14.02.2017

CEPI | New vaccines for a safer world

Coalition for Epidemic Preparedness Innovations

Responses to CfP1 questions sent to cfp@cepi.net by 3 February 2017

Contents

Overview

Below you will find answers to questions that the CEPI Secretariat received by 3 February 2017. There will be one more round of answers published for questions submitted to cfp@cepi.net by **20 February 2017**. One set of responses to all questions will be emailed to those who submitted questions. All responses to the two rounds of questions will be published here.

Please note that these responses are in addition to the previously published application guidelines and frequently asked Questions on the CEPI Website.

Scientific questions

1. Do you accept applications from individual organisations that provide services or tools needed for vaccine development or do you prefer that such organisations be part of consortia with vaccine developers?

The scope of the present call is on developing specific vaccine candidates through Phase II, and targeting one or more of the three CEPI prioritised diseases. Proposals from organisations or consortia that do not provide a comprehensive team to meet the requirements to pursue development into clinical trials should indicate partners/organisations to enable this.

2. Will CEPI be considering passive antibody therapy as part of the call for proposals? Or is the focus on vaccine development alone?

Passive antibody therapy will be outside the scope of the present call, which focuses on developing specific human vaccine candidates through Phase II, and targeting the three CEPI prioritized diseases.

3. Will CEPI consider proposals related to the development of vaccines for use in animal species involved in zoonotic transmission as being on topic?

The current call for proposals focuses only on the development of vaccines for use in humans. We recognise the validity of developing animal vaccines as part of a comprehensive approach to prevent zoonotic transmission and disease burden in humans. The Scientific Advisory Committee may in the future consider revisiting this standpoint, depending on funding and CEPI's achievements in the first phase of operation.

4. Is the CEPI grant program more interested in proposals for "a la carte" pieces needed for the complete development of novel vaccines (e.g. structural design of an immunogen, a clinical center, or a BSL-4 lab that can do immunization studies), or only fully integrated programs; design-to-testing-to-implementation. Eg, would CEPI mix and match scientists to create the team you wish from the collection of applications received or only focus on a pre-formed team?

The scope of the present CfP1 is on developing specific vaccine candidates through Phase II, and targeting one or more of the three CEPI prioritised diseases. Proposals from organisations or consortia that do not provide a comprehensive team to meet the requirements to pursue development into clinical trials should indicate partners/organisations to collaborate with to compensate for this and

ensure future product development. Applicants are encouraged to be as specific as possible. Please see Section 2 of the Project Description Template for more information.

5. We want to know whether CEPI will strictly require preclinical/clinical data obtained with the specific virus of interest, or whether it will be acceptable to provide data obtained with an appropriate surrogate model system (e.g. a virus relevant to one of the pathogens in the scope).

A key entry criterion for being funded through CfP1 is to have data from a relevant animal model demonstrating immunogenicity and likely protective immunity for one of the three pathogens in the call or on a pathogen relevant for these.

6. Will CEPI consider eligible for funding proposals that are still on early stages of development and will focus mainly on the scientific questions that need to be addressed to develop a vaccine candidate. Or whether CEPI will only consider vaccine candidates that are already at advanced stages of development and ready to initiate preclinical or clinical trials.

A key entry criterion to being funded through CfP1 is to have data from a relevant animal model demonstrating immunogenicity and likely protective immunity for one of the three pathogens in the call or on a pathogen relevant for these.

7. Given the incidence of Lassa fever virus infection and its geographic and temporal occurrence, it may be possible to conduct formal Phase IIb proof of concept or Phase III studies. Would CEPI consider funding such efficacy studies, or only Phase II safety and immunogenicity assessments? If CEPI were to fund efficacy studies, is there a particular study design that it would favor?

CfP1 encourages vaccine developers to present a clinical development plan taking into account the process until (and including) phase II trials, and to outline plans until (and including) stockpiling for phase III trials and emergency use. Phase III trials for Lassa are feasible but this call only focuses on phase I/II clinical trials.

8. What criteria will be used to judge the acceptability and preference for the challenge model selected? What level of detail on the correlates of protection will need to be demonstrated in preclinical models? How much (and what type) of data will be needed to bridge preclinical animal model data to immunogenicity data in humans?

