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| [Full Study Title] | | | |
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| **Sponsor Imaging Manual – V 1.0**  **Clinical Research Imaging Facility (CRIF)** | | | |
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| *Short Title* | |  | |
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| CONFIDENTIAL | | | |

**Prepared by: CI/PM/CRIF lead Approved by: CI/Sponsor Rep**

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2. Introduction

The purpose of the Sponsor Imaging Manual is to describe the technical procedures and general trial logistics as they apply to category 2 and 3 imaging tests as defined in SOP 51.033 using FORM 51.033A. These may be standard imaging protocols that have specific trial requirements or non-standard imaging protocols specific to the research trial.

Routine imaging tests conducted in the trial by local NHS radiographic staff at a participating site are not covered by this document. The process of handling these images is described in the protocol and as per local procedure.

*[If the local NHS radiographic staff require access to the electronic Case Report Form (eCRF) include details of obtaining eCRF access and Data Centre Provider contact.]*

Ensure all Imaging trial documentation references the identifiers and protocol version it relates to:

|  |  |
| --- | --- |
| Full trial title |  |
| IRAS ID |  |
| NHS GG&C R&D number |  |
| EudraCT/Other study Reg ID |  |
| Protocol Version |  |
| [subsequent amendments] |  |

**3 Contact Information**

|  |  |
| --- | --- |
| **Role** | **Name & contact information** |
| Chief Investigator (CI) |  |
| PM (PM) |  |
| Sponsor R&D representative |  |
| Imaging contact (image receipt) |  |
| Courier Details |  |

|  |  |
| --- | --- |
| **Participating Site** | **Contact information (person responsible for images)** |
|  |  |
|  |  |

**4. Purpose of trial image acquisition and image analysis**

*[Describe in this section the details of the images being collected. For example: safety, primary endpoint, eligibility or experimental.]*

**5. Procedures**

The analysis or evaluation of clinical trial images in accordance with this manual should be overseen by the CI who assumes responsibility for various components. Oversight of the image analysis is likely to be delegated to one of the Research Radiographers, Radiologists or Physicists associated with the Clinical Research Imaging Facility. This role should be described.

|  |  |  |
| --- | --- | --- |
| **Named person** | **Role** | **Procedure** |
|  |  |  |
|  |  |  |
|  |  |  |

**5.1 Categorisation of trial images**

State each Image test by category

|  |  |
| --- | --- |
| **Category** | **Description** |
| Category 1 | Standard imaging protocol used by service |
| Category 2 | Standard imaging protocol with specific trial requirements |
| Category 3 | Nonstandard imaging protocol specific to research trial |

|  |  |
| --- | --- |
| **Imaging Test** | **Category** |
|  |  |
|  |  |

Detail of any non-standard requirements for image acquisition or image analysis e.g. Work in Progress sequences (WIPs), software released by agreement with Vendors, novel coils or specific analysis software.  Include processes for contracting, implementation and use, even when this is in accordance with the Imaging department’s standard practice.

**5.2 Communication related to Safety**

Lines of communication with the CI must be detailed to ensure that any issues that may impact on study participant’s safety are reported without delay. This includes the reporting of out of the range results and significant deviations from the protocol or the study specific Imaging Manual. If there are no potential safety issues, this should be stated in the manual.

*[Detail the steps to be taken in the event of a deviation which should include:*

* *Imaging staff contact designated PM*
* *PM will contact CI and study Monitor*
* *The study Monitor is responsible for contacting the Imaging staff and opening and completing a protocol deviation form as required (Form 51.008A). ]*

**5.3 Communication related to changes with scanner/ coils**

The imaging protocol is specified for the trial. MRI facilities that upgrade their scanner software or hardware (coils and gradients) after Sponsor has approved them may need to readjust their sequence parameters to maintain consistent image characteristics. Therefore it is important to contact Sponsor in advance if a scanner hardware/software upgrade is planned. Similarly please contact Sponsor as soon as possible in the event of a scanner/coil repair.

All scans for an individual subject **will usually** be performed on the same scanner and coil throughout the trial. Any change of scanner for reasons of servicing or upgrade must be communicated to Sponsor in advance. If other scanning arrangements are permissible then this **must** be clearly specified.

