ECTU Central Office SOP_TM_03: Obtaining Approvals

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Authorship and Approval			
Name and Designation	Author/Reviewer /Approval/ Authorisation	Date	Signature
Julia Boyd, Senior Trial Manager	Author	15 Dec 2023	See Retained Approval Email dated 15 Dec 2023
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Tanya Tharakan QA Manager	QA Authorisation	15 Dec 2023	See Retained Approval Email dated 15 Dec 2023

Document Revision History		
Version No.	Effective Date	Summary of Revisions
1.0	14 Jun 2012	Initial creation
2.0	13 Jan 2015	Amendments after scheduled review to section 3.1 Submissions for Welsh sites added to section 3.4 Added Section 3.5 Gaining Approvals
3.0	23 Nov 2017	Updated after scheduled review. Document Title changed. Extensive changes to all sections of document due to changes in approvals process.
4.0	21 Oct 2019	Amendments at scheduled review. Document moved to new SOP template. Section 3.4.2 and 3.4.4 updated to incorporate changes to the approval process. Minor alterations throughout.
5.0	05 Nov 2020	Updated after scheduled review. Change to author and reviewer. Information on Data Protection Impact Assessments added to section 3.1. Review process

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		detailed in section 3.2 updated. Section 3.5 updated as amendment submission process has changes.
6.0	22 Jan 2024	Updated to new SOP template V3.0, responsibilities section and details of new QA manager added. Updated throughout to reflect changes in approvals processes.

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1.0   PURPOSE

This Standard Operating Procedure (SOP) describes the process to be followed in order to determine which approvals are required for a particular study, which documents should be included in the submission for approval and gives guidance on the submission process to the relevant bodies and authorities for that particular study.

2.0   SCOPE

This SOP applies to all studies where ECTU has Trial Management responsibilities including the responsibility of submission of the application/s for approval to the relevant bodies and authorities.

3.0   RESPONSIBILITIES

The Trial Manager or designee is responsible for the following:

- Determining which approvals are required for a specific study
- Determining which documents are required for each submission
- Completing/collating application form and associated documents
- Ensuring documents are reviewed by appropriate individuals and collating comments
- Submitting the applications and associated documentation to the relevant bodies and authorities
- Preparation and submission of amendments to the relevant bodies and authorities

4.0   PROCEDURE

Approvals will be required for all studies but the types will vary considerably and include overall approval on the conduct and safety of a study, specific approval on documentation used to collect data or provide information to the participant, approvals to ensure safe administration of IMP, NIMP or use of a Medical Device and approval on the collection, storage and appropriate use of patient identifiable and confidential data. It is important that the study design is reviewed and approved by the appropriate individuals and bodies in order to ensure that the study is conducted ethically and the data obtained is suitable for analysis.

4.1 Approvals Required

The relevant initial approvals must be in place before commencing a study. The approvals required will depend on the nature and design of the study (e.g. CTIMP or non-CTIMP studies, multi-centre or single-site studies, UK or international). Following the research governance review, the sponsor will advise on the approval/s needed for each specific study.

Approvals that may be necessary are as follows:

Sponsor Approval – Agreement to act as the sponsor will normally take place during the grant application stage and is formalised in the Sponsorship Agreement. The sponsor is required to review and approve all submissions during the course of the trial including the initial submission and all subsequent amendment submissions. Sponsor approval should be sought before any applications are submitted.

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Research Ethics Committee (REC) Approval – Initial REC approval is required for all ECTU trials. Subsequent amendments may or may not need REC approval,. Details of the approvals required can be found in section 4 of the completed Amendment Tool and in the Sponsor Classification email.

MHRA Approval – If the study involves a CTIMP or Medical Device, MHRA approval will be required before the study can start. Subsequent amendments may or may not need MHRA approval. Details of the approvals required can be found in section 4 of the completed Amendment Tool and in the Sponsor Classification email.

Non-substantial amendments do not need to be submitted to the MHRA or the REC but they should be informed in the covering letter of the next amendment submitted.

HRA Approval for NHS England and Wales – HRA approval is required for studies led from England and/or involving English/Welsh sites. Each site will need to confirm local capability and capacity before participating in the trial.

NHS Management permission in Scotland and Northern Ireland – NHS R&D Approval is required for each site participating in the study in Scotland and Northern Ireland.

Data Protection Impact Assessment – the sponsor will advise whether a DPIA should be completed for the study following the research governance review. If required contact the University's Data Protection Office (dpo@ed.ac.uk) who will set-up access to the online tool. Please provide them with UUN and name of all individuals requiring access. Check with the sponsor early whether a DPIA is required as this can take time to complete and gain approval.

Confidentiality Advisory Group (CAG) Approval - If the study requires confidential patient information to be accessed by individuals outside the direct care team for patients in England and Wales, without explicit consent, then CAG approval may be required. The CAG pre-application checklist can be used to determine whether approval is necessary but it should also be discussed with the sponsor. If required the CAG application is completed on IRAS. If there are sites in Northern Ireland, you will need to apply to the Privacy Advisory Committee (PAC) approval.

