Standard Operating Procedure			**53.012**
Monitoring Clinical Research – Site Close Out Monitoring visit			
Version	**1.0**		
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1. SOP Category

NHS GG&C Sponsor Governance

2. Staff Category

- Sponsor Research Coordinators
- R&I Lead Clinical Trial Monitor
- R&I Clinical Trial Monitors
- R&I Sponsor Pharmacy
- R&I Research Governance Manager
- R&I Project Management Unit
- GU Project Managers
- Innovation Project Managers
- Innovation Contracts Manager
- Principal Investigators

3. Scope

This standard operating procedure applies to all NHS Greater Glasgow & Clyde Research Governance staff, working within the Glasgow Clinical Trials Unit (GCTU).

4. Purpose

The purpose of this SOP is to describe the procedures that will be used by the Clinical Trial Monitors (CTMs) acting on behalf of the sponsor to perform the Site Close Out Visit (COV) for non-commercial clinical trials, clinical investigations of a medical device and non-CTIMP studies, Sponsored or Co-sponsored by NHS Greater Glasgow and Clyde (GG&C). If monitoring on behalf of a non-GGC Sponsor, this standard operating process will also be used, upon agreement with the Sponsor.

The Project Manager will notify the CTM when a site is ready to close, this may happen at any time throughout the course of the study however sites will be asked to refrain from final archiving until the end of trial notification has been submitted and the site is formally closed. The Project Manager will inform the CTM when the last patient has completed their participation at the site. The CTM will liaise with the appropriate data management and PV team to ensure all data queries have been resolved and SAEs followed up. Sites which do not recruit any participants may be closed remotely as discussed further in the SOP. The purpose of the COV is to verify that the trial has been conducted according to the protocol and in compliance with GCP guidelines, regulations and any other applicable requirements, ensuring that the Investigator Site File is complete. This should verify that all regulatory and local requirements for retaining documents have been met, all outstanding actions arising from previous monitoring visits have been resolved, and that the site is fully prepared to finally archive its files. If a date/time for a COV is not suitable for a particular part of the team then the site/pharmacy can be performed independently or if workloads/resource are an issue then site/pharmacy can be prioritised by the monitoring team.

5. Procedures

The core monitoring tasks for the COV are to:

- Ensure the ISF is complete and reflects the trial conduct.
- Ensure all Informed Consent Forms are present and complete ensuring the original consent form is present
- Ensure that all subjects have completed their participation in the trial, ensuring procedures and withdrawals have been fully completed.
- Ensure all Case Report Forms, including data queries are complete and filed.
- Ensure all safety reports and SAEs have been followed up to completion where possible.
- Ensure that all events meeting protocol defined reporting criteria have been reported as SAEs
- Ensure that all events meeting endpoint definitions as per the protocol have been appropriately reported.
- Ensure all source data are filed within the subjects' notes and removed from the ISF/CRFs in preparation for archival.
- Check retained samples have been sent to laboratory or destroyed as per ethics approval.
- Verify any supply equipment has been returned, if required.
- Ensure the Delegation Log has been completed and signed off by the PI and all staff have an end date to their responsibilities.
- Ensure all training evidence is filed with current evidence of Curricula Vitae along with GCP certificates ensuring these are dated within the last two years or per their own local GCP policy.
- Ensure all actions from previous monitoring visits have been addressed and any outstanding objectives from the Monitoring Plan are completed.
- Ensure all protocol deviations and GCP non-compliances deviations have been documented and reported.
- Confirm IMP accountability for all subjects entered at site.
- Ensure temperature logs for storage of IMP are filed within the pharmacy site file or the location of these logs is indicated by file note.
- Ensure any IMP approved by Sponsor to be destroyed has been and is fully documented.
- Ensure the End of Trial Declaration has been submitted; or will be submitted in good time.
- Ensure the CI/PI understands arrangements for archival.
- Ensure the CI/PI understands the timeline for the End of Trial Report.
- Ensure the PI and the monitor sign the Agreement on Delegation of Responsibility for Archiving (Form 51.024B) (only applies if a multi-centered CTIMP study).
- Update SReDA to document the study has been closed by the monitoring team, detailed in 5.3.

