Standard Operating Procedure		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).		
Version **1.0**		
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1. SOP Category

NHS GG&C Sponsor R&D

2. Staff Category

Members of Clinical Research Imaging Facility (CRIF) Working Group
Lead Research Radiographer
Chief Investigators
Senior R&D Managers
R&D Research Co-ordinators
NHS GG&C Sponsor Project Management Unit& Project Managers

3. Scope

This procedure applies to clinical trials of investigational medicinal products (CTIMPS) sponsored by NHS Greater Glasgow & Clyde (NHS GG&C) or co-sponsored by NHS GG&C and the University of Glasgow (UoG) which involve radiological research imaging. This includes trials sponsored or co-sponsored by NHS GG&C even if NHS GG&C is not a participating site or when the imaging and/or data handling is not conducted by NHS GG&C and/or Clinical Research Imaging Facility (CRIF).

4. Purpose

The performance and analysis of research imaging in subjects participating in a clinical trial forms a key part of the clinical trial process. It is a requirement for all imaging departments that perform work in support of clinical trials to implement appropriate measures to assure the quality and integrity of the data they produce and to exercise due diligence to ensure that the trial subject' rights are not compromised. In order to meet this requirement a Trial Specific Imaging Manual (Form 51.034A) is required for all Clinical Trials of Investigational Medicinal Product (CTIMP) sponsored by NHS GG&C or co-sponsored by NHS GG&C and UoG. The Trial Specific Imaging Manual will include standard imaging, but have specific requirements or non-standard research imaging or central imaging functions – category 2 & 3 tests as defined in SOP 51.033 using Form 51.033A.

The Trial Specific Imaging Manual must only include work that is covered by the clinical trial protocol. It should contain sufficient detail to allow accurate reproduction of techniques for non-standard, research imaging undertaken on trial participants. Generic SOPs and processes in operation within imaging departments will still be followed. A trial may require more than

one Imaging Manual depending on the number of imaging departments and imaging procedures specified within the Clinical trial protocol.

5. Procedures

The Trial Specific Imaging Manual should be written by the Chief Investigator (CI) or delegate in conjunction with the named individual(s) performing and reporting the images at the lead centre. The process will be coordinated by the Project Manager. The manual requires to be approved by the CI, sponsor representative (usually the Project Manager) and Lead Research Radiographer. The Trial Specific Imaging Manual should be filed in the laboratory section of the Sponsor TMF, and in the trial Investigator Imaging Site files.

The performance and analysis or evaluation of clinical trial imaging in accordance with the Trial Specific Imaging Manual should be overseen by named individual(s) who assumes responsibility for the conduct of the work. The CRIF Working Group should approve the classification of Research Imaging Tests and the Trial Specific Imaging Manual itself. The CRIF Working Group should provide feedback to ensure that it captures the training and expertise required of those performing the roles and responsibilities assigned to them.

Appropriate Imaging costs for the project will be approved as per SOP 52.007 "Authorisation for NHS resource use in R & D submission".

5.1 Categorisation of Research Imaging

Prior to trial commencement, imaging procedures detailed within the trial protocol should be classified according to the following criteria. Form 51.033A should be completed for each imaging outcome listed within the protocol and this should be filed in the laboratory section of the Sponsor TMF, and in the trial Investigator Site files detailing**:**

Category 1: Standard imaging protocol i.e. in use in clinical practice within NHS
Category 2: Standard imaging protocol, with specific requirements or
Category 3: Nonstandard imaging protocol specific to research trial

The Trial Specific Imaging Manual must detail any non-standard requirements for taking images or conducting image analysis e.g. Work in Progress sequences (WIPs), software released by agreement with Vendors, novel coils or specific analysis software. When this is the case, the Trial Specific Imaging Manual must detail the processes for contracting, implementation and use, even when this is in accordance with the Imaging department's standard practice.

5.2 Safety

The Trial Specific Imaging Manual must detail the communication plan to be followed with the CI to ensure that any issues that may impact on a trial participant's safety are reported to them without delay. This must include the reporting of any incidental findings and significant deviations from the Clinical Trial protocol or the Trial Specific Imaging Manual. If there are no potential safety issues, this be stated in the Manual.

5.3 Communication related to changes with scanner/ coils

The Trial Specific Imaging Manual must detail how the site communicates with the sponsor in advance of any hardware/software changes or upgrades or major scanner/coil repairs that may affect imaging quality or scheduling.

5.4 Consent and withdrawal of consent

The Trial Specific Imaging Manual must detail how the trial team or Project Manager will refer the patient to the Scanning Department once the patient has been recruited. It must also detail any actions to be implemented by imaging staff if notified by the trial team or PM that a participant has withdrawn consent.

5.5 Visit Schedule

The Trial Specific Imaging Manual must detail visit schedules, acceptable scanning windows, re-scanning windows and how incidental findings are reported/ followed up. 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 must not be performed without confirming details with the Project Manager.

5.6 Local Site Initiation Requirements

All sites participating in the Trial shall have completed the Trial Specific Imaging Manual and provide a **Trial Specific Acquisition Imaging Protocol** as Form 51.034C and **Imaging Parameters** as Form 51.034D that details scanning parameters, if required. The Trial Specific Imaging Manual shall detail local quality control of equipment, Dummy run and quality control checks (including use of phantoms). In addition, a protocol must be specified as to how acquired image data, once transferred to the workstation, is de-identified. Local clinical reporting requirements must be specified.

