FIEBRE
Febrile Illness Evaluation in a Broad Range of Endemicities

Request for Proposals (RFP) for Utilization and/or Storage of the FIEBRE Study Research Sample Archive (Round 1)

We are pleased to invite potential partners to submit a proposal for the utilization of research samples obtained during the FIEBRE study, a UK aid-funded multi-country research study on the causes of fever. The purpose of this RFP is to identify potential partners who are seeking well-characterised samples from a diverse study population for translational research (such as evaluations of in-vitro diagnostics or novel biomarkers) with global public health objectives aligned with that of the FIEBRE study. FIEBRE samples are not commercially available, but invited proposals for their use are those with existing funding or a clear route to potential funding for the proposed research, as well as for the management, processing and shipment (where applicable) of the requested samples. Applicants with existing or proposed capacity and/or funding for future storage and responsible management of the sample archive are particularly desirable.

Project Background:

The FIEBRE (Febrile Illness Evaluation in a Broad Range of Endemicities) study is a comprehensive multisite prospective observational study led by the London School of Hygiene & Tropical Medicine (LSHTM) in collaboration with partners from Laos, Malawi, Mozambique and Zimbabwe. The primary objective of the FIEBRE study is to investigate the underlying causes of fever across diverse populations and epidemiological contexts in Africa and Asia. Detailed information about the FIEBRE study can be found at: https://www.lshtm.ac.uk/research/centres-projects-groups/fiebre.

The study has yielded a collection of research samples from over 10,000 participants (adults and children >2 months old), including both inpatient and outpatient fever cases as well as age- and location-matched controls. Participants have well-described clinical phenotypes (see appendix 3), and they have been extensively tested for infectious pathogens in specialist reference laboratories, as described in the protocol paper available at: https://bmjopen.bmj.com/content/10/7/e035632. The final number of cases and controls recruited to the study by country are shown below.

Country	Fever cases	Controls
Laos PDR	1,972	485
Malawi	1,773	908
Mozambique	2,182	572
Zimbabwe	1,924	436

Archived Sample Types:

The FIEBRE sample archive consists of various specimen types for both cases and controls, which are being stored for a limited time period at LSHTM: Serum (d0 and d28), venous blood in PAXgene tubes (Laos, Malawi and Mozambique in a subset of participants), whole blood and cell pellets. Plasma may also be available (TBC). Availability per participant varies. There are 0-18 (median, 7) aliquots of serum (mean residual volume 0.2ml per aliquot; range 0.05-1ml) and 0-2 (whole blood samples (mean volume per sample 0.5ml; range 0.05-1.5ml) per participant.

Objectives:

1) To identify external partners who can effectively leverage the research sample archive to conduct high-quality research that addresses essential public health needs.
2) To ensure that the utilization of the samples aligns with the ethical principles and guidelines established during the original FIEBRE study.
3) To establish a fair and systematic process that prioritises proposals with a clear potential for benefiting the populations represented by the participants in Laos, Malawi, Mozambique and Zimbabwe.
4) To identify external partners who may have the funding and/or capacity to support continued storage of the samples either through supporting staff time at LSHTM or at an external biobank facility.

Submission Details:

To submit a proposal for the use of archived FIEBRE samples, **please complete this short online form** with your details and declarations of interests **and send a 1-2 page proposal** to fiebre@lshtm.ac.uk no later than **31st October 2023 23:59 UTC**.

Proposals should consider the following guidelines:

1. Research focus: Proposals should outline a compelling research question or hypothesis that aligns with the primary goal of addressing public health challenges related to fever in the regions of Laos, Malawi, Mozambique and Zimbabwe.
2. Population benefit: Strong proposals will demonstrate potential benefits of the proposed research to the populations represented by the study participants and clearly describe the scope of those benefits, particularly with respect to *treatable and/or preventable infections*. This could include improvements in diagnosis, clinical management, prevention and public health interventions, or overall health outcomes.
3. Ethical considerations and approvals: Proposals should consider the remit of consent given by participants for use of the samples (see appendix), any existing ethical approvals for the project, and plans for obtaining any additional approvals from the relevant in-country institutions where required.
4. Research plan: Proposals should briefly outline the research methodology, including which type(s) and volume of samples are being proposed for use, data analysis, and potential outputs. For proposals of evaluations of in-vitro diagnostics or biomarkers, sufficient detail regarding the diagnostic is important, including stage of development and a summary of prior performance data.
5. Funding and timeline: Existing or anticipated funding available for the research or plans to apply for funding (with details of any funding calls) should be outlined, with a budget summary where possible.
6. Capacity and expertise: Proposals should highlight the expertise, infrastructure, and other resources available for the proposed research. Proposals to support the storage and management of a subset (or all) of the sample archive would be highly desirable.
7. Collaboration: Proposals involving formal collaborations with local research institutions and stakeholders from the study countries or regions are strongly encouraged, noting that all outputs should involve investigators from the FIEBRE study sites.