We acknowledge the importance of relevant, predictive and reproducible animal challenge models, and the efforts required to develop such models. We encourage applicants to collaborate to utilise the most suitable models to facilitate future regulatory approval. The extent of data required to bridge from preclinical to human immunogenicity is within the authority of regulatory agencies to define.

9. Which population(s) would be targeted in Phase II studies in terms of age, special populations, etc.? (e.g., adults alone or children too; HIV positive individuals)

This call encourages vaccine developers to present a clinical development plan taking into account the process until (and including) phase II trials, and to outline tentative plans for stockpiling for phase III trials and emergency use. The current call intends to fund until phase II trials, both in high income countries and potentially in countries where the 3 diseases are endemic or likely to occur. The target

population will be captured in a Target Product Profile under development by World Health Organization (WHO).

10. How many stockpiled doses is the project intended to end up with? What form should those doses take (e.g., labelled, packaged, etc.)?

This will be pathogen specific and based on input from the work of WHO and other stakeholders. A CEPI stockpiling working group has been established to give guidance on these issues.

11. If the capability exists to produce a Tetravalent Hemorrhagic Fever vaccine [Lassa, Ebola (Zaire), Ebola (Sudan) and Marburg], may a proposal for a tetravalent vaccine containing Lassa be submitted or should it be a proposal for only Lassa?

Any vaccine candidate that provides protection against one or more of the 3 priority pathogens are encouraged for submission to CfP1.

12. May a proposal be submitted with the primary goal of a Lassa vaccine but a secondary goal of another vaccine that could be added using the same delivery vector platform e.g. Ebola (Zaire), Ebola (Sudan) and Marburg vaccine?

Any vaccine candidate that provides protection against one or more of the 3 priority pathogens are encouraged for submission to CfP1.

13. Are clinical trial sites supported, especially in preparation for phase 3 trials, or is this call just for getting early stage vaccine candidates to phase 1 or 2?

This call encourages vaccine developers to present a clinical development plan taking into account the process until (and including) phase II trials, and to outline tentative plans for stockpiling for phase III trials and emergency use. The current call intends to fund until phase II trials, both in high income countries and potentially in countries where the 3 diseases are endemic or an outbreak is likely to occur. Funding to operate clinical trial sites required to fulfil the clinical development plan is within the scope of this call, if critical for the overall development of the vaccine candidate.

14. We have a vaccine candidate that has shown vaccine efficacy in animals, but needs further fine tuning to be most effective against future Lassa Variants. Is refinement/ improvement/ development work supported?

The strategic objective of CEPI is to have vaccine candidates tested in phase II trials by the end of the five year period. Proposals need to describe how they achieve the proposed goal with their candidate, and what measures will be taken to reach this. A key entry criterion for being funded through this call is to have data from a relevant animal model demonstrating immunogenicity and likely protective immunity. These data should preferably be based on studies with the pathogens targeted in this call, or on a pathogen relevant for vaccine development for these.

15. Are there any limitations on the number of Phase 1 or Phase 2 clinical trials that may be included in the proposal budget?

No, but funding is limited. The proposal should reflect the scope of the 3 priority pathogens and not serve as proof of concept for the technology. This call encourages vaccine developers to present a clinical

development plan taking into account the process until phase II trials, and to outline tentative plans for stockpiling for phase III trials and emergency use.

16. The CfP describes the scope for development activities through a Phase 2 clinical trial and the generation of a vaccine stock for a Phase 3 clinical trial. Is there a distinct size of vaccine stock defined for Phase 3 trials or emergency use.

This will be pathogen specific and based on input from the work of WHO and other stakeholders. A CEPI stockpiling working group has been established to give guidance on these issues.

17. Since it is a common practice to complete process validation for manufacturing of Phase 3 clinical trial material, should process validation performance, including validation of all analytical methods be included in the proposal?

This call encourages vaccine developers to present a vaccine development plan taking into account the process until (and including) phase II trials, and to outline initial plans for stockpiling for phase III trials and emergency use. This could include process validation for a GMP product intended for phase III trials; however, the process validation should be clearly specified and presented separately. Please see Section 2 of the Project Description Template for more information.

