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1. Background

The primary role of all the LSHTM Research Ethics Committees (RECs) is to safeguard the rights, safety, dignity and well-being of all actual and potential research participants. This includes protecting participants from physical, psychological, social/cultural, economic and legal risks of harm.

All research projects undertaken by staff or students involving humans, their tissue and/or their data ***must*** undergo ethical review by one of the LSHTM RECs before the research project begins. Research is defined as the attempt to derive generalisable new knowledge**,** and includes studies that aim to generate hypotheses as well as studies that aim to test them. Further information can be found on the Research Governance and Integrity Office (RGIO) website.

In addition, the LSHTM REC will also review projects involving primary data collection. This includes audits and service evaluation where surveys, interviews or case note review takes place. The Research Governance and Integrity Office (RGIO) will triage and distribute these projects to the appropriate committee, as required.

The LSHTM RECs are responsible for considering the ethics of human research, whether it be clinical, physical, behavioural, attitudinal, economic or psychological. Note this list is not exhaustive, as it will depend on the nature of the research, and its population.

The RECs at LSHTM are independent of all institutional, faculty, departmental, and financial interests.

These Terms of Reference and Procedures are aimed at ensuring a quality and consistent ethical review of projects undertaken by and for LSHTM staff and students.

2. Standards

The LSHTM ethics committees review all submitted research projects against recognised international ethical standards, such as the Belmont Report (1979), World Medical Association's Declaration of Helsinki (1964, as amended (currently 2013)), ICH Good Clinical Practice (R1, 1997 & R2, 2016), CIOMS International Ethical Guidelines for Health-

related Research Involving Humans (2016), as well as other established standards in biomedical research. Links to these guidelines are included in the references.

In addition, the Interventions, Observational A, and Commercialisation and Rapid Response (CaRR) committees comply with the US Federal Policy for the Protection of Human Subjects (also known as the Common Rule, ie 45 CFR part 46). The Interventions committee complies with the Food and Drug Administration regulations Protection of Human Subjects (21 CFR 50) and on Institutional Review Boards (21 CFR 56).

LSHTM, as an institution engaged in human research conducted or supported by the US Health and Human Services (HHS), submits a written assurance of compliance to the Office for Human Research Protection (OHRP). This assurance is submitted by the RGIO on behalf of LSHTM to assure the HHS that LSHTM will comply with the requirements set forth in the regulations for the protection of human subjects at 45 CFR part 46. The Federalwide Assurance (FWA) is the only type of assurance of compliance accepted and approved by OHRP.

Organisation Ref: IORG0002178
FWA: FWA00003028
Interventions cmte: IRB00008403
Observational A cmte: IRB00002708
CaRR cmte: IRB00012035

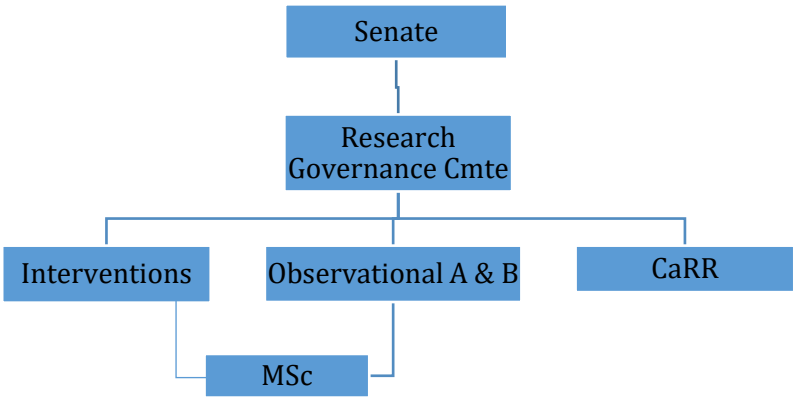
The committee endeavours to ensure that all studies carried out by LSHTM staff and students meet these standards by reviewing projects against the four essential ethical principles: beneficence, non-maleficence, justice and autonomy. In addition, the research project must be based on good quality, valid science, risks must be minimised, and not exceed the potential benefits to the individual or community.

