MRC Clinical Trials Unit

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SITE EVALUATION AND ACTIVATION

VERSION 1.0

APPROVALS

Author and Position	Signature	Date
Hanna Bryant Trial Manager	DocuSigned by: Hanna Bryant CE0791103EDD410...	18-Jun-2021
Alex Robbins Trial Manager	DocuSigned by: Alex Robbins 50A2996566794D7...	21-Jun-2021
Reviewer(s) and Position	**Signature**	**Date**
Ellen Owen-Powell Trial Manager	DocuSigned by: Ellen Owen-Powell E2D10E2B1AE7423...	21-Jun-2021
Cheryl Pugh Clinical Project Manager	DocuSigned by: Cheryl Pugh 56F91EF32C4E40B...	21-Jun-2021
Malissa Richmond Trial Manager	DocuSigned by: Malissa Richmond 0A17137B6EDD483...	21-Jun-2021
Approver and Position	**Signature**	**Date**
Fleur Hudson Head of Trial & Study Management	DocuSigned by: Fleur Hudson 9928360F606E467...	28-Jun-2021

UPLOAD TO SOPBOX BY SOPBOX ADMINISTRATOR

Name	Signature	Date
Clare Shakehaft	DocuSigned by: Clare Shakehaft BB6C2416F21D4EE...	28-Jun-2021

All appropriate approvals must have been completed prior to uploading to SOPbox. The effective date of this SOP is the day on which it was signed by the SOPbox Administrator and is available to use.

For the Revision History please see the Version History Summary in SOPbox.

SITE EVALUATION AND ACTIVATION SOP

TABLE OF CONTENTS

The following symbols may be used in this SOP:

Indicates a link to a related document

Indicates instructions to document trial-specific processes elsewhere

Throughout this document 'MRC CTU' will be used to refer to the MRC Clinical Trials Unit at UCL (MRC CTU at UCL).

1 PURPOSE

The purpose of this SOP is:

- To define the roles and responsibilities involved in the site selection and activation process, for example, new studies or sites or following protocol amendments.
- To outline the procedures for site selection and activation in order to ensure that:
  - The site has the required resources, facilities, infrastructure and appropriate patient population to conduct the study.
  - Investigator(s) are qualified by training and experience and have adequate resources to properly conduct the study.
  - The site receives the appropriate documentation to gain all necessary approvals and that essential documents are in place prior to the site starting recruitment.
  - Investigator(s) assume responsibility for the enrolment of eligible patients and for the conduct of the study in accordance with the protocol and applicable regulations.

2 RESPONSIBILITY AND ROLES

The following table lists the roles relevant to this SOP and a brief description of their responsibilities.

This SOP will be circulated to be Read and Understood to all appropriate roles identified in the training matrix.

ROLE	RESPONSIBILITIES
Trial Management Team (TMT)	▪ Identification of appropriately qualified potential investigator(s)/institution(s) for the study and providing the contact details and relevant information to the Trial Manager for evaluation. ▪ Checking the institution has the facilities, infrastructure and required patient population to run the study. ▪ Ensuring the institution and the Sponsor has the essential documentation in place before initiating or restarting recruitment into the study. ▪ Checking the institution has the required approvals in place before initiating or restarting recruitment into the study. ▪ Checking all aspects for the green light process and giving the site the green light for activation. ▪ Participation at investigators' meetings (if any). ▪ Engage and collaborate with other relevant departments within the institute as required, for activating a new site e.g. finance and contracts department.
Trial Management Group (TMG)	▪ Identification of appropriately qualified potential investigator(s)/institution(s) for the study and providing the contact details and relevant information to the Trial Manager for evaluation. ▪ Participate in the site evaluation and selection process. ▪ Participation at investigators' meetings (if any).
External Collaborators (e.g. international collaborators)	Where appropriate: ▪ Recommend potential investigator(s)/institution(s) for the study. ▪ Participate in the site evaluation and selection process. ▪ Participate in investigators' meetings (if any).