Caldicott Guardian/HSC Public Benefit and Privacy Panel (HSC - PBPP) Approval – In Scotland, if personal identifiable data (including CHI number) is being collected and held Caldicott Guardian and/or HSC-PBPP approval may be required. Contact the NHS Lothian Caldicott Guardian for further advice (caldicott.guardian@nhslothian.scot.nhs.uk). Applications for single centre studies (Lothian only) can be submitted to ACCORD@nhslothian.scot.nhs.uk. For multi-centre studies in Scotland, National Caldicott Approval should be sought by applying for HSC-PBPP approval. Applications are submitted on eDRIS. Contact phs.edris@phs.scot to discuss prior to submission.

The Caldicott Guardian/HSC-PBPP would only be notified of a study amendment if it involves a change to the personnel, project duration, data sources/data variables or method of transfer. Submit HSC-PBPP amendment request form via eDRIS.

Check with the sponsor early whether a Caldicott Guardian/HSC-PBPP approval is required as this can take time to complete and gain approval. The process is described in ACCORD

SOP GS008 Patient Identifiable Information: Caldicott Approval and Information Governance Review.

IT Security Risk Assessment - The sponsor will notify the TM team if completion of the IT security risk assessment is required. This may be required if personal data is being transferred to a non-NHS organisation or a web-based system is being used to capture personal data. Check with the sponsor early whether NHS Lothian IT security approval is required as this can take time to complete and gain approval.

Administration of Radioactive Substances Advisory Committee (ARSAC) Approval – Studies that involve the use of radioactive substances (e.g. most commonly studies where participants are subject to a scan for research purposes) must be provided with an ARSAC certificate for the overall study and for each scanning site prior to study commencement. ARSAC approval is valid until the date on the certificate, or until the research project is completed (whichever is sooner). An amendment which changes the scanning protocol may require a new certificate of approval from ARSAC.

Further guidance on the approval process for each of the above can be found on the HRA and ACCORD websites (see section 5 for details)

4.2   Guidance with regard to design and review of documentation
Prior to finalising and submitting any documentation for approval it is important that these are reviewed by the relevant study team. The following members of the study team may be consulted (if applicable) during the review process:

Chief Investigator (CI) – The CI should be involved in all aspects of the review process throughout the study as they will be ultimately responsible for the study conduct.

Trial Statistician – It is imperative that the Statistician is included in the review process throughout the study (for both initial submissions and any amendments) to ensure that the study is conducted within the correct parameters to ensure effective analysis of the outcomes and that any changes made during the study do not negatively impact this.

Health Economist – As with the Statistician, if data is being collected for analysis by the Health Economist, it is imperative that they are consulted for initial submission and amendments to ensure the data is collected correctly and that any changes made during the study do not negatively impact analysis.

Research Nurse – It is useful to include a member of the study team who will consent and collect data from participants in the review process as they may be able to identify any potential pitfalls in the design of Consent Forms or CRFs.

IT Programmer/IT and Systems Manager – The IT Programmer who will build the study database should be consulted during the review process to ensure that the database can be designed according to the specifications of the protocol. If data linkage after study completion is required, then this should also be discussed with the IT and Systems Manager.

Data Manager – The Data Manager will assist and advise on the design of the pCRF/eCRF in accordance with the study protocol to ensure consistency throughout the study.

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Patient and Public Involvement (PPI) Representatives- It is useful to involve people with relevant experience in the design and development of research as it can improve its quality and relevance. The Patient and Public Involvement Team at the Edinburgh Clinical Research Facility can help with PPI participation if there are no PPI representatives directly involved in the study.

Other Key Collaborators – If the research involves specialist expertise such as Qualitative Researchers or Process Evaluation then these collaborators should be involved.

The TM will be responsible for co-ordinating and overseeing the design and review of the study documentation throughout the study. Any draft documents annotated with comments or changes to a document will be collated by the TM and filed on the drive, with a file note referencing it location filed in the Trial Master File (TMF). Key emails relating to significant changes to a document should be filed in the TMF.

Some funders (e.g. NIHR) will expect to review and approve the protocol before submission. Please check specific requirements with the funder of your study.

4.2.1   Studies with an Imaging Protocol

If the study involves participants attending for scans as part of the study protocol, the review process for the imaging centre will need to be completed before any scans can be booked. If scans are completed at Edinburgh this can be arranged with Edinburgh Imaging. If other imaging centres are participating, they should be contacted individually.

4.3   Preparing study documents for approval

Refer to ACCORD SOP CR007 Study Documents. The following study documentation will require review and approval prior to study commencement:

- Protocol
- Consent Form
- Patient Information Sheet (PIS)
- Participant Questionnaires
- Letter templates (e.g. GP letters)
- Participant Study Cards
- Any documentation used/seen/given to participants
For risk Assessed Studies only:
- Case Report Forms (CRF)

The documentation to be approved will differ depending on the nature of the study. In a CTIMP the Summary of Product Characteristics/Investigator Brochure and IMP labels will also require review and approval. Not all documents will require approval from all bodies (e.g. in a risk assessed study the Sponsor will generally review and approve all study documents but the REC does not usually review the CRF).

