

**Lassa epidemiological studies
for preparation of clinical trials
in affected countries**

Expression of Interest

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Summary

The Coalition for Epidemic Preparedness Innovations (CEPI) is funding the development of multiple Lassa vaccine candidates, some of which will begin testing in phase I clinical trials at the beginning of 2019. If these initial trials are successful and vaccine candidates are deemed safe to proceed to the next stages of testing, we will want to start vaccine trials in affected countries and potentially prepare for a phase II trials. To prepare for these trials, we need better epidemiological data to support trial design. Epidemiological research can also help strengthen site and investigator capacity to conduct these trials. CEPI will therefore provide grants for epidemiological studies that contribute to data for vaccine development in terms of trial design, appropriate endpoints and site selection. All work conducted under this and subsequent calls is expected to involve local investigators, and to contribute to clinical research capacity strengthening.

To ensure efficient use of time and resources, CEPI wants to identify research groups that are interested in performing such studies via this expression of interest. Selected groups will be involved in the preparation of a harmonized study protocol and funding call. Groups are eligible if they have strong local presence in Lassa-endemic regions and previous experience with Lassa field studies. The expression of interest will serve as a prequalification to receive funding through a forthcoming request for proposals on Lassa epidemiological studies. We expect the applicants selected through this expression to provide input on harmonizing the core study protocol.

The deadline for submission of an application to the expression of interest is **12.00 CEST on 30 August 2018**. All requested forms should be completed and uploaded via <http://cepi.net/expression-interest>.

Background

Lassa fever: disease characteristics and epidemiology

Lassa fever (LF) is an acute viral haemorrhagic illness caused by Lassa virus (LASV), first identified in 1969 in Nigeria. It is an important rodent-borne disease estimated to cause up to 300,000 infections in West Africa per year, resulting in approximately 5,000 deaths. The case fatality rate is estimated to be around 15% among those who develop severe disease and are hospitalized. Lassa fever patients who recover may experience hearing loss as well as other neurologic side effects.

Several aspects of LF's epidemiology remain unclear, such as its incidence in different areas and age groups, the prevalence of sequelae among survivors, and differences in clinical presentation. Outbreaks are frequently reported in Nigeria, Liberia, Sierra Leone, and Guinea, but the virus is probably also endemic in other West African countries. The limited existing surveillance infrastructure means that the disease is likely significantly under-reported and that incidence rates in countries with known endemic disease are imprecise.

CEPI is funding the development of several Lassa virus vaccine candidates. We expect that some of these candidates could be ready to initiate phase II safety and immunogenicity clinical trials in affected counties at the beginning of 2020.

Epidemiological data needs to facilitate vaccine development

CEPI's efforts to characterize LF's epidemiology will focus on generating data that can inform vaccine trial design, the location of trial sites, the selection of appropriate endpoints, and ultimately, how much vaccine to stockpile for pivotal trials and outbreak control. The epidemiological studies will strengthen local capacity ahead of the planned clinical trials and will contribute to community engagement. We anticipate that sites and investigators that participate in epidemiological studies will be well positioned to participate in vaccine trials, either in the inter-epidemic period or during an outbreak.

To ensure we can leverage all available data, it is essential to have a standardised core study protocol for all selected sites, including elements like target population, inclusion and exclusion criteria, laboratory procedures, minimum data requirements including data management, sampling times and duration. This standardised protocol will be developed together with the pre-qualified groups identified via this expression of interest and will focus on the primary endpoints identified by a CEPI facilitated expert opinion. We expect each site to collect these key endpoints in a harmonized way, analyse them using a standardised methodology and share them between sites and with CEPI to allow comparison across sites and countries. For the most part, we envision investigators will share governance of the scientific process and team publication of results regarding the core data to be collected. In addition, local and national needs can be addressed in the proposed studies and we encourage inclusion of relevant authorities early in the process.

The core study proposal will need to address the following elements:

- Define the incidence of infection with Lassa virus
- Determine sero-prevalence of Lassa virus
- Strengthen the knowledge base around clinical parameters such as scope of disease presentation and kinetics of viral loads, viral shedding and virus-specific IgM/IgG, as well as other markers of immune response among individuals with confirmed Lassa infection

Expression of interest

To be as efficient as possible, we aim to leverage existing sites and networks in countries in West Africa. We are therefore requesting any groups interested in performing Lassa epidemiological studies to submit an expression of interest application; this document explains the eligibility criteria, requested information and template for submission. This expression of interest serves as a **prequalification for the request for proposals** on Lassa epidemiological studies.

All applications received through this expression of interest will be reviewed based on the eligibility and evaluation criteria by an expert committee, which consists of CEPI secretariat members, CEPI scientific advisory members with relevant expertise and a WHO representative. This expert committee will also provide technical input for the core study protocol and review the submitted proposals.

