LSHTM Ethics Application & CARE Form

Project Information

Staff members/students based at:

- (•) LSHTM
- ( ) MRC Gambia@LSHTM (For LSHTM staff/students requiring SCC/MRCG EC review, please select this option)
- ( ) MRC Uganda@LSHTM
- ( ) Other external applicant applying to the SCC/MRCG EC only

1. Full project title

Wolbachia, dengue fever and randomised test-negative studies

2. Is this Project in fulfillment of a degree?

(•) Yes ( ) No

2a. Degree registered for

MSc

2e. Indicate student type

- ( ) Distance Learning
- (•) Face-to-Face or Intensive Online

2f(MSc) Is this an original submission, or are you responding to a request for clarification or insufficient information notification from the LSHTM Ethics Committee?

- (•) Original submission
- ( ) Responding to the Ethics Committee

Student Details

3a. Student details

Title	First Name	Surname
Mr	Jerome	Johnson

Telephone: 07904225210

Email: 2005647@student.lshtm.ac.uk

3a(i). Please provide your student ID number

2005647

3a(ii). MSc course

Medical Statistics

3a(iii). Indicate proposed project length:

- (•) Standard
- ( ) Extended

3b. Are you studying as a full or part time student?

Full time

3c. Supervisor's name.

Nicholas P. Jewell

3c (i). Supervisor's email address (if more than one, please only provide the email address of your main supervisor)

Email: nicholas.jewell@lshtm.ac.uk

3 c(ii). Supervisor's institution

- (•) LSHTM
- ( ) MRC Gambia or Uganda
- ( ) Other

3e. Supervisor status

Confirmed

Project Type

Note: Completing the filter will enable and disable sections of the form so you may not see all questions.

4. Does the research involve primary data collection, analysis of data/samples that have already been collected, or a mix of both?

- ○ Primary
- ◉ Previously collected data/samples
- ○ Mixed

4a(iii). Select type of project:

Project using data from secondary sources

4c. Does the project involve extraction of data from patient records (e.g. medical, social care, service user records)? (This refers to primary data collection from records and does not include data that was previsously collected and is now being used in a secondary analysis).

- ○ Yes
- ◉ No

6. Does this project require review by the Commercialisation and Rapid Response (CaRR) ethics committee? (please see info icon for the remit of this committee)

- ○ Yes
- ◉ No

Samples

6a. Does this research project involve the collection, or use of previously collected, human tissue samples e.g urine, stool, blood etc? (Please select yes even if the samples are not considered relevant material under the Human Tissue Act)

- ○ Yes
- ◉ No

6b. Will this project involve living animals (either laboratory, livestock or wild animals) AND/OR biological material that has been obtained from animals in the experiments planned?

- ○ Yes
- ◉ No

Fast-Track

7. Does this project use anonymised and unlinkable secondary datasets only? (If yes the application may be eligible for fast-track 7b.)

- ◉ Yes
- ○ No

7a. Will this project be conducted in conjunction with NHS staff, premises or any other connection to the NHS?

- ○ Yes
- ◉ No

7b. Is this application for fast-track? Please see information icon for which projects are eligible. Note: MSc applications are not eligible for fast-track.

- ○ Yes
- ◉ No

Vulnerable Groups

8c. Does this research project involve vulnerable groups? Vulnerable groups include: children, individuals with mental disability or learning difficulties, pregnant women, prisoners etc (see information icon for full description).

- ○ Yes
- ◉ No

Security Sensitive Research Material

9. Does this research involve access to and/or storage of security sensitive research material? Please note that while some data is considered sensitive, such as HIV status, it is not necessarily considered security sensitive. If you are using data that could be considered sensitive, but not security sensitive please answer no to whether your research involves access to and/or storage of security sensitive research material. Please see information icon for what is considered security sensitive material.