18. The CEPI Call for Proposals indicates that "a key entry criterion for being funded through this call is to have data from a relevant animal model demonstrating immunogenicity and likely protective immunity" (page 3). Could you provide any guidance on CEPI's expectations for the degree of preclinical information required? Does CEPI expect information from multiple studies? Does CEPI consider an animal model to be "relevant" only if it is considered an optimal model for vaccine testing (e.g., wild-type virus challenge of nonhuman primates), or would information from other accepted but less rigorous models (e.g., rodent-adapted virus challenge of small animals) be adequate?

Applicants should submit what they believe is adequate evidence of preclinical immunogenicity and protection. Applications will be assessed based on the package on preclinical data as indicated in the Project description template guidance. We recognise the importance of relevant, predictive and reproducible animal challenge models, and the efforts required to develop such models. We encourage applicants to collaborate to utilize the most suitable models to facilitate future regulatory approval.

19. Does the Call for Proposal (CfP) include execution of a proof of concept Phase IIb efficacy trial?

This call encourages vaccine developers to present a clinical development plan taking into account the process until (and including) phase II trials, and to outline tentative plans for stockpiling for phase III trials and emergency use.

20. Does the CfP encourage inclusion of a One Health approach to prevent transmission (e.g., camel vaccine trials)?

The current call for proposals focuses only on the development of vaccines for use in humans. We acknowledge animal vaccines as part of a comprehensive approach to prevent zoonotic transmission and disease burden in humans. The Scientific Advisory Committee may in the future consider revisiting this standpoint, dependent on the funders and CEPIs achievements in the first phase of operation.

21. Is ease of vaccine delivery included as an assessment criterion? If so, what weight will it be given?

Yes. It is important and it will be considered, along with other equally or more important parameters of likelihood of successful vaccine development and anticipated target product characteristics.

22. Do you have an estimated timeline for proposals focusing on Zika vaccine development?

CfP1 is focussed on developing vaccines for Lassa fever virus, Nipah virus and Middle Eastern Respiratory Syndrome. Due to the intense investment and potential commercial market, at this stage it is not yet decided if there will be a call for proposals related to Zika.

23. Is CEPI willing to fund platform technology proposals that are not related to the 3 pathogens mentioned in the CfP? Will CEPI consider funding a modified mRNA vaccine?

CfP1 is focussed on developing vaccines for Lassa fever virus, Nipah virus and Middle Eastern Respiratory Syndrome. If the modified mRNA vaccine candidate targets one of these 3 diseases and progress till phase II is feasible with this candidate within the timeframe of the call, CEPI will consider the proposal. In addition to CfP1, CEPI is in the process of developing calls related to vaccines for filoviruses and for platform technologies.

24. Will there be a future CEPI CfP for vaccine platforms rather than a specific pathogen?

In addition to CfP1, CEPI is in the process of developing calls related to vaccines for filoviruses and for platform technologies.

25. Is CEPI interested in setting up repositories for emerging pathogens where valuable pre-clinical and clinical materials may be deposited both for ongoing activities but also as a legacy for future needs?

CEPI acknowledges the need for reference materials, standards and validated assays for the Prioritized Pathogens, but this is not within the scope of this call. This need will be explored for future consideration for investment.

Budgetary / financial questions

26. Can you provide me with more information about the intended budget per project within the CEPI-CfP-001 call? In what range of proposed budget do you expect proposals to be successful?

We have not defined a target or expected budget per project at this stage. CEPI has secured funding US$460 million of funding to support its mission for the period 2017 – 2021. Part of this funding will be allocated to projects selected for funding under this Call for Proposals (CfP). In addition to CfP1, CEPI is in the process of developing calls related to vaccines for filoviruses and for platform technologies. The Board will decide on allocation of funds to projects under CfP1 based on the SAC's recommendations about fundable projects that have a reasonable likelihood of success, taking into account CEPI's overall objectives.

27. Is there a maximum amount of funding available for a single proposal?

See response to question 26.