*[Detail the steps to be taken in the event of a change in scanner/coil which should include:*

* *Imaging staff contact designated PM*
* *PM will contact CI and trial Sponsor]*

**5.4 Consent & withdrawal of consent**

*[Detail how the patient once recruited will be referred to the scanning department. Describe how the study team (PM will notify the Imaging staff of what actions to implement if a participant withdraws consent. For instance, when a subject withdraws consent to participate in the trial, a member of the research team (CI, Research Fellow or PM) will contact the relevant staff to inform them of the withdrawal. This will be in writing and will detail the steps to be undertaken with trial images. ]*

If copies of consent forms are required, please detail the process in this section

**5.5 Visit schedules, acceptable windows, re-scanning windows & incidental findings**

**5.5.1 Visit schedules**

The visit schedule for pre-defined imaging tests should be captured in a table, as below:

**Example of Table with visit schedule and when imaging tests should be conducted**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Base line/Screening** | **Month 12** | **Month 24** |
| **Imaging test 1** | **🗸** | **🗸** | **🗸** |
| **Imaging test 2** | **🗸** | **🗸** | **🗸** |
| **Imaging test 3** | **🗸** | **🗸** | **🗸** |

In addition there may be specific imaging time points such as End of Treatment (EOT) imaging (when a patient prematurely discontinues treatment), End of Study (EOS) or Unscheduled visits (UV). Such requirements should be specified in the imaging protocol.

**5.5.2** **Acceptable windows**

Stipulate the acquisition windows (as specified in the trial protocol) in relation to the treatment period or other key events eg:

Month 12: +/- 14 days relative to the scheduled visit

Month 24: +/- 14 days relative to the scheduled visit

EOT (End of Treatment): N/A

EOS (End of Study): N/A

UV (Unscheduled Visit): N/A

When a dummy run is required for quality control (QC) purposes, ensure that sites plan sufficient time for transfer of the dummy scan, scan receipt, QC reporting by the Sponsor and potentially a repeat scan before a patient visit is scheduled eg

Screening: Day -45 to Day -8

**5.5.3** **Re-scanning windows**

In the event that a scan needs to be repeated, it should be reacquired as soon as possible. If a re-scan is necessary for the **screening v**isit, it is imperative that it is acquired as soon as possible and **before** the first study dose, as applicable.

**5.5.4** **Incidental findings**

Unless, it is specified in the trial protocol that all scans will be reported for incidental findings, the evaluation of scans for incidental pathology is a local responsibility that should be handled according to local practice. For NHS Greater Glasgow and Clyde, incidental findings will be reported according to SOP 58.006 using GUI 58.006A if an incidental finding is detected.

5.5.5. **Confirmation of attendance and completion of imaging**

If non-attendance or technical failure impacts on research imaging used in eligibility criteria, primary, secondary or safety endpoint analysis the Project Manager must be promptly notified. Likewise if participant details do not match the request form then the research imaging should not be performed without confirming details with the Project Manager.

**5.6 Local Site initiation requirements**

**5.6.1 Local Quality Control of equipment**

It is the responsibility of the local imaging Facility to have a standard program of quality control and preventative maintenance of their equipment and that such routine checks are properly documented. These scanner maintenance reports should be kept on site, such that they can be easily retrieved in the event that Sponsor requests a copy of a report for a given time frame.

**5.6.2 Acquisition Imaging Protocol**

Each site requires a description of scanner-specific scanning parameters and where possible, step-by-step instructions for implementing these parameters on the console for different scanner manufacturers. See FORM 51.034C Study Specific Imaging Protocol and FORM FORM 51.034D for imaging parameters (if required).

Information about patient positioning should be provided. Sometimes it is helpful to provide examples of acceptable and unacceptable images. If planning images must be kept from the screening visit to facilitate re-positioning of patients at subsequent visits, these images must be stored according to local data protection rules.

**5.6.3 Dummy run and quality control checks**

Dummy Runs are conductedto ensure that adequate image quality can be achieved at each site, irrespective of the scanner used. Dummy runs may involve phantoms, healthy volunteers or sometimes patients. In some cases, patient positioning and measurement reproducibility are obtained through the use of appropriate sequence parameters.

If a dummy run is required, the images must be approved by Sponsor **prior**to scanning trial subjects.To facilitate the Dummy Run process, the PM will contact sites to discuss the process. A phone training session will also be scheduled with the Imaging technologist at each site. Prior to this the PM will send out the Scanner Specific Console Setup Instructions, which are to be used as the starting point for setting up the imaging protocol. The Scanner Specific Console Setup Instructions is a separate document from this Manual and contains the parameters required for the Imaging sequences in the trial.