It is expected that an independent scientific review/peer review of the research project is conducted prior to submission to the ethics committee.

Projects deemed to be high-risk under the UK Prevent duty guidance will undergo a risk assessment and additional scrutiny prior to review by the ethics committee.

3. Committees

There are five research ethics committees at LSHTM: Interventions, Observational A, Observational B, CaRR (Commercialisation and Rapid Response) and MSc. In addition, there is a fast-track review route for studies that meet the criteria for Chair's Action review.



3.1. Interventions Committee

The Interventions Committee will review all projects submitted by staff and research degree students which meet the definition of interventional: studies where participants or group of participants are given treatments (of any nature) or diagnostics that they would not otherwise be receiving in the ordinary course of events and which are allocated by the investigators. This includes all trials based on random or non-random allocation. The Interventions Committee will comply with section 3 of ICH GCP as well as 21 CFR 56.

3.2. Observational Committee A (High-risk)

The Observational Committee is responsible for reviewing applications submitted by staff and research degree students which are observational in nature, ie where no intervention takes place. The Observational Committee A will be constituted so that it is compliant with The Common Rule (45 CFR 46) and thus will be under the Federalwide Assurance (FWA). It therefore will review higher risk projects, and those that require FWA-compliant review (eg with US funders, or with US collaborators). High-risk observational studies include all research with vulnerable groups (excluding secondary analyses of existing datasets), and research involving the removal and storage of human tissue.

3.3. Observational Committee B (Low-risk)

The Observational Committee B will NOT be constituted to be compliant with Federalwide Assurance, and therefore will only review low-risk projects or those that do not require FWA-compliant review (eg not with US funders, or with US collaborators). Low-risk studies will include secondary analyses of existing datasets that include personal identifiable data, surveys and interviews with non-vulnerable groups.

3.4. Commercialisation and Rapid Response (CaRR) Ethics Committee

The CaRR Ethics Committee primarily reviews all projects undertaken under Chariot Innovations, as well as studies undertaken by the Rapid Support Team. This committee is available only for research undertaken by these groups which is of a commercial nature, where Chariot have been contracted to undertake the research, and/or where a research project will be undertaken by the Rapid Support Team which requires a quick review due to the nature of infectious outbreaks. The CaRR ethics committee will review projects on a rolling basis, with a turnaround of two weeks. The CaRR ethics committee will be constituted so that it is compliant with The Common Rule (45 CFR 46) and thus will be under the Federalwide Assurance (FWA). .

3.5. MSc

The MSc committee is a sub-committee to the interventions and observational ethics committees. All MSc students, whether distance learning or face-to-face, who are undertaking a research project as part of their MSc, must complete a CARE (Combined Academic, Risk and Ethics) form. This form is submitted to the RGIO for determination of whether full ethical review from the MSc committee is required.

3.6. Chair's Action (fast-track review)

Fast-track review is available to staff and research degree students (not MSc students) in limited situations only. See section 5.2 for further details.

4. Composition of the committees

The composition of the Interventions, Observational A, and CaRR ethics committees are in compliance with requirements of the Federalwide Assurance as stipulated by the Office for Human Research Protection, and meets the standards outlined in the International Council on Harmonisation Good Clinical Practice (ICH GCP), as well, conforms to the FDA's requirements as detailed in 21 CFR 56.107.

Deans of Faculty are asked to nominate members of the Ethics Committees, with all School invitations to express interest sent out by the Deputy Director and Provost, as required.