- ○ Yes
- ◉ No

Geography

10. List the countries where the research project is to be conducted (For example: if you are conducting a secondary data analysis for your project and you will be based in the UK, select UK regardless of where the original data has come from):

United Kingdom

Please be aware that all primary health research conducted in the UK requires a sponsor. Please contact the RGIO at RGIO@lshtm.ac.uk for more information on sponsorship.

Outline

Note: Please do not copy and paste directly from the protocol. Applications where large portions of text have been copied and pasted directly from the protocol, and therefore do not properly answer the question, will be invalidated

12. Give a lay outline of the proposed project, including background to the proposal. Include information from any systematic reviews that have been conducted. Sufficient detail must be given to allow the Committee to make an informed decision without reference to other documents, and the outline should be written in such a way that lay members of the committee can make an informed decision.

A novel intervention to reduce, or eliminate, infection with the dengue virus using deployment of Aedes Aegypti mosquitos transinfected with the common in sect bacteria, Wolbachia has recently been completed in Indonesia with the data now available. The study design used a novel application of a cluster randomised intervention complemented by a test-negative recruitment of participants suffering from symptoms compatible with dengue infection. The study, and primary data analysis has now been completed with the data now available for various important secondary analyses. The primary results showed a very high reduction in dengue incidence associated with the intervention.

The specific objectives of the project include several possible data analyses: (i) analysis of how the intervention efficacy changes over time as control contamination with Wolbachia increased, (ii) comparisons of spatial clustering of dengue infections across intervention and control areas, and (iii) examination of the performance of specific statistical efficacy estimates for specific sub-strains of the dengue virus (there are four) where the data becomes much sparser.

12a. Upload the study protocol (compulsory for staff and doctoral students), including data collection forms, questionnaires and topic guides. Please upload each document separately, ensuring that the date and version number of each document is correct.

Documents

Type	Document Name	File Name	Version Date	Version	Size
Protocol / Proposal	20191014_Yogya CRT protocol_v5.1	20191014_Yogya CRT protocol_v5.1.docx	14/10/2019	5.1	2.0 MB

13. State the intended value of the project, detailing why the topic is of interest or relevance. If this project or a similar one has been done before what is the value of repeating it? Give details of overviews and/or information on the Cochrane database. This area is of increasing importance – please ensure you give a full response.

It is important to assess the impact of the Wolbachia intervention in reducing dengue incidence and, in particular, determine the impact of the intervention on local clustering of specific dengue serotypes. This will inform implementation of the intervention in new sites.

14. Hypothesis statement.

The Wolbachia intervention reduces spatial-temporal clustering of dengue infections in addition to reducing overall incidence.

15. Overall aim of project

Analysis of spatial-temporal clustering of dengue incidence in intervention and control areas in the AWED trial.

16. Specific objectives of project

Apply statistical methods to analyse how the intervention efficacy changes over time as control contamination of Wolbachia increases, compare the spatial clustering of dengue infections across control and intervention areas, and to examine the performance of specific statistical efficacy estimates for certain sub-strains of the dengue virus where the data becomes sparse.

Methods

Note: Please do not copy and paste directly from the protocol. Applications where large portions of text have been copied and pasted directly from the protocol, and therefore do not properly answer the question, will be invalidated

18. Specify the procedures/methodology to be conducted during the project. Please include outcome measures and plans for data management and analysis. For literature reviews, include details on search strategy, search terms, inclusion and exclusion criteria.

Spatial clustering analysis of dengue serotype incidence data using two statistical methods to quantify spatial-temporal clustering. The methods will be applied to the AWED data and compared using simulated incidence data.

23. Proposed start date of the project

01/06/2021

24. Proposed end date of the project

01/09/2021

25. In terms of the feasibility of your project, what could stop this project from succeeding, or prevent you from achieving your objectives? *Please indicate any aspects of your proposed approach which could potentially experience difficulties, e.g. delays with permissions, data collection or storage problems, lack of sufficient comparable information, etc. You may also wish to mention any wider matters which could affect your project, e.g. civil unrest, natural disasters, transport availability.

