Site assessment, selection and initiation guidance

General Guidance

Potential sites may be identified by contacting investigators who have previous experience in the therapeutic area, recommendations by colleagues, or via publications, professional groups, or research networks. Each Principal Investigator (PI) must be qualified in education, training, and experience, which is evidenced in the form of a CV, and each site must be adequately resourced to properly conduct the study.

Initial contact with a potential new site may be via an 'expression of interest' form. This is usually a brief document containing a short description of the study, participant population, and expectation of site requirements.

The Chief Investigator (CI) will conduct a sites selection assessment of all potential sites (including the selection of Barts Health NHS Trust (Barts Health) as a site).

Details of any pre-initiation contact to assess site suitability should be documented and any issues raised must be addressed by the CI or delegate. Once information has been collected from the site, the CI should review and make a suitability decision. This process should be documented. If an assessment is deemed unnecessary, particularly if the site staff and facilities are already known to the CI or sponsor, the reason and decision for not performing an assessment must be documented in the Trial Master File (TMF).

International Sites

When research is to be conducted in countries within the EU, the CI should provide the Joint Research Management Office (JRMO) Good Clinical Practice (GCP) & Governance Manager with sufficient justification as to why additional countries are needed outside of the UK, how they will be funded, along with a short summary of each country's clinical management. The CI must identify a national coordinating centre (NCC) for each international site. The NCC(s) will be delegated regulatory and oversight responsibilities for their country as part of the sponsorship contracting process. Each country will be asked to comply with the relevant EU directives, have contracts written under the jurisdiction of the Law of England and Wales, and agree to complete all the necessary submissions to their national research ethics committee and competent authorities on the sponsor's behalf. The CI should consider the resource and management implications and may consider contracting to a contract research organisation (CRO) for the management of international studies.

When research is to be conducted in countries outside of the EU, and in addition to the above, the CI and team must provide the JRMO GCP & Governance Managers a short summary of the regulatory status of all countries, including differences to the EU Directive regulations and other relevant laws (for example, the Data Protection Act (DPA) and the General Data Protection Regulations (GDPR)).

The following additional information will need to be provided to the sponsor when seeking approval for including non-EU countries in all studies:

- Copies of the risk assessments made, including internal and any conducted by external organisations (e.g. CROs).
- If not covered in the risk assessment, provide a written account of the CI's and collaborators' experience of managing trials in these non-EU countries.

- Any known issues of working in these countries and how they are managed or mitigated (e.g. additional administrative, regulatory or legal issues that are not relevant within the EU).
- Confirmation that the sites selected are not within the areas that the Foreign and Commonwealth Office (FCO) currently advise against travel (see Foreign and Commonwealth Office website for details).
- Confirmation that the sponsor (or delegated organisation) is able to freely audit the sites, given the FCO travel advice.

Confirmation of plans for shipment and distribution of the IMP and investigational medical devices, and the additional considerations for the transfer of samples, data, and supplies to and from the selected countries. This information must be sent to the JRMO Costing and Contracting Officer and JRMO Research Governance & GCP Managers.

What is a Site selection assessment?

Site Selection assessment is a process of comprehensive analysis and planning, including risk assessment and contingency planning.

Aims of a Site selection Assessment

The aims of undertaking an assessment are to review participant recruitment and retention strategies, assess the sites facilities, review availability of resources, staffing, support departments, ethics and R&D approval processes, and contracts and budget requirements.

Requirements/Selection criteria

The CI should define the selection criteria for suitable sites, prior to the start of the selection process. For example:

- The site must have capacity to recruit 10 patients per year
- The PI must have acted as PI on a CTIMP previously
- The Site must have capacity to store 20 boxes of IMP and to have 2 blinded staff.

The assessment

The complexity and scope of the assessment should vary depending on the type of study and location of its sites.

Sites should firstly be assessed as known or unknown. It is likely that if the CI or group has already carried out a trial at a particular site, a great deal of information about this site is already available to them, (e.g. existing/previous track record of participant recruitment, previous compliance, etc.). Teams should try to access this information and hereby review the need to conduct further assessment (e.g. if concerns are present or time has elapsed).

Sites should be allowed sufficient time to complete an assessment.

As a minimum, the below should be assessed and the outcome documented:

- Site status (NHS or Non-NHS)

- Site willingness to participate
- Recruitment rate & possible confounding factors in patient recruitment
- Site's ability to complete all site-specific procedures
- Impact of study procedures on Standard of Care
- PI training, experience, and availability
- Investigator/Site experience in conducting similar trials
- Local approval processes
- Staff resources, including the number of PI's active trials
- Adequate facilities/equipment/resources to conduct the study properly
- Availability of potential eligible participants
- Ability and agreements for remote monitoring if applicable

Common Questions

Common Questions for sites to consider prior to agreeing to participate in a clinical trial

The below should be used along with the Site Selection Assessment and report template to ensure the assessments study specific.