4.1. Composition

4.1.1. Interventions, Observational A, and CaRR Ethics Committees

Each of the above committees will comprise of:

- Chair (appointed by the Director)
- Minimum of five members
- Sufficient experience, expertise, and diversity to make an informed decision
- Include both men and women
- Differing backgrounds and expertise
- At least one scientist
- At least one non-scientist/lay-member
- At least one person external to the institution (this may also be the non-scientist/lay member)
- Ideally, at least one physician
- Ideally, at least one nurse
- Ideally, at least one member with pharmacology/toxicology (for CaRR), epidemiology, and/or statistical expertise
- Be independent, ie members may not vote on their own projects

4.1.2. Observational B Ethics Committee

The Observational B committee will be constituted to a similar standard as the Interventions, Observational A, and CaRR committee except will not have a mandatory lay member nor a mandatory external member present, nor will there be a requirement for a physician or nurse, although this will be recommended, as will someone with pharmacology/epidemiology/statistical expertise. Thus, the committee membership for Observational B and CaRR committees will be:

- Chair (appointed by the Director)
- Minimum of five members
- Sufficient experience, expertise, and diversity to make an informed decision
- Include both men and women
- Differing backgrounds and expertise, particularly from various scientific disciplines
- Ideally, one lay-member
- Ideally, one member with clinical/medical expertise
- Be independent, ie members may not vote on their own projects

The Observational B committee does not conform to the standards of ICH GCP, nor does it have a FWA, and does not meet the FDA requirements as detailed in 45 CFR part 46. Therefore, the Observational B committee is unable to review interventional trials, nor studies that obtain US funding.

4.1.3. MSc Committee

The MSc Committee typically only reviews projects that do not pose any additional risk above the everyday risk for participants, eg secondary data analyses of existing studies, therefore the MSc committee does not conform to the standards of ICH GCP, nor does it have a FWA, and does not meet the FDA requirements as detailed in 45 CFR part 46. The MSc committee membership is comprised of sufficient volunteers from each Faculty required to undertake the review for the academic year, as well as a Chair. The Chair of the MSc Committee will be selected by the Chair of the Observational A/Observational B/Interventions/CaRR committee as the MSc Committee is a sub-committee of the others, as depicted in section 3.

Should an MSc student wish to undertake a clinical trial or other type of interventional study as part of their project, they would need to submit to the Interventions Committee for compliance with ICH GCP.

4.1.4. Conflict of Interests

Committee members must inform the Chair if they have a financial or personal interest in a project, or a project funder. The Chair will decide whether the interest disqualifies the member from reviewing a project. The register will be maintained by the RGIO.

4.2. Member Responsibilities

All members, regardless of the committee to which they belong, must undergo appropriate training for their role as a member of an ethics committee. The Ethics Facilitator will retain certificates of training from each member, as well as the list of training providers that meet the minimum requirements for members, as per the training procedure. Members will not review any project until the certificate is submitted to the RGIO. Members will be required to update their training every three years.

4.2.1. Chair

The Chair for the Obs A/Obs B/Interventions and CaRR committees is appointed by the Director for a three (3) year term. The Chair for the MSc committee is selected from volunteers by the Chair for the main committees (Obs A/Obs B/Interventions and CaRR) for a three (3) year term. Both Chairs are responsible for the following:

- Promoting and protecting the interests of participants and the public in research conducted by LSHTM staff and students
- Reviewing applications and listing any ethical concerns for the research project (as listed below under members. For MSc committee, the Chair will review a similar quota to the members)
- For the Interventions, Observational A & B, and CaRR Committee, make a final decision, taking into account the committee's views (ie favourable, unfavourable or provisional/request for clarification)