3 PROCEDURES

3.1 IDENTIFICATION OF POTENTIAL CLINICAL SITES AND PRINCIPAL INVESTIGATORS (PIS)

For many MRC CTU at UCL studies, site selection is based on historical evidence of prior study participation, especially in instances where the patient population is limited (e.g. paediatric HIV). However, there are numerous ways in which potential sites and Principal Investigators (PIs) might be identified. These include but are not limited to:

- Use of Local Clinical Research Networks (LCRN) to identify and contact potential sites within their region.
- Some sites/investigators may already be included as investigators on a trial grant.
- Discussion at Trial Development Group (TDG)/ Trial Management Group (TMG) meetings where members discuss and put forward suggestions for new sites/PIs.
- Potential sites might contact the Trial Management Team (TMT) requesting to participate in the study.
- Sites who may not have been involved in MRC CTU at UCL studies previously but have a specific patient population or special knowledge of a disease area.
- Sites identified by international collaborators; this might include sites taken on as part of capacity building activity.
- Satellite sites or Patient Identification Centres (PIC) from previous MRC CTU studies with greater experience therefore able to run future studies independently.

Potential sites and PIs are generally selected early in study development, however new sites can continue to be selected once the study is open. Suitability of interested sites for inclusion in the study must be assessed by the TMT.

3.2 SITE SELECTION

Early in the development of a new study the TMT will identify the requirements for potential clinical sites and PIs wishing to participate in the study. These requirements are captured within the Site Evaluation Form, which cover the following categories where appropriate: patient population, investigator and staff experience, facilities, pharmacy, laboratory and electronic data capture (eDC) capability. This may be updated throughout the study for new sites introduced later, if required.

Site Evaluation Form (MRC_CTU_TT_0110)

Many of these requirements will be standard across all studies, but there may also be specific facilities or expertise required in some studies. Appropriate expertise should be sought from outside of the TMT to confirm special requirements e.g. clinical expertise from the TMG, Database Programmer and Data Scientist on eDC studies or a Pharmacist in a study with an unlicensed IMP. The Site Evaluation Form should be personalised for each study to document study-specific requirements.

When working with international sites, the site selection process may be delegated to international collaborators such as a local CTU, but oversight should be maintained by the TMT, if UCL are the Sponsor, or if delegated to do so by the Sponsor. There may also be additional requirements to consider when including international sites. For example with US sites, the TMT should ensure that

the site is not listed on the Clinical Investigators – Disqualification Proceedings Database published by the Food and Drug Administration (FDA).

3.3 SITE EVALUATION

Potential clinical sites and PIs should be assessed against the study-specific requirements as outlined in **Section 3.2.**

Sites should be asked to complete a Site Evaluation Form, and this may be sent alongside a trial summary or the protocol (if available). The Site Evaluation Form must be completed by the proposed investigator or their delegate and returned to the TMT for review and assessment.

Site Evaluation Form (MRC_CTU_TT_0110)

When opening a new trial arm or comparison in multi-arm multi-stage (MAMS) trial (unless all previously opened sites are expected to be included) or a nested sub-study within a trial, a similar site evaluation process can be performed, and should be risk assessed by the TMT. The Site Evaluation Form can be adapted for this purpose. Key points to include may be information about the target population and the capacity available, and this could be compared to the general site performance (e.g. data returns, protocol deviations and site participation in other sub-studies) in the main trial, and any queries or clarifications must be resolved prior to confirming participation.

Completed Site Evaluation Forms will be discussed at TMT meetings where members with different areas of expertise can provide comments and assess site suitability for inclusion in the study. It may also be necessary to consult the TMG for their input. Discussions must be documented in the TMT meeting minutes and the relevant section of the Site Evaluation Form completed. To fully assess site suitability it may be necessary to conduct a site evaluation visit or to discuss details of the study with them further. Any queries or clarifications must be resolved and documented prior to confirming site participation.

Any decisions to include (or not) a site should be documented in the Trial Master File (TMF). It is recommended that the TMT keep an electronic tracker detailing the list of potential sites, evaluation forms and responses received, TMT decisions and justification for any decisions. Plans for site evaluation must be documented in the Monitoring Plan.

Monitoring (MRC_CTU_SOP_060)

Once site suitability has been confirmed, if they have not already been provided, the TMT should provide the site with the following documents (at a minimum): a copy of the protocol, a study summary and if available the Summary of Product Characteristics (SPC)/Investigator Brochure (IB) (as applicable).