28. Will there be a funding ceiling applied to each proposal?

We have not defined a funding ceiling per project at this stage. However, preliminary proposals will be assessed and compared against total vaccine development cost estimates, including size of budget required to achieve the stated objectives of each project, additional cost estimates above and beyond each project including for regulatory approval, stockpiling and emergency use.

29. What is the budget cap over 5 years?

See response to question 28.

30. The cost guidance document describes indirect eligible costs but does not specify whether they have a cap. Will CEPI cover the total of eligible ID costs already fixed by the Institution of the applying investigator?

CEPI will negotiate the level of indirect cost coverage on a case-by-case basis. Under certain circumstances, such as in the case of fully dedicated programmes to CEPI, we may fund up to 100% of indirect costs, which should be, in any case, identifiable and justified by awardees' accounting systems as being incurred in direct relationship with the direct eligible costs attributed to projects.

Dedicated programmes are defined as research, development and manufacturing capacities and capabilities committed to CEPI, in the form of facilities or technology platforms, whereby any revenues generated directly due to CEPI investments will be re-invested into the sustainment of the dedicated programmes. Programmes can be fully or partially dedicated to CEPI, and CEPI's cost coverage of these programmes will vary according to the share of capacity dedicated to CEPI. CEPI reserves the right to negotiate joint management and shared ownership options of dedicated programmes.

31. If an employee is hired to the organization specifically to work full time on a CEPI funded contract, is the full salary costs of the employee allowable? (e.g. Does funding cover time when the employee is completing training, attending management meetings, public holidays, vacation time, etc. which are all included as part of the annual salary of the employee?) Please advise.

If the salary cost meets the criteria provided in the guidance as a direct eligible cost and the employee has allocated 100% of their time to the CEPI funded project, then the full salary costs of the employee are allowable, please see CEPI cost guidance document (updated 14/02/2017).

32. Do you have any known salary caps that must be considered in the submission?

See answer to question 31.

33. Is the preliminary proposed budget binding for the duration of the multistage proposal process?

Yes. The preliminary budget needs to remain as close as possible to the full budget but we understand that in certain circumstances, there will be variation between the two as the proposal develops, however there is no guarantee variations will be accepted.

34. If an activity has multiple cost types (e.g., personnel, lab supplies, contracts), should multiple individual lines be inputted on the table to reflect each cost type?

Yes, direct activity costs should be broken down by cost type.

35. Does the line "Procurement of R&D Services" in the budget template include sub-awards and contracts?

Yes, procurement of R&D is defined as the purchase of R&D services, this should include sub-awards and contracted services for R&D expenditure, e.g. CRO costs.

36. How would multiple indirect/overhead rates be entered? The application provides only one field for one rate but our organization has multiple rates.

Applicants should enter an overall indirect cost percentage of the total direct costs of their projects, supplemented by explanatory text in the designated cells of the budget and financing plan template, justifying the types of such costs this total percentage figure includes.

37. May the license fees/upfront payments related to the licensing rights to a specific vaccine that are due during the development program timeframe be included in the CEPI proposal budget?

If you are in-licensing from another company it would be an eligible cost, but ineligible if it was background IP already developed in-house.

38. For potential subcontractors (eg. those providing clinical development services), is breakout of direct and indirect costs required for budget submission? More specifically, will submission of a subcontract budget under a fixed unit pricing model, consistent with a commercial services proposal that does not require formal breakout of direct and indirect costs, be acceptable?

A breakout of direct and indirect costs of subcontractors is not required at this stage of the application process but CEPI may request further information on this if the proposal is shortlisted for further consideration.

39. Are in-kind contributions required or suggested?

Full reporting on in-kind contributions is required.

40. If we need to hire new FTE to work directly on the project, would their recruitment costs be reimbursable?

Applicants can enter recruitment costs at their discretion, please see CEPI cost guidance document (updated 14/02/2017).

Contractual and procedural questions

41. What level of product development is considered to be suitable for subsequent stockpiling and emergency phase III?

This will be pathogen specific and based on guidance and scientific and regulatory advice from regulators and WHO.

In emergency situations, some national and regional regulatory authorities (NRAs) and the WHO have developed specific emergency evaluation pathways and procedures that may allow for time-limited emergency use authorization of products based on a risk/benefit assessment of more limited available data, which are usually less than those required for a full authorisation under non-emergency situations.