- What previous clinical trial experience does the PI have?
- Were previous recruitment targets met for other similar studies?
- Do you have other competing studies?
- What is your study population?
- Size of cohort?
- How many participants may be excluded?
- What recruitment strategies do you have?

Here is a checklist for sites to consider prior to agreeing to participate in a clinical trial:

- Validating Enrolment Potential
- Subject population
- Is the PI aware and willing to conduct the study?
- What track record does the PI have at meeting recruiting successfully?
- Has the proposed PI been a PI on a non-commercial CTIMP/ Clinical Investigation before?
- Has the PI undergone an MHRA inspection before?
- Are any research passports needed for lead site staff to enter the site? If so, request contact details of person who arranges at the site / local R&D office.

Participant Recruitment

- Who will be responsible for driving recruitment at the site?
- Do other departments/people need to be contacted to make them aware of the study (think of the patient pathway)? Who will do this?
- Is there anything in the protocol design or inclusion/exclusion criteria which may impact recruitment?
- How many patients are currently seen a) Per month b) Per year
- What is the anticipated screen failure rate?
- Length of recruitment

- Proposed recruitment target
- Is the start and end date appropriate for the study?
- Any similar/conflicting studies in the department?
- Review and evaluate inclusion/exclusion criteria
- Any circumstances that would affect recruitment?
- What is the expected screen failure ratio?
- Is there a patient stipend?
- Are vulnerable populations involved?
- Do you have access to special testing/monitoring required by the protocol?
- What potential problems does the PI foresee with your site with recruitment? Are they realistic?
- Can the PI meet the recruitment timelines and targets?
- Are there any seasonal issues at the site that may affect recruitment?

Healthy Volunteer studies

- Phase 1 studies – consider using the MHRA requirements of the site and PI: https://www.gov.uk/mhra-phase-i-accreditation-scheme#principal-investigator-in-first-in-human-fih-trials
- Is the site registered with the Over Volunteering Prevention System http://www.hra.nhs.uk/about-the-hra/our-committees/the-over-volunteering-prevention-system/
- Is the site/CTU located with an NHS Trust? What emergency provisions are available if not? Has this been risk assessed and documented?

Laboratory issues

If using local labs, do they have:
- Accreditation/certificates
- Training and certification for handling dry ice

If using central labs, do they have the:
- Staffing for processing of samples or previous experience of central lab kit management
- Handling/training
- Sponsors will want to see evidence of Investigator and staff trained in GCP. Copies of certificates or training logs and documented on CVs.
- Does the site have access to any specialist departments and diagnostics require in the protocol, if so, are they willing to be involved in clinical trials and what additional information do they need?

Pharmacy

- Which Pharmacy will be used at the site?
- Does Pharmacy have adequate storage facilities for the IMP?
- Do they have the capacity?
- Is there anything unusual about this drug/drug regime?
- Will Pharmacy have to source drugs or are these provided by Sponsor?
- Will these drugs be paid for by the Sponsor?

- Will there be out of pharmacy storage? Has this been risk assessed by the GCP Manager and Sponsor Pharmacist

Other Support Departments requirements

- Which support services/departments will you be using at the site?
- Clinical Research Facility (CRF)
- Imaging/Radiation Radiology procedures (How many scans required & frequency & the number of patients. If a lot of patients or several scans required within a very narrow timeline, please flag this as an issue to the site to discuss with Radiology as soon as possible)
- Medical Photography
- Clinical Physics/Medical Physics

Protocol Considerations

- Do you have previous experience with the site/PI?
- Does the PI have experience in the therapeutic area?
- Is the PI qualified/experienced to make the safety reporting assessments? (SAEs/SUSARs) for the relatedness of the IMP/NIMPs or investigational devices?
- Are the procedures consistent with the site's standards of care?
- Is study drug dosing complex (e.g. dose escalation)?
    - Are follow-up visits reasonable and are the visit windows feasible at this site?
- Randomisation consideration for the site
- Unblinding considerations for the site
- Where will patients be seen (different departments)?
- Will patients need to be sedated at any point (e.g. colonoscopies)?
- Radiology procedures (How many scans required & frequency & the number of patients. If a lot of patients or several scans required within a very narrow timeline, please flag this as an issue to the site to discuss with Radiation/imaging department at site as soon as possible)
- What are the interventions outside routine clinical care?
- Will any equipment be required for the purposes of the trial?