- For Chair's Action or Fast-track applications, review submission and make sole and final decision for project
- Chair the face-to-face ethics committee meetings
- Act as point of contact for appeals or disputes from applicants. These will then be forwarded to the Research Governance Committee as per the appeals procedure
- Promote the effective working of the committee as a cohesive group
- Review and agree procedures for ethics review
- Monitor the standard and application of research ethics across LSHTM via discussions at the face-to-face meetings
- To make recommendations to the Research Governance Committee, and to meet with them as required
- Author the annual report to be submitted to the Research Governance Committee annually (Chair of Interventions, Observational A&B, CaRR only)
- Review potential conflicts of interest
- Assure compliance with the LSHTM policies and procedures for the ethics committee as written by the RGIO, and agreed by the Research Governance Committee
- Provide advice to the researchers on all aspects of welfare and safety of research participants
- To maintain confidentiality of documents obtained and discussions during the review process
- Be familiar with and keep up-to-date with ethical guidelines such as the Declaration of Helsinki, CIOMs and others (eg ICH GCP), as required.

4.2.2. Deputy Chair

The Deputy Chair will act as Chair in the Chair's absence and cover the above responsibilities.

4.2.3. Members

Each member is responsible for the competent review of all applications and listing any ethical concerns for the research project. Specifically:

- Undertake review free from bias and influence
- Provide advice to the researchers on all aspects of welfare and safety of research participants
- Check and ensure that all information given to the research participants is clear and easy for them to understand, honest and does not have a negative impact on the participant's autonomy (with reference to the LSHTM SOP on informed consent)
- Maintain confidentiality of documents obtained and discussions during the review process
- Develop the necessary skills to understand the scientific and ethical issues for each project, or request that an external expert join for the review.
- Assess the social value of the research, and identify any possible harm that may occur to vulnerable participants.
- Allocate appropriate time for reviewing the proposals
- Monitor the standard and application of research ethics across LSHTM
- Promote and protect the interests of participants and the public in research conducted by LSHTM staff and students

- Comply with Chair's overall views as a consolidated view from the collective review of the committee, incorporating individual responses
- Compliance with the LSHTM policies and procedures for the ethics committee as written by the RGIO, and agreed by the Research Governance Committee
- Commit to reviewing projects each and every month, endeavouring to review at least 10 of the 12 months (MSc committee will commit to reviewing a similar number as other members, pro-rata)
- Have full knowledge of ethical guidelines such as the Declaration of Helsinki, CIOMs and others (eg ICH GCP), as required.

4.2.3.1. Lay member

A lay member means someone who is not currently professionally qualified in healthcare or works in healthcare research or as a scientist. The lay member reviews projects as above in 4.2.3.

4.2.4. Student representative

The student representative does not currently review projects but attends the termly meetings only and acts as a representative across all the committees except for the MSc Committee. The student representative may have access to the online application system (LEO) in a read-only capacity, but will not comment on projects in terms of the official review process. The student representative acts as a bridge between the committee and the student body to help with the flow of information between the parties.

4.3. Responsibilities of the Secretariat (RGIO)

The RGIO are responsible for providing all secretariat services for the ethics committees, including acting as secretary to the committee, administration of the applications, and minute-taking during the meetings. In addition, the Ethics Facilitator will:

- retain all relevant records (eg the Terms of Reference, membership lists, submitted documents, minutes of meetings, and correspondence)
- Ensure that studies submitted via the LSHTM Ethics Online (LEO) system are validated within five (5) working days
- Ensure that members review applications within the set timelines, sending reminders as required
- Ensure that responses are sent to applicants in a timely fashion
- Ensure quorate for each meeting is reached
- Maintain register of interests of members

Other duties undertaken by the RGIO with reference to ethics include, but not limited to:

- Develop and implement the Good Research Practice policy, as approved by the research governance committee and Senate
- Plan, monitor and audit compliance of the policy and adherence to conditions of ethics approval
- Oversee provision of training and advice on research ethics to members and to the LSHTM community
- Oversee the procedures for the committee to ensure compliance with the assorted regulations, including GCP, with our FWA and 21 CFR 56.107 (as required).

- Monitor the standard of research ethics across LSHTM, and develop training programmes to best assist the School.
- The RGIO will not comment on individual projects as part of the ethics review process, but may help applicants prior to submission, and may comment on legal/research governance aspects of the study

4.4. Length of Service

Members joining after September 2015 will serve for a minimum of three years. There will be no maximum service time.

