CEPI | New vaccines for a safer world

Coalition for Epidemic Preparedness Innovations

Call for proposals (CfP) Step2

Topic: Vaccine development against Lassa, MERS-CoV and Nipah

Reference number: CEPI-CfP-001-Step2

Given a successful review of preliminary proposals under step1 of the CEPI Call for proposals for vaccine development against Lassa-MERS-Nipah, CEPI hereby invites shortlisted applicants to submit a full proposal for funding. This document describes the requirements and processes for full proposal submission, full review and final selection for CEPI funding.

The deadline for submission of full proposals will be **4 p.m. CEST 12 July 2017**

1. Step 2: Guidelines for full proposal submission

1.1. General instructions

Applicants invited to respond to step 2 of this Call for Proposals (CfP) must submit their full proposals to CEPI via the online application system of the Research Council of Norway before **4 p.m. CEST[1] on 12 July 2017**.

Applicants are encouraged to discuss their proposal with the CEPI secretariat prior to the submission deadline in order to ensure alignment between the proposals and CEPI's objectives. Applicants can contact cfp@cepi.net in case of questions on the electronic submission system, access to proposal form templates, technical and administrative issues related to this invitation, including scheduling of any teleconferences to address potential clarifications raised in letters of invitation to step 2 received from CEPI.

1.2. Full proposal submission

Applicants invited to submit full proposals must create a new online application form, but can copy and adjust the data submitted under step 1 of this CfP. Applicants are requested to prepare and upload as attachments all the following completed documents:

- A full project description form *(max 50 pages)*
- A budget narrative *(max 5 pages)*
- A detailed budget plan *(excel by email cfp@cepi.net)*
- A milestone template with stage gates for key activities by phase of development *(2-3 pages)*
- Any CVs or bio sketches that are relevant and have not been submitted previously *(max 2 pages per CV/bio sketch)*

Templates, which include detailed guidelines, for the required attachments are accessible via the CEPI and RCN websites. **The project description form cannot exceed 50 pages, the budget narrative cannot exceed 5 pages and the proposal should only include documents listed above.** Submissions that exceed any of these limits will be excluded from consideration. All uploaded documents must be converted to pdf format. In addition, the budget plan (excel) should be send to cfp@cepi.net.

Please present us with a proposal for base funding on a rolling base with options for subsequent tranches of funding based on milestones designated by stage gates using the budget template and its milestone structure. The base funding will carry the project up to the first stage gate review, with funding for subsequent milestones made at each designated stage gate. The staged funding should also match the Milestone Template.

2. Step 2: Review of full proposals

2.1. Review criteria

Full proposals in Step 2 will be assessed against the following criteria that are listed below. Performances of full proposals against these criteria will be evaluated through the evidence provided on all aspects listed under each criterion below. The level and quality of the information made available by applicants to CEPI against these aspects is therefore critical to help CEPI determine the expected performance of full proposals and guide its subsequent funding decisions. The basis for selecting full proposals for funding will be technical performance (criteria 1, 2, 3, 4 and 5), commensurate with the

[1] Please be aware that the given dead-line is absolute. Potential applicants are recommended to complete and submit the proposal in good time before the dead-line. Please use the "Check-Page" function frequently during creation of the electronic application.

total costs and timeframes for completing the projects (criteria 6 and 7), the realism and reasonableness of which will also be considered.

1 APPLICANT COMPETENCY, EXPERIENCE AND TRACK RECORD

Extent to which the applicant organization or consortium is capable of performing the proposed activities of the project. The applicant competency, experience & track record is assessed in relation to the evidence provided by applicants to demonstrate:

1.1 Technical competency/expertise based on provided CVs, lists of vaccine development achievements and research results

1.2 Experience in preclinical testing of vaccines, including on non-human primate models

1.3 Experience in conduct of Phase I/II clinical vaccine trials, including on:

- Phase I/II clinical vaccine trials in High Income Country settings
- Phase I/II clinical vaccine trials in Low and Middle Income Country settings
- Phase I/II clinical vaccine trials in disease outbreak settings
- Testing of the proposed technology platform in clinical settings

