regarding the completeness of the submission. All applications will be stored in a restricted access repository.

No costs incurred by the applicants for the development and submission of proposals will be covered.

6. Review criteria

Proposals will be assessed against the criteria listed in Table 2 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.

Table 2: Review criteria

Criterion	Aspects to consider where appropriate
1. Applicant competencies, experience and track-record	▫ Technical competency/expertise of project staff ▫ Experience in preclinical testing of vaccines ▫ Experience in conduct of clinical vaccine trials in LMIC settings ▫ Experience in regulatory interactions with competent authorities and licensing of vaccines ▫ Manufacturing capabilities and skills
2.Technical feasibility	▫ Soundness of the theoretical concept ▫ A preclinical data package which will support rapid initiation of Phase I clinical trial development. ▫ Scientific appropriateness of the clinical development, epidemiology/modelling study(ies) and regulatory approach and quality of the available data
3.Manufacturing scalability and speed	▫ Significant evidence that the proposed manufacturing process is viable for the candidate vaccine ▫ Current status/availability of manufacturing ▫ Suitability of the process for scale-up.
4. Use potential for target pathogens	▫ Suitability of the candidate vaccine for reactive use during outbreaks ▫ Suitability of the candidate vaccine for preventive use in countries disproportionally affected/LMICs

5. Use potential for other pathogens	▫ Potential of the technology platform to be used for other pathogens on the WHO R&D Blueprint list ▫ Suitability of the technology platform for other pathogens beyond the R&D Blueprint list
6. Cost	▫ Each cost response will be reviewed for cost realism, reasonableness, and overall best value ▫ Proposals will be reviewed to determine if the costs proposed are based on realistic assumptions, reflect a sufficient understanding of the technical goals and the objectives of the call and are consistent with the proposed technical approach ▫ Applicants who are able to provide co-funding, complimentary funding, or in-kind support will be considered favourably.

7. Review and due diligence process timeline

The Secretariat will assess whether received applications fulfil the published eligibility criteria of the call, and then will send the eligible proposals to internal and independent external experts for 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. CEPI's Scientific Advisory Committee will advise on the selection of proposals to be considered for funding.

Applicants may be invited for interviews when required to ensure that any outstanding questions are resolved prior to concluding the full review. CEPI will cover reasonable travel costs for this purpose[4]. 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 and financial due diligence and pursued to recommendations for funding to the Board by Q4 2022. 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 in a timely fashion.

8. Award conditions from funders

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

[4] CEPI will cover travel costs for three consortium members for those invited to a bid defense meeting if applicants are selected for funding.

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, please contact CEPI at CfP-311-RVF@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

9. 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 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 take into account 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.

10. Technical and administrative questions

Technical and administrative questions about CfP3ii should be directed to CEPI Secretariat (CfP-311-RVF@cepi.net). A summary of frequently asked questions and answers (FAQs) will be posted on CEPI's website.