No, data is already available.

25a. What alternative plans do you have in case you encounter any of the potential problems you have identified? Please troubleshoot all points raised in question 25.

N/A

26. What specific facilities or resources will you personally expect to make use of for your project (eg a local university library, lab facilities, project placement with a specific organisation etc)?

Computing facilities

27. List key references (no more than 5), including for methods to be used.

K. L. Anders, Z. Cutcher, I. Kleinschmidt, C. A. Donnelly, Ferguson, N. M. and Nicholas P. Jewell, “Cluster randomized test-negative (CR-TND) trials: A novel and efficient method to assess the efficacy of community level dengue interventions,” American Journal of Epidemiology, 2018, 187(9), 2021-2028.

N. P. Jewell, S. Dufault, Z. Cutcher, C. Simmons and K. Anders, “Analysis of cluster randomized test-negative designs: Cluster-level methods,” Biostatistics, 2019, 20, 332-346.

Peter J Diggle, Statistical Methods in Medical Research 2006; 15: 325–336 Spatio-temporal point processes, partial likelihood, foot and mouth disease

Experience

30. State the personal experience of the applicant and of senior collaborators in the research project in the field concerned, and their contribution to this project. Indicate any previous work done related to the project topic including student and/or professional work, or publications

Currently do not have experience as I am an MSc student.

30a. Upload the CVs for all main investigators working on the project. For MSc students, please upload your CV only.

Documents

Type	Document Name	File Name	Version Date	Version	Size
Investigator CV	Jerome Johnson CV	Jerome Johnson CV.docx	12/04/2021	1	24.4 KB

30e. Have the main investigators undertaken any Research Ethics/Human Subjects Protection training (either online or face to face)? It is recommended that all applicants and members of their research team should complete ethics training at least every 3 years to account for changes in guidelines and regulations. Links to online training can be found in the information icon. (Please note this is not the same as GCP training).

- (•) Yes
- ( ) No

30e(i). Please upload a copy of the certificate(s)

Documents

Type	Document Name	File Name	Version Date	Version	Size
Other	citiCompletionReport4715196_Jewell	citiCompletionReport4715196_Jewell.pdf			153.3 KB

Informed Consent - Secondary Data

34. Is participant consent in place for secondary use of the data?

- (•) Yes
- ( ) No

34c. Please give details of the participant consent that was obtained when the original project(s) took place. Please upload copies of the original consent form(s). If there are no original consent forms (e.g. for audit or DHS data) please explain this.

I do not currently have access to the original consent forms. However, informed consent was obtained and is described in Section 7.2 of the protocol attached to this question. The informed consent document was reviewed and approved by the Institutional Review Boards of Universitas Gadjah Mada, Yogyakarta, and Monash University, Melbourne prior to the start of the trial.

Documents

Type	Document Name	File Name	Version Date	Version	Size
Consent form	20191014_Yogya CRT protocol_v5.1	20191014_Yogya CRT protocol_v5.1.docx	14/10/2019	5.1	2.0 MB

Confidentiality & Data

40. State how your data will be stored and what will be done with it at the end of the project.

Data is stored securely by project administrators - we have access to the data, but no jurisdiction over its provenance

Funding

46. Do you have external funding for this project?

- ○ Yes
- ◉ No

46b. How will the project go ahead without funds?

It is a secondary analysis for an MSc project

46c. Are you in receipt of any funding from the United States? Or will you be collaborating with (or with individuals from) a US Institution/organisation?

- ○ Yes
- ◉ No

47. Has the project been sent out for peer/independent scientific review (please select yes if the project is being sent to the SCC)?

- ○ Yes
- ◉ No

47a. If no, why has the project not been sent peer/independent scientific review?