1.4 Experience in regulatory interactions with competent authorities and licensing of vaccines, including on:

- Track-record of licensing vaccines in the last 10 years through standard regulatory pathways in High Income Countries
- Track-record of licensing vaccines in the last 10 years through standard regulatory pathways in Low and Middle Income Countries
- Track-record of registering vaccines in the last 10 years through the WHO Prequalification Programme
- Track-record of licensing vaccines through alternative regulatory pathways for product registration and/or delivery for emergency use to national (e.g. US FDA's animal rule) or supranational organizations (e.g. WHO EUAL)

1.5 Infrastructures and facilities in-house, or alternatively contract manufacturing partnerships for clinical lot and scale-up production

1.6 Clinical / regulatory capabilities in-house or through consortium of partners (e.g. Contract Research Organizations, Contract Manufacturing Organizations, other service providers, etc.), where this is relevant

2 TECHNICAL FEASIBILITY

Extent to which the development of the vaccine candidate can reach successfully end of phase II and readiness for phase III or EUAL. The feasibility of vaccine development through end of phase II is assessed in relation to the evidence provided to demonstrate:

2.1 The soundness of the theoretical concept/scientific rationale of the proposed vaccine R&D candidate:

- mode of action of the candidate vaccine
- type of immune response induced
- mode and route of application
- If an adjuvant is used, rationale for the use/selection or testing of adjuvants (if applicable)

2.2 Availability/completeness/quality/validity of the integrated product development plan from research through clinical development and potential EUAL (or full approval) l, including on:

- Soundness of critical development path and clarity of project milestones, core activities to reach milestones, go/no-go criteria by milestone and plans for overlapping subsequent preparatory activities to allow seamless and speedy transitions between milestones
- Identified risks and quality of risk mitigation plan

2.3 Current development status/technical readiness of the proposed vaccine R&D candidate

- Preclinical development status: available data on immunogenicity in small animals; protection in relevant animal models; passive transfer protection; toxicology data
- Availability of platform toxicology data
- Availability of toxicology batches
- Clinical development status or readiness
- If not in clinics, time to First In Humans (FIH)
- Qualified and validated assays suitable for routine use

2.4 The soundness of the clinical development approach through phase II, regulatory/prequalification pathway and strategy for obtaining emergency use approval::

- Clinical plan phase I/II, Contract Research Organization (CRO) engagement, timelines and cost per subject
- Establishing clinical trial sites and planning for clinical trial execution
- Obtaining regulatory advice with respect to clinical development
- Identifying/selecting an appropriate regulatory pathway to licensure
- Engaging with the WHO on prequalification requirements or EUAL requirements

3 MANUFACTURING SCALABILITY AND SPEED

Extent to which the platform technologies and manufacturing processes in this project can achieve CMT supply early enough to conclude phase 2 within 5 years or less; and readiness to supply sufficient quantities for emergency use in time to impact emerging disease outbreaks. Manufacturing scalability and speed is assessed in relation to the evidence provided by the applicant to demonstrate:

3.1 The soundness/scientific rationale of manufacturing processes/technologies supporting the candidate vaccine:

- Principle of antigen presentation, formulation, delivery and administration
- Method of delivery and administration

3.2 Current status/availability of manufacturing:

- Master cell bank/working cell bank and master seeds/working seeds established
- In absence of master cell bank and seeds, previous evidence for the technology platform (cell bank/vector/adjuvant/targeted MOA)
    - Human trial data up to licensure (number of people exposed, doses administered, repetitive dosing)
    - Number of licensed vaccines (where?) and research projects leveraging this platform;

- Clarification whether the platform resides in-house or with a Contract Manufacturing Organization (CMO)
- Human trial data with platform incl N of individuals dosed, N of doses given, data on repetitive dosing

3.3 Manufacturing capacity and yield at '(if previous experience exists with the proposed technology platform)

- pilot scale' (10 Ltr)
- 'medium scale' (50 Ltr)
- 'large scale' (1000 Ltr and above)