Close-out visits may be conducted in person, by telephone or remotely by asking the site to complete a checklist for both Pharmacy and Site. Where adequate monitoring has been conducted and objectives have been achieved, and provided there are no concerns regarding the safety of participants or the integrity of the data, close out visits may be done remotely. At times, the Remote COV may occur due to other reasons, for example, travel restrictions due to a pandemic or a non-recruiting site. In such cases a trial specific Remote Closure Form will be developed based on FORM 22.016A for pharmacy or Form 53.004L for the site and sent to sites and Pharmacy departments seeking confirmation that the files and actions are complete. The CTM will ask the site to have this returned signed by the Principal Investigator and signed off by the delegated member of the research team within 30 calendar days. If not received, the CTM will email the site and wait 5 working days for a response, if there is no response from

the site, this will be escalated to the Lead Clinical Trial Monitor and then the Research Governance Manager if the site has failed to respond. The CTM will record the communication in the notes section of Q-Pulse ensuring dates of communication with the site are documented. The form will include confirmation of the arrangements and contacts for archiving.

Where the trial has been of a complex nature, there have been specific issues attributed to a site or there have been issues of concern noted at routine monitoring visits, the Clinical Trial Monitor may be required to visit the site in person to verify that the trial has been completed to an acceptable standard and that any relevant corrective or preventative actions have been completed. If an in-person visit is not possible due to any restrictions, remote visits where the site has had specific issues can be done with Microsoft Teams, ensuring a video link in order to see the site and the folders. If the COV visit is conducted over Microsoft Teams, the CTM will ensure their NHS identity badge is shown to the site and, they declare they are in a room by themselves ensuring confidentiality.

5.1. Recruiting Trial Sites

5.1.1. Recruiting Pharmacy Close-out

If the trial has involved the supply of IMP to sites, Sponsor Pharmacy will give permission for remaining stock to be destroyed before the site Pharmacy can be closed out (as per SOP 21.010 Destruction of Investigational Medicinal Products). Once the correct accountability documentation has been received and checked by Sponsor Pharmacy, permission will be given to destroy any IMP remaining at site (as per SOP 21.003 Sponsor IMP Management and Accountability). The CTM will review the current Monitoring Plan for the study (FORM 53.004A) ensuring all monitoring has taken place for the study and monitoring objectives achieved, a decision will be taken whether the pharmacy can be closed remotely or an on-site visit is necessary to achieve monitoring objectives as per the specific study Monitoring plan (FORM 53.004A). If the site wishes to close early, pharmacy will be closed at the same time and the reason the site being closed early will be documented within the monitoring follow up letter (FORM 54.004H) and evidenced in the notes section of Q-Pulse. If a date/time for a COV is not suitable for the pharmacy department, this can be performed independently or if workloads/resource are an issue then pharmacy can be prioritised by the monitoring team.

If an on-site visit is scheduled this would usually include a site COV as-well. The CTM would ensure full accountability has taken place and the pharmacy investigator site file is complete with all essential documents prior to archival. If a remote visit is planned, the CTM will send a trial specific Pharmacy Investigator Site file checklist based on FORM 22.016A of the pharmacy index. However, this document will be detailed with pharmacy trial specific documents and versions. This must be completed by a pharmacy representative on the delegation log and will capture both a site pharmacy signature and PI signature on the document and instruction to be returned to the Monitor within 30 calendar days timeframe of sending the COV checklist to the site. The CTM will email the site and wait 5 working days for a response, if there is no response from the site, this will be escalated to the Lead Clinical Trial Monitor and Sponsor Pharmacy Representative and then the Research Governance Manager. The timeline will be evidenced in the note section of Q-Pulse. A remote phone or video call will be scheduled with the site pharmacy team ensuring all procedures for the COV have been achieved. The pharmacy monitoring visit log should be completed by the monitor and a delegated pharmacy representative (FORM 22.027A) regardless of the visit type.