It will be reviewed by project supervisor, Professor Nicholas Jewell

49. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

- ○ Yes
- ◉ No

50. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

- ○ Yes
- ◉ No

Local Approval

69. For projects using previously-collected human data, give details of all approvals under which the original project(s) took place. Please quote names of Ethics Committees and approval reference numbers (required even if previous approval was from LSHTM); if possible give web link to original project application. If there are no original approvals (e.g. for audit or DHS data) please explain this.

This study has gone through Human Subjects Review at two institutions:

Monash University, Ethics Approval: #2017-0960-9526
University of Gadja Mada, Indonesia, Ethics Approval “KE/FK/159/EC 06 February 2017

69a. Will your analyses be for purposes entirely covered by the original ethics application where the data was collected, as detailed above?

- (•) Yes, this falls within the aims and scope of the original project
- ( ) No, the analyses and aims differ from the original project

69a(i). Summary of purpose and methods of the original project(s)

Purpose: Does large-scale deployment of Wolbachia-infected Aedes Aegypti mosquitoes lead to differential spatial-temporal clustering of dengue incidence in people living in release areas, compared to those living outside release areas?

69b. Indicate how you will obtain permission to use the data from the principal investigator responsible for each original project

This MSc project only uses publicly available surveillance data. Professor Jewell is the study statistician for the project and has access to non-identifiable study data.

Data Sources, Results & Permissions

70. If you expect to use existing data, how will you obtain it? *Indicate who holds the data, who specifically you will contact, and by when. Any contact so far, especially anything confirmed in writing, should be mentioned.

Professor Jewell is the study statistician and has access to non-identifiable study data.

70a. Please upload any documents confirming that you have requested/been granted permission to use any existing data. This can include email correspondence as well as formal letters of permission. (This is mandatory for projects using existing data).

Documents

Type	Document Name	File Name	Version Date	Version	Size
Other	CARE Confirmation	CARE Confirmation.png	25/03/2021	1	58.2 KB

71. If you expect to use any public domain data, please give further details. *Make clear how you will gain access. Public domain data must be freely available to any member of the public, without any restrictions or requirement for special permission, and must not enable the identification of living people.

N/A

71a. Please provide the links to all public domain data that you expect to use.

N/A

72. Will any specific data rights permissions or usage limitations be required regarding data to be used or collected in the project?

- ○ Yes
- ◉ No

73. Will any agreements be required regarding data to be used or collected in the project (for example, material transfer agreements or data transfer agreements)?

- ○ Yes
- ◉ No

74. Are there any existing obligations regarding ownership of results to third parties (e.g. employer)?

- ○ Yes
- ◉ No

Type of risk

75. Where will the project be carried out? *Note that work away from LSHTM, your primary residence, or outside the UK means any form of work for your project, not just primary data collection. Some courses may have specific restrictions on this.

All work will take place either at LSHTM or my primary residence

76. Please indicate which locations you expect to work at. Check all that apply.

- ☐ Field Work
- ☑ Desk-based (Home, LSHTM, Office, Library)
- ☐ Lab Work
- ☐ Other work away from home

77. Will the project involve working with or handling any of the following materials?

- ☐ Pathogenic organisms
- ☐ Human tissue
- ☐ Animal tissue
- ☐ Radiochemicals
- ☐ Genetically modified organisms
- ☐ Toxic chemicals
- ☑ None of the above

78. Are any other potentially hazardous activities likely to be carried out during the project?

- ○ Yes
- ◉ No

Well-being

111. If you will be conducting research away from the School, and have a disability that may require support, you are encouraged to contact Studentadvice@lshtm.ac.uk in good time to discuss support options.

☑ I have read and understood the above information

112. Your wellbeing is of paramount importance and if your project research will mean spending time away from usual support networks, and if you think that you could find this challenging, we strongly encourage you to seek support and advice well in advance. You can book a confidential appointment (link to appointment booking form available in the information icon) with one of the Student Counsellors to discuss any concerns. The Counselling Service is available to all students and you do not have to have a diagnosed condition to seek support.