The first quality control step is for the local imaging technologist to build the imaging protocol into the scanner and export the protocol from the scanner as a pdf or text file for Sponsor review and a dummy run phone consulting session to enable the fine-tuning and customisation of the sequences prior to acquisition of the dummy run scan. The second quality control step is to send the dummy scan to the Sponsor for review. The Sponsor will send each site a dummy run report within XXX days and a dummy run Approval letter, if a repeat dummy scan is not required.

**5.6.4 De-identification of image data once transferred to the imaging workstation**

Subjects should be registered on the imaging console using a subject- and scan-specific ScanID, which could take the following form:

**GN ID\_<Site ID>\_<Subject ID>\_<Visit>**

**GN ID:** refers to the protocol number

**Site ID:** is a 4-digit number assigned to the site by Sponsor.

**Subject ID:** refers to the unique patient identification number for the trial

**Visit** refers to the visit name of the scan, FOR EXAMPLE:

• Enter **Screening** for the screening scan

• Enter **m12** for the month 12 scan

• Enter **m24** for the month 24 scan

• Enter **EOT** for the End of Treatment visit

• Enter **EOS** for the End of Study visit

• Enter UV for the unscheduled visit

**5.6.5 Local Clinical reporting requirements**

As per trial protocol, local reporting and archiving of images and reports should be specified in the imaging protocol. All trial scans must be archived twice – once using standard imaging archival procedures and the other through the trial archive.

**5.7 Image Export and Transfer to the Central Imaging Laboratory**

**5.7.1 Image anonymisation**

The Sponsor will only receive scans and accompanying documentation (Form 51.034B Data Transmittal) that have had identifiable patient information removed (i.e. subject full name, initials or date of birth). Once stripped of patient identifiable information, the clinical trial images must be labelled in such a way as to allow their unequivocal identification at all times in the analysis or evaluation process (see 5.7.2). The date and time of when the imaging took place must be recorded.

Receipt of images or documentation **with patient identifiers** must be reported to the PM immediately.

**5.7.2 Data Shipment**

The Data Transfer Log (Appendix 2) must be completed for all shipments and a copy retained at site. Because this contains identifiable information, the Data Transfer Log must NOT be sent to Sponsor. The original digital data for all of trial images must be sent to Sponsor in a standard DICOM format which may be submitted using:). Compress the DICOM files of the examination into one ZIP file. The filename of the ZIP file should follow the naming convention:

TRIAL NAME\_<SiteID>\_<SubjectID>\_<Visit >.zip

• **CD**: please review the data CD before shipment to ensure all sequences were successfully exported and label the CD according to trial convention, clearly s

• **Secure FTP (sFTP):** This is thepreferred method of transfer. Please ask the PM to set up your account (sFTP server address, username and password pecifying 1) the Trial, 2)the site ID, 3) the subject ID number, 4) scan type and 5) date of scan acquisition.

*[Detail the shipment requirements and shipping address for CDs.]*

**5.8 Image analysis through the Central Imaging Laboratory**

**5.8.1 Receipt and reconciliation of trial images**

Receipt of images through sFTP or by CD must be documented on the Image Transfer Log (Appendix 2). If images are poorly labelled, missing or if unexpected images are receipted this should be recorded on the FORM 51.034E Data Transfer Log and the PM should be contacted to investigate and resolve the issue. Data Transfer Logs should be stored locally and centrally in the Central Imaging Laboratory Site File.

**5.8.2 Analysis of trial images**

Trial images should be uploaded by a member of the radiographer team to the University of Glasgow secure server to be accessed for review and reporting on workstations in the University of Glasgow. These workstations are accessible only by those with a password protected account and secure keycard entry to the reporting room.

[*Describe any other arrangement*]

A research analysis report (linked to each individual patient by anonymised subject numbers) will be prepared for each patient following each scan.

*[Describe:*

*- Personnel and qualifications of personnel responsible for image analysis.*

*- Software (if used) to facilitate analysis.*

*- How source analysis data is retained and archived*

*- How analysis data is transcribed to eCRF]*

**5.8.3 Inter-observer analysis**

When more than one observer is required to assess each image manually, a random selection of scans (10%) will be analysed independently for assessment of inter-operator variability and quality assurance. The selection of scans for review will be randomly chosen by the Clinical Trials Unit once the final patient has completed follow-up and all scans have been performed.

