SITE INITIATION AND SPONSOR AUTHORISATION

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1 INTRODUCTION

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 A Site Initiation Visit (SIV) and Sponsor Authorisation to Open (SATO) are required to prepare and set up a research site to conduct a clinical research study. Training will be provided to site staff on required sponsor Standard Operating Procedures (SOPs), and it will be ensured that the study team have access to the sponsor SOPs and related documents, and that there is appropriate resource in place to begin the trial. The study protocol and Good Clinical Practice (GCP) will also be discussed. The SIV will be scheduled according to the monitoring plan and the SIV procedures must be complete before sponsor authorisation can be granted and the site opened for recruitment.

1.3 SIVs and sponsor authorisation will take place for new study sites where the combined risk assessment (SOP GS002) has deemed that an SIV is required.

2 PURPOSE

2.1 To document the procedure for SIVs and SATO for sites that will participate in combined risk assessed studies sponsored by NHSL and/or the UoE.

3 SCOPE

3.1 This SOP applies to the Senior Clinical Trials Monitor, Clinical Trials Monitor or any other individual who will conduct and document SIV, and grant SATO on behalf of the sponsor(s). This SOP also applies to ACCORD research governance staff, including Clinical Research Facilitators and Research Governance Co-ordinators who act as Lead Sponsor Representatives.

4 RESPONSIBILITIES

4.1 The Clinical Trials Monitor, or designee, is responsible for conducting the SIV (including reporting and follow up) and for providing SATO in accordance with this SOP.

4.2 The Senior Clinical Trials Monitor is responsible for allocating a member of the monitoring team to perform the SIV, for reviewing SIV reports and for granting

and reviewing SATO, as required. They are also responsible for liaising with the Lead Sponsor Representative to ensure the monitoring team are kept informed with study progress.

4.3 The Lead Sponsor Representative is responsible for liaising with the Senior Clinical Trials Monitor, or designee, throughout the facilitation process, ensuring the ACCORD monitoring team is informed of study progress.

5 PROCEDURE

5.1 Collaboration with Lead Sponsor Representative

5.1.1 The Lead Sponsor Representative and Senior Clinical Trials Monitor, or designee, will discuss when the SIV and sponsor authorisation process should commence.

5.2 Before Site Initiation Visit

5.2.1 The SIV will be conducted prior to first participant being enrolled onto the trial.

5.2.2 The Senior Clinical Trials Monitor or designee will:

- Liaise with the Principal Investigator (PI), or site contact, to arrange an SIV for each site, as required in the monitoring plan.
- Outline the requirements for the SIV, in terms of attendance of the study team and in terms of time and resources.
- Ensure that all required approvals are in place or document clearly what approvals are outstanding at the time of the SIV.
- Provide clear instruction that sites can not open to recruitment without confirmation of SATO (CM001-T02).
- Ensure that a Trial Master File (TMF) and/or Sponsor File are created for the study. It is the PI's responsibility to ensure that an Investigator Site File (ISF) is in place for their site as per SOP CR001 (Establishing and Maintaining Trial Files).

5.2.3 The following must be completed before conducting the first SIV for the trial:

- Monitoring and Source Data Verification (SDV) plan according to SOP CM004
- Initial Case report form (CRF) review according to SOP CR013
- Submission to R&D for local approval
- Feasibility Questionnaire (GS013-T01) according to SOP GS013

5.3 During Site Initiation Visit

5.3.1 The PI and all relevant trial team members, as identified by the PI, will attend the SIV. Representatives from any supporting departments will attend as

necessary e.g. pharmacy, radiology, laboratories. Those who are unable to attend the SIV in person, training will be provided and documented in the ISF.

5.3.2 The PI is responsible for ensuring that the study team has received training on the protocol. Protocol training will be provided by the Chief Investigator (CI), or designee, and documented at SIV unless otherwise agreed by the Senior Clinical Trials Monitor. Protocol training must be provided prior to site opening to recruitment.

5.3.3 In accordance with the monitoring plan and where deemed necessary by the Senior Clinical Trials Monitor, the Clinical Trials Monitor, or designee, will attend the protocol training provided by the CI or designee.

5.3.4 The Clinical Trials Monitor, or designee, will provide training with respect to the sponsor's SOPs and will discuss the study protocol and GCP as required.