Staff Requirements

- Dissect the protocol and use the event schematic to evaluate all tasks involved.
- Is it feasible in light of current work load?
- Do you have qualified and 'dedicated' research staff?
- Do you have training needs?
- Review CRFs and patient questionnaires (frequently not available at feasibility stage to review). Will the participant or staff complete the questionnaires?
- Does the PI have adequate time and scheduling availability to devote to the supervision of the trial?
- Will it involve out of hours work for enrolment?
- Are their adequate sub-investigators?
- Consider ancillary or speciality staff needs
- Is there a back-up co-investigator?
- Nurse/doctor approaching patient?

- Who will be taking consent?
- If a research nurse, check they are involved in the patient's clinical care - if they are not, they cannot search patient database/notes until consent is signed by the patient
- How many studies are currently being run by the department?
- Are there any competing studies at the site?

Facility Considerations

- Is adequate clinic and office space available?
- Is any special equipment required?
- Is access to emergency equipment necessary?
- Do you have enough storage?
- Do you have archiving facility/off-site?
- Adequate storage for investigational devices?
- Adequate computer systems for trial-specific software?

Supplies

- What will the sponsor supply?
- Does the site have access to all equipment needed for the protocol?
- Will the site be supplied with a device? Is it CE Marked/ UKCA marked?
- Is the device routinely used?
- Is the sponsor Loaning or gifting the device to the site? Or is it already used/delivered into the site?
- Is the device supplier registered on the DoH Master Indemnity Agreement Registry?
- http://nhsmia.bipsolutions.com/index.php
- Will electronic or remote data capture be used?
- Central lab kits, shipping, invoices
- Supplies to pharmacy for CTIMP preparation

Site facilities

- Does the department have adequate staff to conduct the study?
- Do the PI and other staff have adequate time to conduct the study?
- Does the site have Internet access/e-CRF experience?
- Does the site have the equipment available as required by the protocol and a record of equipment calibrations?
- What archiving facilities are in place?
- If other support departments are required for example? Pharmacy
- Do they have adequate storage for the study drugs?
- What staffing do they have?
- What training have they undertaken i.e. GCP

A site selection report should be prepared for each site. *See SOP 46 Template 1 Site Selection Report Template*

Site Initiation and minimum requirements guidance

The PI, lead research staff (i.e., site research nurses), and site pharmacist must be present during the SIV (separate SIVs can be conducted if they all cannot attend on the same date/time). It is best practice to include the CI where possible in SIVs (if they are different to the PI).

Associated Document 3: Site activation checklist, *Associated Document 4: SIV presentation template and Associated Document 5: Site initiation report*, or alternatives that have been agreed by the JRMO GCP & Governance Manager, should be used to conduct the meeting, and document the visit in a report format.

The person delegated by the CI to conduct the SIV should be thoroughly trained in the study and protocol, including having a good understanding of all study procedures, consent forms, CRF, expected AEs, unblinding procedures (for IMP), investigational devices and / or imaging as appropriate) and SOPs. This should be documented and reflected on the coordination delegation log (*SOP 45: Essential documentation including TMFs and files for all external sites and facilities*).

During the visit, the following should occur as a minimum:

- A meeting with the PI, pharmacy, and key staff (i.e., monitor, site research nurse(s), trial coordinator), to discuss and review the protocol and all trial procedures. Pharmacy representatives can be met with separately.

- A study initiation presentation should be given to the PI and their research team (for topics that should be included in the presentation *see associated document 4: SIV Presentation template*). This should include the PI and site team's responsibilities.

- The study team should be provided with the opportunity to ask questions. Any issues highlighted at the SIV which are not resolved during the visit need to be documented and followed up before the site is activated.

- A visit and review of any sample processing or storage areas.

- An agreement of which documents and systems constitute "source data" and their location. This should be documented in the ISF (*SOP 45: Essential documentation including TMFs and files for all external sites and facilities*).

- An assessment of local computerised systems (*SOP 38a: Use of computerised equipment, software, and systems in clinical research*).

- Training the team of study specific software, equipment, or devices, including the requirements for calibration and verification before the study starts, and maintenance once the study is open.

- Completion of the trial delegation log.

CTIMP SIVs should also include:

- A visit to (and meeting with) the pharmacy and / or any out of pharmacy storage areas. This visit must ensure that they are familiar with the IMP documentation and satisfied with the IMP management plan (and any other IMP related documents). Request details of the IMP storage arrangements and, where necessary, review IMP storage facility at the site.

Clinical Investigation SIVs should also include:

- Training on the use of the investigational device and the associated investigator brochure, instructions for use and any clinical investigation agreements.

- Confirmation that the site has an adequate number of investigational devices and can store them appropriately.