Sites may also be provided with a copy of a local information pack or equivalent, which would include documents required for local approvals and essential documents required for green lighting (see section 3.4 for essential documents list). These may be provided to the site or they may be directed to the study website where the relevant documents are available to download. The contents of the local information pack may vary dependent upon the time of site initiation and if they are UK or international centres.

Further information on the Health Research Authority (HRA) website

Where necessary, the pharmacy evaluation and initiation process should be conducted in line with the Pharmacy Initiation, Training and Closure SOP.

Pharmacy Initiation, Training and Closure (MRC_CTU_SOP_100)

Where necessary, the laboratory evaluation and initiation process should be conducted in line with the Laboratory Principles and Sample Management SOP to ensure that laboratories have the appropriate accreditation.

Laboratory Principles and Sample Management (MRC_CTU_SOP_069)

All significant correspondence between the site and the study team must be documented and included in the TMF and Investigator Site File (ISF).

Once a site has been evaluated and selected to participate, they should collaborate with the TMT to commence the relevant submissions for regulatory and ethics approvals. The timing and extent of this may differ across international sites. If involving several countries this might involve several different approvals; study teams should be familiar with each country's regulatory processes.

Ethics Committee Approval SOP (MRC_CTU_SOP_004)
Regulatory Approval SOP (MRC_CTU_SOP_003)
HRA Local Capacity and Capability (MRC_CTU_SOP_082)

If not already started, negotiation of any Clinical Trial Agreement, including budget, between the site and the Sponsor should also commence.

Research Contracting (MRC_CTU_SOP_027)
Research Costing (MRC_CTU_SOP_076)

3.4 ESSENTIAL DOCUMENTS

When activating a site, the TMT must ensure the following essential documentation is stored in the TMF at the CTU (unless otherwise stated) and retained in the ISF at site.

- Documentation of site evaluation (e.g. Site Evaluation Form)
- Signed Clinical Trials Agreement between involved parties
- Confirmation of favourable ethics/regulatory opinion
- Confirmation of HRA approval (NHS England requirement only)
- CV of PI (Co-Investigator(s) CV(s) may not be required centrally (ISF only is adequate) – this can be risk assessed by the TMT)

- GCP certificate of PI (Co-Investigator(s) GCP certificates may not be required centrally and can be filed in the ISF only)
- Contact details and a signature and delegation log for all study personnel at the site
- Completed training log for all study personnel at the site
- Investigator Statement signed by PI at the site (if applicable)
- PIS and ICF on local headed paper (and translations with translation certificate as applicable)
- GP Letter on local headed paper (if applicable)
- Confirmation of receipt of IB/SmPC and acknowledgement of the Reference Safety Information (RSI) (if applicable – this can include Read and Understood confirmation)
- Confirmation of receipt of IMP (if applicable)
- Laboratory accreditation certificates (if applicable)
- Source Data Identification Log

Completion of the ISF must be verified by the TMT before a site can commence recruitment to a study. This can either be verified during an initiation visit using a Site Initiation Visit Report, or sites can be asked to complete an ISF Self-Assessment Form which is returned to the TMT and can then be reviewed centrally. A copy of the completed ISF self-assessment form must be filed in the ISF and the TMF. Pharmacy initiation report and Pharmacy Site File (PSF) must also be in place prior to site activation, see Pharmacy Initiation, Training and Closure SOP for related tools and templates.

Template Site Initiation Visit Report (MRC_CTU_TT_0111)
Template Trial ISF Self-Assessment (MRC_CTU_TT_0113)

Pharmacy Initiation, Training and Closure (MRC_CTU_SOP_100)

The TMT must also ensure that a Source Data Identification Log is put in place with each site, which may be part of the green light process. This will define the source documents and the data therein, together with the location of these source documents and any applicable plans for transmission of source data between the site and the Sponsor/delegated institution. For new studies or new sites opening during an ongoing study, this document must be completed by each site prior to initiation. For ongoing studies, a Source Data Identification Log must be completed by all participating sites at the next appropriate opportunity, as assessed by the TMT. An example of this might be when implementing a protocol amendment, as part of the document pack a site is required to complete before they are permitted to continue with recruitment. A template log is available and can be adapted to suit the study's needs if required, or sites can use local templates if appropriate.