5.1.2. Recruiting Site Close-out

The CTM will review the current Monitoring Plan for the study (FORM 53.004A) ensuring all monitoring has taken place for the study and monitoring objectives achieved, a decision will be taken whether the site can be closed remotely or an on-site visit is required to achieve monitoring objectives as per the specific study Monitoring plan (FORM 53.004A). If a site wishes to close early before recruitment finishes, the CTM will document this in the notes section of Q-Pulse. If an on-site visit is scheduled this may include a pharmacy site COV depending on the pharmacy objectives for the plan. At the COV, the CTM will ensure all further

monitoring objectives are achieved and all procedures as outlined above have taken place at the COV. If a remote visit is planned, the CTM will send an Investigator checklist to the site for completion and signature by the site research personnel and the Principal Investigator. The Investigator site file checklist is developed from FORM 53.004L and should be completed within the 30 calendar day turnaround by the site. If the checklist has not been returned, the CTM will email the site and wait 5 working days for a response, if there is no response from the site, this will be escalated to the Lead Clinical Trial Monitor and then the Research Governance Manager if it has still not been completed. The timeline will be evidenced in the notes section of Q-Pulse. A remote follow up phone or video call will be scheduled with the site team to ensure all monitoring objectives have been completed. Regardless if on site or remote, if the study is multi-centered, the CTM will ensure the PI is clear on responsibilities of archiving and signs FORM 51.024B.

Once this has been received and checked and all actions completed, the Clinical Trial Monitor will liaise closely with the Project Manager, Pharmacovigilance Office and Data Management to ensure the site is ready to be closed. The Project Manager will give permission for the site to archive their documentation. At all site visits, the monitor will ensure the monitor visit log is completed by the monitor and a delegated member of research staff (FORM 53.004G)

5.2. Non-recruiting Trial Sites

5.2.1. Non-recruiting Site Pharmacy

Non-recruiting site Pharmacy close-out will be carried out in the same way as listed above for recruiting Pharmacy close outs, but this may be completed during the trial if the site decides to close to recruitment or immediately on the trial closing.

5.2.2. Non-recruiting Site

Sites that did not recruit to the trial may be closed before the end of the trial. If a site opened to recruitment but did not recruit patients, including patients who were screened but not recruited, site close-out will be carried out in the same way as for recruiting sites but may be completed during the trial if the site has decided to close to recruitment or immediately on the trial closing. Any non-recruiting site may be closed early and this will be documented within the follow up letter and the notes section of Q-Pulse.

5.3. SReDA

After the visit is completed and all monitoring actions have been confirmed, the monitor must update SReDA to confirm the study is closed, as detailed in SOP 51.024 & SOP 51.025. The monitor will login into SReDA using their username and password. The R&D reference number can be used within the search engine to locate the study, once the monitor confirms the study, navigate to the pharmacy/custom tab, scroll down and update the "Monitor Close out status" by confirming closure. This must be done for each monitored Sponsored CTIMP and Non-CTIMP study monitored by GG&C CTMs. It is good practice to email the archiving assistant to confirm this has taken place.

5.4. Archiving Arrangements

Confirmation of local archiving procedures being in place will be confirmed at the site close out visit ensuring the site remains to have adequate archiving procedures in place. Once all the COV actions have been resolved the trial documents stored in the Monitoring file (as per Monitoring file index, FORM 51.016F) will be returned to the main Sponsor file held within R&I. An end of Trial Monitoring Document Reconciliation form (FORM 53.004O) will be completed listing all documents transferred. These documents will then be archived as part of the sponsor file, as per SOP 51.024 and 51.025.

6. Referenced documents

- SOP 21.003 - Sponsor IMP Management and Accountability
- SOP 21.010 - Destruction of Investigational Medicinal Products and Other Study Products
- SOP 51.024 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
- SOP 51.025 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Non CTIMP
- Form 22.016A - NHS GG&C Generic Pharmacy Site File Index
- Form 22.027A - Monitoring Visit Log (Pharmacy)
- Form 51.016F - CTM File Index
- Form 51.024B - Agreement on Delegation of Responsibility for Archiving Study Documentation Form
- Form 53.004A - Monitoring Plan for a Clinical Trial of an Investigational Medicinal Product
- Form 53.004G - Monitoring Visit Log
- FORM 53.004L - Site Close Out Report.
- Form 53.004O - End of Trial Monitoring Document Reconciliation

7. Related documents

- FORM 53.004B - GGC Monitoring Risk Assessment

8. Document History

Version	Date	Description
1.0	25/08/2022	*First Release*