4.5. Review Frequency

Members will be expected to review each month unless they notify the RGIO in advance (eg annual leave or other disruptions to normal work schedule). Should a member fail to review three (3) concurrent months, they will be respectfully requested to resign from the committee.

5. Review of Applications

All applications submitted for review must be prospective, ie the project should not have started yet in any fashion. The ethics committee will not review projects after they have started, ie retrospectively. Deadlines for review will be strictly adhered to. The review process will be documented via the LEO system. External advice may be sought for specific applications. The review process is undertaken virtually via the LEO system and reports will normally take place electronically, unless an issue requires specific consideration at a meeting.

5.1. Full review

5.1.1. Interventions, Observational A & B, CaRR Committees

Committee members are expected to comment on each application that is submitted to their respective committees. Quorate is 80%. Therefore, the committee will be considered to have provided a full response only once 80% of the members provide their virtual review.

5.1.2. MSc Committee

A risk-based approach is taken for review of the MSc projects as projects are typically secondary data analyses which do not pose any additional risk to participants. For most studies, a single review by a member will take place. Higher risk projects, or those involving primary data collection from vulnerable groups, will be reviewed by two members and consensus must be reached. For secondary data analysis of data from vulnerable groups, one review is required, but members may request an additional opinion from another member.

5.2. Fast-track/expedited review via Chair's Action (not available to MSc committee)

To meet the requirement of fast-track review, applications must meet one of the following criteria:

- Use only anonymised and unlinked data
- Have ethics approval from the NHS REC/Health Research Authority, a UK university, or from the Gambia National Ethics Committee or from the UVRI Ethics Committee + UNCST approval
- Be part of a DrPH OPA attachment

The Chair will endeavour to review these applications within two weeks. The Chair will not issue an unfavourable opinion, but will instead refer to the full committee for review.

5.3. Ethics committee response

Research projects will receive one of the following responses from the committee:

- **Favourable opinion.** The committee is content for the research project to commence, contingent on all other appropriate approvals being received (eg local ethics approval, regulatory approval etc). The authorisation for the project is granted on the basis that the project progresses as stated in the submission. Any changes to the project following a favourable opinion must be submitted via the amendment application.
- **Request for clarification/ insufficient information.** The committee has requested additional information, or for amendments to the research project, before issuing their final verdict.
- **Unfavourable opinion.** The committee does not approve the project. The applicant may re-submit and the process starts from scratch.

The committee may also revoke approval if dissatisfied with the conduct of the research. Where relevant, the reasons for the Committee's decisions/opinions will be provided. Should an applicant wish to appeal the decision made by the REC, there is an appeals process which can be followed (see LSHTM-SOP-003 for further details).

5.4. Review timelines

5.4.1. Interventions, Observational A, Observational B

Applications received by the last day of the month will be circulated to the appropriate committee to be reviewed no later than the 15th of the following month. Quorate will be 80%.

Two batches of amendments will be circulated per month: amendments received by the last day of the month will be reviewed by the 15th of the following month and amendments received by the 15th of the month will be reviewed by the last day of the month.

5.4.2. CaRR

Due to the urgent nature of the projects submitted to CaRR, applications will be sent to the committee on a rolling basis and they will be given two weeks to complete the review. Quorate will be 80%.

Amendments will be triaged, and sent to the committee to be reviewed within two weeks.

5.4.3. MSc

Applications will be packaged to committee members in batches of 10 (pro-rata for part-time staff members) and the committee member will have 2 weeks (14 calendar days) to complete the review. Note that due to the extreme number of applications submitted in a short period of time, it may take a few weeks before the application is sent to the reviewer. Thus, the time to initial review will be approximately 4-6 weeks.

Responses to requests for clarification/insufficient information and for amendments will be provided to the original reviewer and will be given 2 weeks for this further review.