3.4 Time to produce /release sufficient vaccine quantities of vaccine for emergency use in a response to a disease outbreak

- Clarify for different dose scenarios (≤50k doses; ≤200k doses; ≤1m doses)
- Clarify whether technology is warm (in constant use) or cold (would need to be "reactivated")
- Clarify whether fill/finish is a bottleneck, and if so, how this is addressed

3.5 The suitability of manufacturing processes/technologies for large scale production and delivery in an emergency

- Stability characteristics of the DS and DP at different storage temperatures
- Purity features of candidate vaccine/technology platform (focus on residual DNA, host cell proteins; any particular products in the manufacturing process that merit special attention)
- Particular strategies in place (process steps downstream) to remove impurities (host cell DNA) and any evidence of clearance effects, if quantitative assessments have been made
- In depth technology platform validation actions undertaken with regards to purity, safety (viral clearance), BSE risk (use of products of animal origin)
- Expected product validation/qualification actions to be completed by the time stockpiles for phase IIb/III were to be produced

4 USE POTENTIAL FOR TARGETED PATHOGENS

Explain the extent to which the candidate vaccine is likely to meet WHO Target Product Profiles and how this might affect use of the candidate in emergency response and potential routine use (See TPP Lassa, MERS, Nipah on the WHO website. Please note that the TPPs for Lassa and Nipah are drafts and the final version should be published shortly). Use potential for targeted pathogens is assessed in relation to the evidence provided by the applicant to demonstrate:

4.1 The suitability of the candidate vaccine for outbreak control of the targeted disease, with respect to:

- Immunological properties (onset of protection, duration of protection, quality of immune response, type of response, quantity of response. Administration mode, number of doses)
- formulation/presentation characteristics (formulation, presentation , paediatric presentation, storage conditions, shelf-life, storage volume per unit)

4.2 The suitability of the candidate vaccine for routine use (e.g. expanded programmes on immunization), with respect to:

- Safety

- Immunological properties
- Use in primed populations (important for vectors) or re-use of vector for other candidates
- Formulation/presentation characteristics

5 USE POTENTIAL FOR NEW PATHOGENS

Extent to which the platform technology supporting the candidate vaccine is likely to be suitable for other (re)emerging pathogens. Use potential for new pathogens is assessed in relation to the evidence provided by the applicant to demonstrate:

5.1 Suitability of the technology platform for other pathogens of the WHO priority list of emerging infectious diseases

- Types of pandemic/endemic disease the platform may be useful for (e.g., viral, bacterial, mosquito-borne, parasitic, etc.)
- Target diseases for which the platform has been shown proof-of-concept in animal models

5.2 Suitability of the technology platform for other pathogens beyond the WHO priority list of emerging infectious diseases

- Types of pandemic/endemic disease the platform may be useful for (e.g., viral, bacterial, mosquito-borne, parasitic, etc.)
- Target diseases for which the platform has been shown proof-of-concept in humans/is in routine usage for other vaccines

6 TIME-TO-COMPLETION

Extent to which the proposed timeframes for the completion of the project (i.e. advancing the proposed vaccine candidate through phase II and regulatory approval) are based on valid/realistic assumptions, reflect an understanding of the technical milestones and objectives and are generally consistent with the applicant's proposed activities. The technical performance of all proposals against the criteria of feasibility, manufacturing scalability/speed, and use potential, will need to be commensurate with the timeframes of implementing the projects. Therefore shorter timeframes (ideally less than three years and not more than five years) will be positively evaluated under the time-to-completion criterion, and in general shorter timeframes for advancing vaccine candidates through phase II and regulatory approval will impact positively the overall performance of proposals.