Eligibility and evaluation criteria

The minimum **eligibility criteria** for this expression of interest are:

- Principal investigator from a Lassa affected country
- Local co-investigators at each proposed site (if multiple sites are proposed)
- Experience with field research in West Africa
- Experience with Lassa research
- Previous engagement with the proposed sites

All applications will be reviewed based on the following **evaluation criteria**:

- **Applicant consortium competencies, experience & track-record**
 - Partners and their roles within the project
 - Prior collaboration between proposed partners, or rationale for new collaboration
- **Experience with epidemiological field studies in West Africa, in particular Lassa**
 - Previous studies, including study designs and methodology
 - Evidence of community outreach and social mobilisation
 - Evidence of implementation strategies
- **Capacity of the proposed site and suitability to perform epidemiological studies**
 - Proposed site details and demographics
 - Local capacity to perform epidemiological studies, including human resources
 - Laboratory capacity and current Lassa testing algorithms
 - Health care system capacity to integrate epidemiological research
- **Support from local/regional/national authorities**
- **Potential to build capacity for field studies, surveillance and clinical trials**

Information requested

For the expression of interest, we are asking all groups to fill out the submission form and upload this via the online submission portal (<http://cepi.net/expression-interest>). The template includes information related to the proposed research group(s), capacity, standard of practice, data previously or currently collected at the proposed sites, a description of available surveillance data and financial support.

- **Proposed research groups/consortium; description of the following elements:**
 - Description of the applicant, partners and consortium
 - Identification of key personnel, including co-investigators
 - Prior collaboration between proposed partners, or rationale for new collaboration
- **Capacity of the proposed site; description of the following attributes:**

- Site location and extent and quality of demographic data
- Laboratory facility and resources
- Health care facility and resources
- Data management facility and resources
- **Local support**; please provide details on
 - Community engagement, including
 - Previous capacity building activities
 - Letter of support from local / national institutes
 - Previous engagements with local and national ethics committees and regulatory agencies
- Standard of practice, including
 - Case definitions used, both for diagnoses and research
 - Prevention and control, clinical management in health centre
 - Outreach and community control
 - Laboratory testing
- Description of the Lassa data from the area, including
 - (National) surveillance data
 - Previous or ongoing data collection of research studies
- Financial support; please describe the following funding sources
 - Any core / base funding for the sites included in the proposal
 - Any agreed funding for current and imminent Lassa projects
 - Any submissions for funding of Lassa projects

Details can be found in the template for the submission form (<http://cepi.net/expression-interest>).

Next steps

Pre-qualified groups will be expected to support the harmonization of the core study protocol by proposing relevant study designs, providing written input and participating in meetings to discuss the protocol. This core study protocol will include elements that should be included in all final projects to ensure comparability between sites. To enable discussions on the core protocol, we will organise a workshop in the fourth quarter of 2018 (see timelines below) with all pre-qualified research groups and the expert committee. Other relevant stakeholders may also be invited to this workshop, including national representatives, ethics board representatives and other actors working in this space.

When the core study protocol is finalized, we will request the selected groups to submit a project proposal, which should incorporate the core protocol, and specified budget (early 2019). We expect that applicants will take into account the local research needs beyond the harmonized protocol, especially focussed on addition data relevant for vaccine development. After review of the study protocols, the expert committee will select groups and engage with them to discuss and finalise their proposals prior to awarding funding.

Tentative timelines

| Activity | Time | Description |
|--|--------------|---|
| Publication of call for “expression of interest” | 19 July 2018 | Publishing and inviting relevant parties to apply to the expression of interest |
| Submission deadline | 30 Aug 2018 | |
| Evaluation and selection | 30 Sept 2018 | Review of the submitted proposals and selection of research groups |
| Workshop | Q4 2018 | Workshop with selected research groups, stakeholders and CEPI task force |
| Launch call for proposals | Q4 2018 | Based on the workshop and the core study protocol we will launch the call for proposals |
| Deadline call for proposals | Q1 2019 | Submission of proposal and budget |
| Decision of CEPI’s board | March 2019 | Presentation of and decision on research groups and projects by CEPI board |

Submission guidelines

All applications need to be submitted via the online submission system (<http://cepi.net/expression-interest>) by **12.00 CEST on Thursday 30 August 2018**. All submissions must include detailed contact information as requested on the online form and completed submission form. Submissions that are not complete by the deadline are not eligible for consideration.

Communication

Any communication regarding the application or process shall be directed via e-mail to Hinta Meijerink at secretariat@cepi.net.

CEPI will communicate the responses to the questions directly to the contact person. Questions and responses that are relevant for all applicants may be published anonymized as FAQs on our website.

Guidance

Confidentiality: All internal and external experts that participate in the review process will be evaluated for any potential conflicts of interest and are required to sign non-disclosure agreements. All data submitted via this expression of interest will be handled as confidential. Upon selection of research groups, CEPI may publish the names of the primary applicant and principle investigator after acceptance of their pre-qualification.

Funds pre-qualification: CEPI will not cover any costs during the preparation of the study protocol in the pre-qualification phase. For the workshop, CEPI will cover costs for key participants from the pre-qualified groups.

Cancelation: CEPI reserves the right to change the timelines or cancel the grant prior to signature of agreements without obligation to cover any cost for the applicants’ work on the call.

Procurement: Groups awarded the funding for the epidemiological studies, will need to follow CEPI regulations for any procurement not covered by the agreement.

Applicant organizations: This expression of interest is open worldwide to relevant entities that bring the relevant expertise and experience to address challenges within the scope of this call. Funding beneficiaries must be legal entities, or consortia of at least two legal entities. CEPI may conduct due diligence reviews for feasibility verification, legal, business and financial compliance before awards are made.