Projects involving primary data collection with vulnerable groups will be sent to two reviewers to be reviewed within the 2 week deadline.

5.5. Sub-forms: Amendments, annual reports, and SUSAR/Protocol Violation Form
The committees will also review amendments, annual reports, and SUSAR/Protocol Violation Forms, as required.

5.5.1. Amendments
All changes to a research project must be notified to the appropriate ethics committee. This includes both substantial and non-substantial amendments (see LSHTM-SOP-007 for definitions and further information). The RGIO will triage the project for substantialness and refer substantial amendments to the ethics committee for review. Where the RGIO deems the amendment to be non-substantial, this will be confirmed in writing.

No deviations from, or changes to, the protocol and associated documents should be initiated without prior written approval from the REC or the RGIO for an appropriate amendment, except when necessary to eliminate immediate hazards to the participants.

5.5.2. Annual progress reports
All projects submitted to the Interventions, Observational A & B, and CaRR committees are expected to submit an annual report on the anniversary of the confirmation of favourable opinion. This is to ensure that the ethics committees of LSHTM maintain appropriate ethical oversight of its research.

The MSc committee will not expect an annual report as MSc students will complete their projects within one year of receiving a favourable opinion. If this is not the case, ie in the case of part-time students, the student is expected to submit an amendment to clarify the extended period of the project.

5.5.3. SUSAR/Protocol violations
Should a SUSAR (Suspected Unexpected Serious Adverse Reaction) or protocol violation (see SOP LSHTM-SOP-008, LSHTM-SOP-009 and LSHTM-SOP-012 for definitions and further information) occur, the ethics committee will expect that the research team notify the committee within seven (7) days via the SUSAR/protocol violation form.

Note: Serious Adverse Events (SAEs) and Serious Adverse Reactions (SARs) should be submitted via the annual progress report.

6. Meetings
The observational, interventions and CaRR committees meet three times per year, once per term in a joint meeting. The MSc committee will meet at least once per year, but its

frequency is determined by need. A meeting shall be deemed to be quorate when three members of each committee and the Chair are present.

7. Reporting to the Research Governance Committee

The ethics committees will compile a single report for the Research Governance Committee, to be submitted annually. The ethics committee reports to the Research Governance which in turn reports to Senate.

8. References

21 CFR 56: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56

45 CFR 46: www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

Belmont Report (1979): www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

CIOMS International Ethical Guidelines for Health-related Research Involving Humans (2016)
http://cioms.ch/ethical-guidelines-2016/WEB-CIOMS-EthicalGuidelines.pdf

ICH Good Clinical Practice R1 (1997):
www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

ICH Good Clinical Practice (2016) R2:
www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

LSHTM Standard Operating Procedures: https://lshtm.sharepoint.com/Research/Research-Governance/Pages/standard-operating-procedures-(sops).aspx

OHRP: https://www.hhs.gov/ohrp/

Prevent: www.gov.uk/government/publications/prevent-duty-guidance

WMA Declaration of Helsinki (2013):
www.wma.net/en/30publications/10policies/b3/index.html

Document Control	
Applicable to	All staff
Procedure owner	Research Ethics Committee
Date reviewed by Research Ethics Committee	05 May 2020 (with minor edits following meeting)
Date approved by Research Governance Committee	20 October 2021
Date document to be reviewed	20 October 2023

Procedure Chronology		
Version	*Date*	*Reason for change*
1.0	18/11/2015	N/A – first approved version
2.0	25/07/2017	Update to include new committee, clarification of standards
2.1	23/01/2018	RGC request for all primary data collection to be assessed and reviewed by REC if appropriate
2.2	25/03/2019	Update to fast-track criteria
2.3	20/10/2021	Update to include that CaRR is included under FWA and in response to new ARMA/UKRIO guidelines.
2.4	22/02/2022	Removal of review of Arctec projects from remit of CaRR committee