☑ I have read and understood the above information

Signature Instructions

The form should be completed and finalised prior to signing or requesting signatures. Incomplete or incorrectly filled in forms will be invalidated and this may cause a delay with your review. For external applicants/supervisors, please ensure that they have registered for an account prior to requesting the signature.

Please ensure that you obtain all signatures on this page. Failure to obtain all required signatures will result in the form not submitting and a delay to the processing of your application. If you have trouble signing/requesting signatures please contact ethics@lshtm.ac.uk or MScEthics@lshtm.ac.uk (for MSc students).

For MSc students:

- Please indicate that you have read and understood each statement under the student declaration before adding your signature using the blue sign button at the end of the student declaration.
- Once you have signed, please request your supervisor signature using the request signature button under the supervisor signature section. For external supervisors, please ensure that they have registered for an account prior to requesting the signature.
- Once your Supervisor has signed, please request your Course Director/Project Module Organiser signature using the request signature button under the Course Director / Project Module Organiser Signature section.
- Check whether any further signatures are required (these will show under the Course Director / Project Module Organiser Signature section) and request as required.
- Please ensure you have obtained all required signatures are your form will not submit without these. If you have any trouble please contact MScethics@lshtm.ac.uk

Signature - Applicant

Student Declaration

- [x] I have read and understood, and agree to abide by the LSHTM Good Research Practice policy as well as all applicable Standard Operating Procedures, including on informed consent
- [x] I undertake to abide by all regulations, guidelines and standards of good practice, including but not limited to the Data Protection Act 2018, GDPR, and the Declaration of Helsinki
- [x] I undertake to abide by all local rules/laws for non-UK research
- [x] I agree to conduct my project on the basis set out in this form, and to consult staff (initially, my Supervisor) if making any subsequent changes
- [x] I agree to inform the ethics committee of any changes made to this form, and will not implement any changes until approval from the ethics committee has been received
- [x] I undertake to adhere to all conditions set out by review bodies in giving approval and will not start the project until all required approvals are in place
- [x] I agree to comply with the relevant safety requirements, and will submit a separate request for LSHTM travel insurance where relevant
- [x] I agree to inform the Faculty Safety Officer and/or the Off-Site Safety Advisor (as required) if there are any changes to the risk assessment
- [x] I confirm that there are no conflicts of interest that preclude my participation in the project

Student signature

Signed: This form was signed by Mr Jerome Johnson (lsh2005647@student.lshtm.ac.uk) on 24/06/2021 11:54 AM

Signature - Supervisor

Supervisor signature

I declare that:

- I agree that the information submitted in this application is a reasonable summary of the proposed project.
- I agree that this form correctly indicates whether or not ethics approval will be required.
- I agree that this form contains adequate information for the ethics committee to form an opinion of the proposed project.
- I agree that all required supporting documentation is attached to this application.
- (For MSc projects only) I agree that responses in the Risk Assessment section address the main risks connected with a project of this nature
- I have reviewed the risk of the project, including travel, and agree that it is an acceptable risk to the student
- I confirm that there are no conflicts of interest that preclude my role as supervisor for this project
- I Have read and understood, and agree to abide by the LSHTM Good Research Practice policy

Signed: This form was signed by Professor Nicholas Jewell (nicholas.jewell@lshtm.ac.uk) on 14/04/2021 8:16 PM

Signature - Course Director/Project Module Organiser

Course Director / Project Module Organiser Signature

I declare that:

- I agree that the proposed project's academic content is suitable for this MSc

Signed: This form was signed by Ms. Kathy Baisley (kathy.baisley@lshtm.ac.uk) on 14/04/2021 9:35 AM

Signature - Other

Note:

The form will automatically submit upon receipt of all required signatures.

After submission, you will receive a confirmation email with further details.

If you have not received a confirmation email within 5 working days please email ethics@lshtm.ac.uk (staff) or MScethics@lshtm.ac.uk (students) to check the status of your submission.