4.4   Submission of Initial Applications for Approvals

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The Trial Manager (TM) will usually be responsible for completing and submitting the IRAS forms on behalf of the Chief Investigator (CI).

4.4.1   Sponsor

The sponsor will review all documents and forms before they are submitted to external bodies for approval. IRAS forms require sponsor approval before submission.

The sponsor reviewer will determine what approvals are required for the study and inform the CI/TM team.

The CRF for risk assessed studies will be reviewed by the sponsor (usually the Monitor) before database validation is completed.

4.4.2   MHRA/REC/CAG/ARSAC/HRA

Submissions are prepared by completing an online set of forms on the Integrated Research Application System (IRAS) which are submitted to the various regulatory bodies and agencies electronically along with any relevant study documentation.

The IRAS System is provided by the Health Research Authority (HRA) on behalf of their partners and the combined review removes the need for separate applications to be made to each individual organisation.

On completion of an initial set of filter questions within IRAS, the submission forms and approvals that will be required for the study will be identified (e.g. MHRA, ARSAC etc. as described in section 4.1). A checklist of mandatory documents is included for each form, and any applicable documents are uploaded to the checklist. Once complete electronic authorisation can be requested from the sponsor. Then a slot for REC review must be booked by selecting this in the IRAS system. Once this is completed the application can be submitted and will be sent to the various bodies (REC, MHRA, study wide review). Instructions on how and where to submit other application forms are provided in the submission tab of each form within IRAS and also the IRAS help section.

4.4.3   NHS Research Permissions for multi-centre studies led from Scotland/NI/Wales

For multi-centre studies the IRAS Form and supporting documents are submitted electronically to the NHS Research Permissions Coordinating centre in the country of the lead site. The lead R&D Office will conduct the study wide review. The NHS Research Permissions Coordination Centre will inform the HRA (if applicable) and all participating sites (not in England) that the NHS Governance checks have been completed.

4.4.4   R&D Approval

Clinical trials conducted on the premises of an NHS organisation, with NHS patients or with NHS staff, require permission from the local NHS R&D office. The UK Information pack is used

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for setting up participating NHS/HSC organisations. Further information can be found on IRAS https://www.myresearchproject.org.uk/help/hlpsitespecific.aspx#UK-Local-Information-Pack. An exception to this is where a study is a single centre study with an NHS/HSC Sponsor (i.e. there is a single participating NHS/HSC organisation and it is the same as the NHS/HSC Sponsor for the study). In this specific scenario a UK Local Information Pack and Organisation Information Document is not required. The process is described in ACCORD SOP GS001 R&D Management Approval.

4.5   Amendments

The current version of the amendment tool should be downloaded from IRAS and completed. https://www.myresearchproject.org.uk/help/hlpamendments.aspx#Amendment-Tool

When the amendment tool is completed the amendment classification and approvals required will be shown in section 4 of the document. Following review and sign off the Sponsor will issue a sponsor classification email which also details the approvals required.

For studies using combined review: create an amendment on IRAS. Complete questions. Upload completed amendment tool and relevant documents. Request review and approval electronically from the sponsor. Once this is granted submit the amendment and it will be sent to the relevant regulatory bodies and agencies for review.

For studies submitted pre combined review: amendments are submitted via the IRAS Identity Gateway, which is separate login to your main IRAS account. The same process and documents need completed as detailed above.

For ACCORD sponsored studies guidance on the amendment approval process is detailed in SOP GS007 R&D Review of Amendments. Details of the amendment should be added to the amendment tracker (TM-T14 Amendment Tracker). Some funders (e.g. NIHR) request that any changes to the protocol are approved by them before submission of the amendment. Please check specific requirements with the funder of your study.

5.0   RELEVANT DOCUMENTS AND REFERENCES
- Clinical Trial Toolkit - http://www.ct-toolkit.ac.uk/routemap/
- Integrated Research Application System (IRAS) - www.myresearchproject.org.uk/
- HRA Approval Guidance- www.hra.nhs.uk/research-community/before-you-apply/determine-which-review-body-approvals-are-required/
- CAG Approval Guidance - www.hra.nhs.uk/resources/confidentiality-advisory-group/determining-need-cag-application/
- ACCORD Sponsor Guidance (for NHSL/UoE studies)
  - CR007 Study Documents
  - GS001 R&D Management Approval
  - GS007 R&D Review of Amendments
  - GS008 Patient Identifiable Information: Caldicott Approval and Information Governance Review

    www.accord.scot/research-access/resources-researchers/sop
- TM-T14 Amendment Tracker
- Edinburgh Imaging: Edinburgh Imaging | The University of Edinburgh

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- Edinburgh University Data Protection Impact Assessment https://www.ed.ac.uk/data-protection/data-protection-impact-assessments
- Patient and Public Involvement Guidance https://www.ed.ac.uk/clinical-research-facility/patient-and-public-involvement

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