Evaluation Process:

Proposals will be reviewed by a dedicated committee consisting of both FIEBRE investigators and independent experts, including study site representatives, and scored based on the criteria listed above. Eligible proposals will be discussed in detail at a shortlisting committee meeting after which members of the committee may request additional information from applicants regarding eligible proposals or further development of a proposal. Committee members will be requested to declare any potential conflicts of interest for each proposal prior to the scoring process and will not score such proposals. *Please note being shortlisted does not constitute acceptance of a proposal nor an obligation of the FIEBRE consortium to negotiate or award a contract or agreement. The committee reserves the right to use all information available to them and to request additional information in writing or during meetings with applicants.*

Timeline

25th September: Issue of RFP
31st October: Submission deadline
15th November: Shortlisting by committee
17th November: Notification of ineligible proposals
17th-30th November: Requests for further information and development of eligible proposals

Contacts:

RFP Coordinator: Dr Elizabeth Fitchett – Elizabeth.Fitchett@lshtm.ac.uk
FIEBRE Scientific Programme Coordinator: Dr Heidi Hopkins – Heidi.Hopkins@lshtm.ac.uk
FIEBRE Principal Investigator: Professor David Mabey – David.Mabey@lshtm.ac.uk

For more detailed information about the FIEBRE study, please refer to the protocol paper at: *https://bmjopen.bmj.com/content/10/7/e035632*.

UKaid from the British people
The FIEBRE Study was funded by UK aid from the UK government.

Appendices:

1. Characterization of samples: summary of variables collected for FIEBRE participants

Variable type	Cases	Controls
Basic demographics (age, sex, location, inpatient/outpatient/control)	☑	☑
Presenting symptoms and history	☑	
Environmental exposures and risks	☑	
Physical exam	☑	
Treatments and resuscitation	☑	
Severity of illness	☑	
Point of care test results (malaria, HIV, CrAg and uLAM)	☑	☑
D28 outcomes	☑	
Microbiology results (blood and urine, where available)	☑	
Reference laboratory testing results	☑	☑

2. Information sheet and consent form signed by FIEBRE participants

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Information Sheet for Future Use of Biological Samples – for Adult Patients

Study title: Causes of Fever (FIEBRE)

Introduction

While you are in this study, samples will be taken of your blood, and from your nose/throat, that may be useful for future research. These samples will be stored for a long time at [local research collaboration facility] and at the London School of Hygiene & Tropical Medicine (LSHTM). Samples may also be shared with other researchers who work directly with the research team.

What will be done with my samples?

Your samples will be used to study infections that cause fever, and the response of the human body to infection. Research on these samples will happen in the future, and any information we get from these studies will not affect your care.

Your samples will be used only for research. They will not be sold or used to make a profit or to make money.

Will my samples be stored confidentially?

The samples will be identified only by study numbers and codes; they will not be labeled with your name or any personal information. We will not put reports about research done with your samples into your medical record.

What are the risks and benefits of storing my samples for future use?

There are no known risks to you from future use of your samples. There will be no direct benefit to you from any future research on stored samples. From studying your samples we may learn more about infections that cause fever. We may learn how to prevent them, how to treat them, or how to cure them.

Can I change my mind?

If you agree today to allow your samples to be stored, you can change your mind at any time about allowing your samples to be used for future research. If you change your mind, contact the study team at [contact information]. We will make sure your samples will no longer be made available for research by destroying the samples. If you decide for us to destroy samples for future research, you are still welcome to participate in the FIEBRE study.

Whom can I talk with if I have questions about providing my samples before, during or after the study?

You are welcome to contact the research team [local investigators' name/s, address, phone number/s, email as appropriate].

What if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The research team can be contacted at [address, phone number/s, email as appropriate].

If the research team cannot address your concerns, and you wish to complain formally, you can do this by contacting [LSHTM staff member Patricia Henley at rgio@lshtm.ac.uk or +44 (0) 20 7927 2626].

Providing consent for future use of biological samples

Thank you for taking time to read this information leaflet. If you would like your samples to be stored for future research, please read and sign the consent form on the next page.

Statement	Please initial or thumbprint* each box
I have had the information about sample storage explained to by study personnel in a language that I understand. I have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	
I understand that sample storage is voluntary and that I am free to withdraw my samples at any time without giving any reason, without my medical care or legal rights being affected.	
I understand that the samples collected from me will be used to support other research in the future, and may be shared anonymously with other researchers, for their ethically approved projects.	
I agree to allow my samples to be stored for future research.	

Printed name of participant	Signature of participant	Date

Printed name of impartial witness*	Signature of impartial witness*	Date

I attest that I have explained the study information accurately in _____ to, and was understood to the best of my knowledge by, the participant and that he/she has freely given their consent to participate* in the presence of the above named impartial witness (where applicable).

Printed name of person obtaining consent	Signature of person obtaining consent	Date

[*Only required if the participant is unable to read or write.]