5.3.5 The Clinical Trials Monitor, or designee, will discuss and verify all items listed in the SIV Report (CM001-T01). CM001-T01 can be made study specific to remove non-applicable sections. For trials subject to combined risk assessment, this requires prior agreement with the Senior Clinical Trials Monitor.

5.3.6 If there is a delay of 3 months or more, or a significant change in study design between the SIV and Sponsor Authorisation to Open (SATO), a documented offer of refresher training will be made to the site team (including the PI). If the site request refresher training this will be provided by the Clinical Trial Monitor, or designee, and documented in a contact report (CM002-T02) or if applicable, a new SIV report will be completed and filed alongside the original report. Where refresher training is not requested by the site a justification of why training is not required will be documented and filed alongside the original site SIV report. The PI will be copied into any updated training materials provided to the site to ensure oversight.

5.4 After Site Initiation Visit

5.4.1 Subsequent to the visit, the SIV report (CM001-T01) and follow-up letter will be prepared by the Clinical Trials Monitor, or designee, who conducted the SIV. The report will be completed with factual information only. No personal opinions or comments will be documented in the report.

5.4.2 Where the SIV involves several different meetings or time points (e.g. training for pharmacy team is provided separately to PI) which take place within 5 working days of each other these will be documented in a single SIV report (CM001-T01). The dates and times of separate training sessions and the individuals in attendance at each will be clearly documented within the report.

5.4.3 Where the SIV involves several different meetings or time points taking place more than 5 working days apart the SIV report will be used to document the

initial SIV meeting and a contact report will be used to capture any subsequent training sessions forming part of the SIV. The content of the contact report will be of the same standard as the SIV report template (CM001-T01) and clearly detail the training session. Relevant sections of the SIV report template will be copied to the contact report to provide structure where necessary.

5.4.4 If any issues are identified requiring a delay to the site opening or any concerns over conduct are raised, these will be escalated to the Senior Clinical Trials Monitor and PI and documented in the SIV report.

5.4.5 The SIV report will be subject to review by the Senior Clinical Trials Monitor, or designee, in accordance with the monitoring plan. The review must be completed by an individual who did not perform the SIV. Both report author and reviewer must sign the SIV report before sending it to the study site for PI signature. All contact reports detailing subsequent training sessions forming part of the SIV are also subject to this review.

5.4.6 A signed copy of the completed report and follow-up letter (CM001-T04) will be sent to the PI by the Clinical Trials Monitor, or designee. If supporting departments were involved in the SIV, or if the report and follow-up letter is relevant to the supporting department, they will be provided with a copy. All contact reports detailing subsequent training sessions forming part of the SIV will also be provided to the PI and relevant supporting departments,

5.4.7 The PI will sign the PI statement on the SIV report and return a copy to the Clinical Trials Monitor, or designee. This signature is required for the SIV process to be complete.

5.4.8 Target times for completion of SIV report, completion of review and sending the report to PI are outlined in the monitoring plan. Where target times are not met, justification will be documented in a file note and filed alongside the SIV report.

5.4.9 The SIV report (and all contact reports detailing subsequent SIV training), follow-up letter and a copy of all training materials used for protocol specific training during the SIV will be filed in the TMF and/or Sponsor File and ISF as appropriate.

5.4.10 Actions identified during the SIV (including subsequent training sessions forming part of the SIV) will be followed up to resolution using the Monitoring visit actions log (CM002-T03).

5.5 Remote Site Initiation Visits

5.5.1 If appropriate, the monitoring plan will specify that remote site initiation will be completed. The Clinical Trials Monitor, or designee, will discuss the necessary

items in CM001-T01 over the telephone (or via another remote communication method) with the study team, provide training with respect to the sponsor's SOPs and discuss GCP and the study protocol as required.

5.5.2 Remote SIVs must document all items in CM001-T01 have been verified. Evidence should be provided by the site where required.

5.5.3 The Clinical Trials Monitor, or designee, who conducted the remote SIV will complete the SIV Report using the information provided by the study team. Where requirements for CM001-T01 cannot be verified remotely, an on-site SIV will be performed.

5.6 Sponsor Authorisation to Open Trial Site (SATO)

5.6.1 Before a site can commence study recruitment, authorisation must be granted on behalf of the sponsor by the Clinical Trials Monitor, or designee.