Realism of time-to-completion estimates is assessed in relation to the evidence provided by the applicant to demonstrate:

6.1 Reasonableness of milestone and activity timelines for non-clinical development

6.2 Reasonableness of milestone and activity timelines for clinical development and regulatory approval

6.3 Realism of overall time-to-completion of the project

7 COST

Extent to which the proposed project budget is based on valid/realistic assumptions, reflects an understanding of the technical milestones and objectives and is consistent with the applicant's proposed activities. The technical performance of all proposals against the criteria of feasibility, manufacturing scalability/speed, and use potential, will need to be commensurate with the cost of implementing the projects. Therefore lower costs will be positively evaluated under the cost criterion, and in general lower costs for advancing vaccine candidates through phase II and regulatory approval

will impact positively the overall performance of proposals. Competitive budgets that represent fair market value and the availability of additional funding sources will be seen as a positive.

Cost is assessed in relation to the evidence provided by the applicant to demonstrate:

7.1 Reasonableness of cost estimates and detailed breakdown of these by milestone and activity for non-clinical development

7.2 Reasonableness of cost estimates and detailed breakdown of these by milestone and activity for phase I and phase II development and regulatory approval

7.3 Reasonableness of detailed cost estimates for stockpiling vaccine product in bulk and fill-finish format under 100 thousand, 500 thousand and 1 million dose scenarios

7.4 Realism and transparency in the justification of overall cost estimates for completing the project, including whether overall costs are competitive and represent fair market value, and whether there are additional funding sources to share the overall cost of completing the project

2.2. Full proposal reviews and confidentiality

Full proposals will be sent to external reviewers for full review. External reviewers have been checked for conflicts of interest and have signed confidentiality agreements. Applicants may be invited for interviews when it is felt beneficial to ensure that any outstanding questions are resolved 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. The SAC will make final recommendations for funding to the Board in September 2017.

2.3. Funding decisions

The Board will make conditional funding decisions for contract negotiations, building on SAC recommendations, business and strategic considerations. The CEPI secretariat will support the SAC and the Board in assessing cost/risk/benefit profiles of shortlisted proposals and in concluding the business case for investment on each of these proposals to the CEPI Board. Final funding decisions will be made only when contract negotiations between CEPI and invited applicants will have been concluded.

3. When will applicants be notified of the award decision?

The anticipated date for notification of results of the proposal process is contingent on the CEPI Board's decision in September 2017. The decision will be published on CEPI's webpages, and applicants will be notified as soon as possible. The CEPI secretariat will facilitate direct negotiations, due diligence, final contracting and follow up of funded proposals.

4. Award conditions

Following Board funding decisions, the CEPI secretariat will provide feedback to applicants receiving an award decision. Applicants and their partners, in case of consortia, are expected to sign a contractual agreement with CEPI within three months from award notification and must designate a representative for contract negotiations with the CEPI secretariat.

Funding will in general be for three years and not for more than five years and must reflect the proposed activities and agreed conditions of the award decision made by the CEPI Board. CEPI reserves the right to terminate agreements according to mutually agreed "go/no-go" decision criteria which are reviewed by the SAC.

CEPI will negotiate with each awardee to optimize and reach an agreement on the ownership and management of intellectual property. Optimal management will safeguard against the use of intellectual property in a manner that impedes equitable access to the vaccine.

More details on award conditions are available online in CEPI policies on:

- Equitable access policy, including data sharing
- Shared risks/shared benefits policy
- Management of intellectual property (IP)

CEPI is currently developing the progress and financial reporting requirements and schedule for awardees, beyond that which is already specified in the Key Funding terms document. These requirements will be published shortly. CEPI reserves the right to request external audits of consortium partners, as well as the right to join regulatory meetings or to participate as an observer to the open part of "Data and Safety Monitoring Board" meetings. The Awardee shall ensure that the control of expenditure under the Award is governed by its normal standards and procedures and is covered by the Awardee's formal audit arrangements. The Awardee shall allow CEPI access to relevant financial records to enable CEPI to ensure auditing compliance.

5. Key dates

Date	Action
12 July 2017	Deadline for submission of full proposals
July - August 2017	Full proposal review
September 2017	Project selection completed, investment decisions made, and award notifications sent (based on CEPI Interim Board Meeting timetable)
Autumn 2017	Contract negotiations.
December 2017	Project start-up expected on signing of contracts.