42. What are the desired endpoints on the licensure dossier level? Any Regulatory guidance yet?

This will be pathogen specific and based on guidance and scientific and regulatory advice from regulators and WHO.

In emergency situations, some national and regional regulatory authorities (NRAs) and WHO have developed specific emergency evaluation pathways and procedures that may allow for time-limited emergency use authorization of products based on a risk/benefit assessment of more limited available data, which are usually less than those required for a full authorisation under non-emergency situations.

43. Which scale/indicative range of stockpiles are envisaged specifically for MERS, Lassa and Nipah?

This will be pathogen specific and based on input from work of WHO and other stakeholders. This will be pathogen specific and based on input from the work of WHO and other stakeholders. A CEPI stockpiling working group has been established to give guidance on these issues.

44. Is profit sharing a condition of acceptance of CEPI funds?

Draft versions of CEPI's policies, including on shared risks/shared benefits are available on the website here. These policies are in the process of finalisation with the Board and will be available shortly.

45. What are CEPI's views about IP rights versus global access agreement

Draft versions of CEPI's policies on equitable access and management of IP are available on the website here. These policies are in the process of finalisation with the Board and will be available shortly.

Application questions

46. Are the Implementation Plan required in the Project Description and the Progress Plan required in the Online Application one and the same? (i.e., should the same document simply be uploaded in two different parts of the application?)

Unless applicants desire to add detail in their implementation plans, applicants may upload the same information into the respective parts of the project description template and online application form. However, in case of consortia of organizations, applicants are required to specify which partner organization will be responsible for undertaking each foreseen activity, in the implementation plan section of the project description template. In any case, it is desirable that applicants clearly describe their activities, milestones and timelines for implementation and achievement of these, respectively.

47. Can CEPI provide a clearer idea of the expected level of detail specifically for the implementation/progress plan in the first stage of the proposal process? Is the expectation that some detail will be deferred to the second proposal stage? In particular, how much detailed information is needed for CEPI purposes versus the significant level of detail required in the routine Norwegian research application format?

Applicants are encouraged to be as detailed as you can keeping in consideration the total length of the application.

48. If the capabilities exist to produce both Lassa and MERS vaccines using the same vaccine platform, may a single proposal to develop both a Lassa vaccine and a MERS vaccine be submitted or should separate proposals be submitted for each vaccine?

You are encouraged to submit separate applications, but where relevant you can demonstrate linkages between the proposals.

49. Would it be of interest and within the scope of this call to include in a single application the side-by-side comparison and testing of two different platform technologies for different vaccines for the same disease?

Yes. This call for proposals specifically addresses the development of vaccines against Lassa fever virus, Nipah virus and Middle Eastern Respiratory Syndrome Coronavirus, and will, within the framework of these, seek to support the further development of technologies suitable for use with newly emerging infectious diseases. In addition to this call, CEPI is in the process of developing calls related to filovirus vaccines and for vaccine platform technologies.

50. Is there a limit on the number of proposals a single company may submit?

There is no limit.

51. What parts of the application (beyond the project summary, which is public) will be shared, and with whom?

No parts of the application under step 1 - preliminary review, other than the project summary, will be shared publicly.

52. Are consortia of 5 or more partners supported?

This depends on the proposal and how the applicant proposes to manage the consortium.

53. Please clarify how to fill in the application forms in case of a consortium of several entities that is applying, all of which parties have important (sine qua non) contributions to the project. Can or should all parties then be Project Owner?

Only one organization can act as the Project Owner. This is mandatory for proposal submission. However, the breadth and depth of individual partner organization contributions within a consortium should be clearly reflected in the project description template.

54. We have previously registered as an organization on the Research Council of Norway website, but I cannot find our organization registration number. Can you please send this to me, or confirm that we need to apply again for a new registration number?

The CEPI Secretariat is collaborating with the Research Council of Norway (RCN) by using their established online application system for submissions. We recommend that you develop a new login for this application.

If your question is in relation to the enterprise number, as indicated on page 7 of the FAQs previously published, it is not obligatory to add your organisation number.