Template Source Data Identification Log (MRC_CTU_TT_0480)

3.5 PATIENT IDENTIFICATION CENTRES (PICS)

In the UK, the HRA defines a Patient Identification Centre (PIC) as an organisation which:

- Identifies potential research participants by processing personal data (e.g. through carrying out a search of a patient records database to identify individuals that meet a study's eligibility criteria).
- Is following the Sponsor(s) instructions in identifying potential research participants.
- Directs these potential participants elsewhere without undertaking any further research activity for that study (i.e. the research occurs at another legal entity).

Further information on the Health Research Authority (HRA) website

Where PICs are used, the TMT should provide a copy of the protocol and the patient information sheet to the Local Collaborator.

The local collaborator should confirm their interest and willingness to participate in the study. NHS permissions should be sought via the Integrated Research Application System (IRAS).

HRA Local Capacity and Capability (MRC_CTU_SOP_082)

According to current guidelines, a PIC is not considered a research site and therefore may be exempt from notification to the Research Ethics Committee (REC). They also do not require the same contractual agreements, training and monitoring as study sites and therefore will not be included in the requirements of this SOP unless explicitly stated.

PICs will also be given documented approval by the TM before starting to refer participants to the referral sites, this must be documented in the TMF.

3.6 SITE INITIATION VISIT

For some studies, a Site Initiation Visit (SIV) may be appropriate prior to activation. For further details on SIVs please refer to the Site Training SOP.

Site Training SOP (MRC_CTU_SOP_105)

3.7 SITE GREEN LIGHT/ACTIVATION PROCESS

Prior to site activation and green light there may be study specific activities required in order to allow the site to commence recruitment, for example whitelisting of the PI (on TMS), activation of user accounts for study specific systems (e.g. databases), triggering drug shipments. This will vary across studies both within the UK and internationally. These processes should be detailed in the Trial Working Practices.

Trial Management SOP (MRC_CTU_SOP_008)

Before a site can open to recruitment, approval must be given by the TM (or delegate) having confirmed that ethical/regulatory approvals are in place, essential activation documentation has been received, training/site initiation visit (including pharmacy) has been completed, any issues identified at site visits or remote assessment have been resolved and all requirements have been met. It is recommended that the study team log this information on an activation tracker. A template activation tracker is available.

Site Training SOP (MRC_CTU_SOP_105)

Pharmacy Initiation, Training and Closure (MRC_CTU_SOP_100)

Site Activation Tracker (MRC_CTU_TT_0479)

Regulatory Approval SOP (MRC_CTU_SOP_003)

PIs, research teams and, if applicable, pharmacy personnel will receive formal Sponsor Site Green Light/Activation (approval to open or reopen the study at the site) via the Site Greenlight/Activation Form and/or the site activation email. A copy of these document(s) must be filed in the TMF and ISF. A list of all approved sites must be maintained in the TMF.

Template Site Green Light/Activation Form (MRC_CTU_TT_0115)
Template Site Opening Email (MRC_CTU_TT_0406)

4 RELATED DOCUMENTS

SOPs
Monitoring (MRC_CTU_SOP_060)
Pharmacy Initiation, Training and Closure (MRC_CTU_SOP_100)
Laboratory Principles and Same Management (MRC_CTU_SOP_069)
Ethics Committee Approval (MRC_CTU_SOP_004)
Regulatory Approval (MRC_CTU_SOP_003)
HRA Local Capacity and Capability (MRC_CTU_SOP_082)
Research Contracting (MRC_CTU_SOP_027)
Research Costing (MRC_CTU_SOP_076)

Tools and Templates
Template Site Evaluation Form (MRC_CTU_TT_0110)
Template Site Initiation Visit Report (MRC_CTU_TT_0111)
Template Trial ISF Self-Assessment (MRC_CTU_TT_0113)
Template Source Data Identification Log (MRC_CTU_TT_0480)
Template Site Activation Tracker (MRC_CTU_TT_0479)
Template Site Green Light Activation Form (MRC_CTU_TT_0115)
Template Site Opening Email (MRC_CTU_TT_0406)

External resources
Health Research Authority (HRA) website - http://www.hra.nhs.uk/