5.7 Image Export and Transfer to the Central imaging Laboratory

The Sponsor requires scans and accompanying documentation to have all identifiable patient information removed. The Trial Specific Imaging Manual must specify how anonymised scans will be labeled to ensure their unequivocal identification at all times in the analysis or evaluation process. The date and time of when the imaging took place must be recorded.

The Trial Specific Imaging Manual shall specify how the **Data Transfer Log** (Form 51.034E) shall be completed. A copy of each **Data Transfer Log** shall be held in local trial investigator site files.

The Data upload requirements shall be detailed e.g. passwords for secure upload of images or shipping addresses for CDs. The **Data Transmittal Form** (Form 51.034B) must be completed and a pdf uploaded by secure file transfer or email, as required. A copy of each Data Transmittal Form shall be held in local trial investigator site files.

5.8 Image Analysis through the Central Imaging Laboratory

5.8.1 Image Receipt

The Trial Specific Imaging Manual shall specify how the **Data Transmittal Form** must be completed and sent. A copy of all Data Transmittal Forms received by the Central Imaging laboratory shall be filed in the Central Imaging Laboratory Site File.

Images and associated documentation being received at a NHS GG&C/ UoG imaging department undertaking central laboratory functions from participating sites must not contain any patient identifiable details. The Project Manager must be notified if patient identifiable details are included.

5.8.2 Method Validation

The Trial Specific Imaging Manual must detail the validation processes to be undertaken for the specified imaging procedures and image analyses. Standard Details to be included are:

a) The process for validating the methods for category 3 tests. For all category 3 tests where externally sourced analysis software, coils or WIPs are used, the detail of the validation and comprehensive testing must be within this section.

If a product is fully validated and CE marked, details of the CE marking must 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 must include an acceptable range of values, confirmation of reproducibility, and limits of variation. These details will be provided in this section or a 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.

b) Definitions of acceptance criteria.

c) Definitions of suitability tests and quality control samples.

d) Definition of limits of inter-and intra-scan variation and accuracy. Inter and intra assay variation is required to be performed during the run of tests where more than 1 product is used, regardless of whether the product is fully validated or not.

5.8.3 Data recording

The Trial Specific Imaging Manual must detail the processes for recording data generated within the imaging departments.

- All data must be recorded directly, promptly, accurately and legibly.
- The date and identity of the person performing and reporting the research imaging should be recorded.
- A quality control procedure must be in place to ensure that all data are accurate and complete.
- An audit process for tracking changes if data are modified or corrected.

5.8.4 Reporting

The Trial Specific Imaging Manual must detail the manner in which the Imaging data will be reported. The format, number, timing and frequency of reports to be generated should also be included.

5.9 Blinding

The Trial Specific Imaging Manual must detail any processes in place to maintain the blind if required. Standard details to be included are:

- Point of contact to receive un-blinded data/reports from the imaging team.

5.10 Data Transfer

The Trial Specific Imaging Manual must detail the processes of data transfer from the imaging department to the data-management centre, e.g. when analyses may be carried out in a central function requiring that batches of data have been held and require transfer. Data may be sent to the Clinical Trial Units or Data Centre Provider as hard paper copy, electronically or both. If data is manually entered onto a worksheet or electronic case report form then the process of auditing this must be defined, e.g., a predefined random proportion of values will be audited or requirements for a 100% check of entries.

5.11 Computerised Systems

The Trial Specific Imaging Manual must detail all computerised systems used for the capture, processing, reporting and storage of data. The processes of development, validation and maintenance of these systems must be detailed. These processes must ensure the validity, integrity and security of the data. Any access that imaging teams require to the electronic case report must be detailed along with how that access is given and removed.

5.12 Retention of Trial Data

The Trial Specific Imaging Manual must detail the processes of retention of trial data.
• Trial specific documents to 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].
• Non trial-specific documents to be retained in accordance with the Imaging Department policies.

5.13 Retention and destruction of trial images

The Trial Specific Imaging Manual must detail the processes to be applied to images at the end of the trial. These will be dependent on the approved detail within the protocol and as defined in the ethical application. The processes may include storage, retention, or destruction when images are not stored for clinical purposes.

5.14 Non-Compliances and Potential Serious Breaches in GCP

The Trial Specific Imaging Manual 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. It may be necessary to define such incidents in the Trial Specific Imaging Manual.

5.15 Protocol Amendments

The Trial Specific Imaging Manual 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 Trial Specific Imaging Manual and ensure updates to it are distributed and implemented accordingly.

6 Referenced documents

• SOP 56.002 – Project Management Trial Set-up
• SOP 51.033 – Research Imaging for Trials involving an Investigative Medicinal Compound (CTIMP) Sponsored by NHS GG&C or co-sponsored by NHS GG&C and the University of Glasgow (UoG)
• Form 51.033A – CTIMP categorisation of Imaging Scans
• Form 51.034A – Sponsor Imaging Manual
• Form 51.034C –CT/MRI Protocol template
• Form 51.034D – Imaging parameters template

• Form 51.034E – Data Transfer Log
• Form 51.034B – Data Transmittal Form
• SOP 52.007 – Authorisation for NHS resource use in R & D Submission
• SOP 51.024 – Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)

7. **Related documents**

- MHRA Good Clinical Practice Guide

8. **Document History**

Version	**Date**	**Description**
1.0	09/03/2020	Release of version 1