**5.8.4 Analysis validation**

Analysis should be performed using appropriately validated methods with defined acceptance criteria.

For category 3 tests the process for validating the methods should be detailed. The analytical methodology should include details of expected range, suitability tests and quality control samples, inter-and intra-assay variation and accuracy. For all category 3 tests where externally sourced analysis software, coils or WIPs are used, the detail of the validation and comprehensive testing should be within this section.

If a product is fully validated and CE marked, details of the CE marking should be provided. An example of this is ‘ready to use’ analysis software (eg. Circle or MEDIS - for cardiac MR analysis). However when a product is not CE marked, an insert or document will be provided from the manufacturer detailing the validation checks that the product has been subjected to. This should include an acceptable range of values, confirmation of reproducibility, and limits of variation. These details should be provided in this section or link to the information.

Where the product has not been previously validated, all validation testing will need to be performed before any research imaging can be performed. These tests should determine reproducibility, accuracy, acceptable range of values, and if any, which control samples are required. The details of these tests should be provided in this section.

Trial specific SOPs for novel analysis methods may be required and should be reviewed and approved by the CRIF Working Group.

**5.8.5** **Image analysis data transfer to the eCRF**

Transfer of image analysis data to the eCRF needs to be described. If this is through manual transcription of results into the eCRF, QA of this process needs to be conducted and described. If transfer of results is through the use of excel spreadsheets, a process of version control is required, such as by pdf. Access to the source data must be described for monitoring or inspection purposes.

**5.9 Blinding**

*[The sponsor must ensure that appropriate measures are implemented to ensure blinded individuals are not exposed to information which can compromise the blinding. In situations in which where images from blinded trials are supplied to a laboratory and the data generated by the laboratory may un-blind the trial, it is important that data is only sent to an established point of contact. This must be fully detailed within the manual.]*

**5.10 Equipment**

Any new equipment must be maintained in accordance with the laboratories standard practice and added to the respective laboratory equipment inventory. Calibration and maintenance documentation should be stored in the Laboratory Master Research File.[*The PM should record the asset details.]*

**5.11 Computerised systems**

All computerised systems used for the capture, processing, reporting and storage of data should be developed, validated and maintained in order to ensure the validity, integrity and security of the data. [*If an eCRF is in use then it may be appropriate for the Laboratory team to have access to this assuming that this will not affect blinding. This section should reference the training provision.]*

**5.12 Retention of trial data**

Trial specific documents should be retained in accordance with the requirements of GCP and national legislation and archived in accordance with the Sponsor archive standard operating procedures [SOP 51.024]: refer to study protocol.

Non trial specific documents should be retained in accordance with the laboratory policies.

All copies of shipping logs/relevant documentation should be retained in study specific files prior to archive.

**5.13 Non compliances and potential serious breaches in GCP**

This section must detail the processes to be followed when incidents occur that are considered to be a noncompliance with GCP and/or potential serious breaches in GCP. Definitions of such incidents may require being included.

**5.14 Protocol Amendments**

This section must detail the processes to be followed when protocol amendments have been made. This must include how the Sponsor will risk assess the impact to the Study Specific Laboratory Manual an ensure updates to it are distributed and implemented accordingly.

1. ***Referenced documents***

* SOP 51.033 – NHS Laboratory Samples within Trials involving an Investigative Medicinal Compound sponsored by NHS GG&C or co-sponsored by NHS GG&C and University of Glasgow
* Form 51.033A – CTIMP Categorising of Imaging Scans
* SOP 51.034 – Writing a trial Specific Research Imaging Manual for Sites Participating in Clinical Trials of an Investigative Medicinal Product (CTIMP) Sponsored by NHS GG&C or Co-sponsored by NHS GG&C and University of Glasgow (UoG)
* Form 51.034A- Sponsor Imaging Manual
* Form 51.034B – Data Transmittal
* Form 51.034C – CT/MRI Protocol Template
* Form 51.034D – CT/MRI Imaging parameters template
* Form 51.034E Data Transfer Log
* SOP 51.024 – Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
* SOP 56.002 –Project Management Trial Set-up
* SOP 52.007 – Authorisation for NHS resource use in R & D Submission

**Form Completed by:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Name** |  | **Signature** |  | **Date** |  |