5.6.2 Where an IMP/agent/device is from clinical trial stock and requires shipment to site, the Clinical Trials Monitor, or designee, will provide authorisation to ship the IMP/device to the site ('Regulatory Green Light') by completing CM001-T03 (Regulatory Green Light Checklist)

5.6.3 Regulatory green light will only be provided once the Lead Sponsor Representative has provided written authorisation to start the clinical trial ('Regulatory Checks Complete') and all local site approvals are in place. The Lead Sponsor Representative will provide written authorisation to the CI as per SOP FA001. (FA001-T03)

5.6.4 Once IMP/agent/device is onsite, the Clinical Trials Monitor, or designee, will confirm (or verify remotely), actions detailed in CM001-T02 and provide SATO. CM001-T02 should be completed by the Clinical Trials Monitor, or designee who attended the SIV. In circumstances where this is not possible, the form will be signed by another member of the Clinical Trials Monitoring team and the reasons for this documented.

5.6.5 If the SIV has been performed remotely, evidence should be provided by site to verify actions have been completed as required.

5.6.6 If any issues are identified requiring a delay to the site opening for recruitment, these will be escalated to the Senior Clinical Trials Monitor and to the PI.

5.6.7 The SATO form (CM001-T02) will be subject to review by the Senior Clinical Trials Monitor, or designee, in accordance with the monitoring plan. The review must be completed by an individual who did not complete CM001-T02.

5.6.8 Once CM001-T02 is reviewed and finalised, the Clinical Trials Monitor, or designee, will send the completed document to the PI to convey permission to open the study at the trial site i.e. SATO. Relevant members of the study team

and supporting departments such as pharmacy will also be provided with a copy.

5.6.7 For studies with a long screening period, initial authorisation can be granted to begin screening participants before IMP has arrived at site. For authorisation to begin screening to be granted, all other actions except IMP in place, shipping records verified and drug labels accurate and consistent with Medicines and Healthcare products Regulatory Agency (MHRA) approval must have been completed in CM001-T02, and written confirmation received that IMP will be onsite before end of screening period.

5.6.9 A second authorisation to begin dosing will be granted once IMP is confirmed as on site and remaining actions in CM001-T02 have been confirmed or verified remotely.

6 REFERENCES AND RELATED DOCUMENTS

- CM001-T01 SIV Report
- CM001-T02 Sponsors Authorisation to open Trial Site
- CM001-T03 Regulatory Green Light Checklist
- CM001-T04 SIV follow up letter
- CM002-T02 Contact Report
- CM002-T03 Monitoring Visit Actions Log
- CM004 Developing a Monitoring and SDV plan
- CR001 Establishing and Maintaining ISFs, TMFs and Sponsor Files
- CR013 CRF Design and Implementation
- FA001 Facilitating a Regulated or Complex Research Project
- GS002 Combined Risk Assessment
- GS013 Site Feasibility
- GS013-T01 Feasibility Questionnaire
- POL012 Data Management
- ICH-GCP E6(R2) Guidelines

7 DOCUMENT HISTORY

Version Number	Effective Date	Reason for Change
1.0	14 SEP 2011	New procedure.
2.0	05 FEB 2016	New SOP template and updated SOP title. Introduction of sponsor authorisation to open process.
3.0	25 JUN 2018	Addition of Regulatory Green Light process and Regulatory Green Light checklist (CM001-T03) at section 5.6. Additional changes made to CM001-T02. Other minor changes made throughout.

4.0	30 JUN 2020	Addition of section 5.2.3 – List of actions which must be completed prior to first SIV. Clarification of regulatory greenlight process. Minor updates to SIV, SATO and Regulatory green light forms.
5.0	15 SEP 2020	Section 5.2.3 updated with the requirement to receive the completed site feasibility questionnaire (GS013-T01) prior to SIV.
6.0	24 FEB 2022	Addition of SIV follow up letter template (CM001-T04). Update to SIV report (CM001-T01) to add checks for archiving (including copy of electronic data), feasibility questionnaire completion and site level vendor identification.
7.0	09 FEB 2024	Section 5.3.6 updated to clarify requirements for provision of retraining to sites during the SIV process. Additional information added to section 5.4 to detail documentation requirements where the SIV is split across multiple training sessions. Addition of Data Management Plan check to CM001-T02 in line with POL012 (Data Management).

8 APPROVALS

Sign	Date
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Gavin Robertson (Jan 24, 2024 12:37 GMT) APPROVED: Gavin Robertson, QA Coordinator, NHS Lothian, ACCORD	Jan 24, 2024
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