CRF & DATA MANAGEMENT (SPONSORED)

Research & Development

Standard Operating Procedure for Clinical Trials Source Data, Case Report Forms and Clinical Trial Data Management in West Hertfordshire Hospitals NHS Trust Sponsored Clinical Trials

SOP Number : SOP-15-06	**Effective Date:** October 2021
Version Number: v06	**Review Date:** Every 2 -3 years

1.0 BACKGROUND

This document sets out the procedure to be followed by all West Hertfordshire Hospitals Trust (WHHT) staff who record data for the purpose of research and in the management of research data of clinical trials sponsored by WHHT.

It provides clear guidance on how data collected in the course of research should be documented and how records should be stored as well as the steps involved in data management to ensure compliance with the Trust's policies.

2.0 PURPOSE

- To provide guidance and templates that will assist in the development of appropriate data collection tools e.g. Case Report Forms (CRFs)
- To define the review and approval process for data collection tools
- To define the data collection process and define source documentation requirements for WHHT sponsored trials
- To provide guidance for the management of trial related data and therefore ensure that all data is collected, verified and analysed to assure that trial data is accurate

3.0 APPLICABLE TO

Any Trust employee involved with the collection and management of data for clinical research including, but not limited to, Unit Heads, Chief Investigators (CI), Principal Investigators (PI), Co-Investigators, Consultants, Clinical Trial Pharmacists, Research Managers, Statisticians, Research Nurses, Allied Health Professionals, Trial Coordinators & Data Managers.

"ICH GCP guidelines state that only appropriately qualified individuals should supervise trial data handling, verify the data and conduct the statistical analyses (ICH 5.5)".

4.0 RESPONSIBILITIES

The Chief Investigator (CI) or Delegated Individual (DI) is responsible for the design and development of CRFs. The CI is also responsible for ensuring that there are CRFs for use in the study in all participating sites. Instructions should be given to all participating sites on how to complete the CRFs to ensure data is collected in a standardised fashion. A CRF completion guide may be useful in a multicentre study.

Prior to study approval, the CRF should be reviewed and approved by Statisticians, CTU, the Research & Development Steering Group (RDSG) and R&D for sponsored trials. Subsequent amendments to CRFs should also receive statistician and RDSG/ R&D approval.

5.0 PROCEDURE

5.1 Management of Source Data in Clinical Trials

5.1.1 The documents containing source data must first be specified within the trial protocol. Where either the CRF or other forms (questionnaires) are to be used to directly record source data, this should be defined in the protocol.

5.1.2 All patient activities from registration on the clinical trial should be fully documented in the health records (paper medical records or electronic medical records). All healthcare record keeping should be compliant with the applicable latest version of Records Management: NHS Code of Practice. For clinical trials, the following areas are examples of what should be recorded as source data:

- Date of registration into study
- Confirmation of eligibility
- Date of consent
- Details of Adverse Events (Graded according to CTCAE)
- Details of all drug administration

5.1.3 For clinical trials, all original recordings and all information regarding clinical investigations should be documented for a patient in the medical records according to protocol.

5.1.4 All original copies of source data should be held as part of the trials essential documents. Where copies are to be used, these should be certified (dated signature) by the investigator or member of the research team.

5.1.5 When using copies of eSource Data, copies are only acceptable when the copy is produced and verified against the eSource data. This process should normally be documented in the form of a local study SOP.

5.1.6 Where original source data is to be scanned and used, the scanning process has to be validated prior to implementation in a trial to ensure that the integrity of the generated record is good. If the scanning process is contracted to an external party, then appropriate agreements should be in place to safeguard key requirements.

5.1.7 Where the protocol specific clinical data is first collected on a paper collection tool (data collection sheets) and then data is entered onto the CRF, this 'transcription' step must have quality control steps.

5.2 Design, Development and Approval of Case Report Forms

5.2.1 Case Report Forms (CRFs) are the usual data collection tool used in a clinical trial and are essential for quality assurance and control. The CRFs can be either in paper format (pCRF) or an electronic CRF (eCRF). The procedures outlined below apply to both CRF formats.

5.2.2 A CRF should be designed to ensure that it captures all the information which is required according to the protocol. **It should not capture additional information which is not specified in the protocol.** For WHHT sponsored trials; the CRF example in appendix 2 can be used as a template. This CRF template can be adapted by the study team to suit the requirements of the study. It is recommended that the study team also request review of the study CRF by an independent Data Manager.

5.2.3 The CRFs should be version controlled and a clear amendment history should be possible to follow/ view in the Trial Master File (TMF).

5.2.4 The CRF should follow the schedule of clinic visits and should be consistent with the treatment schedule in the protocol. Preferably the CRF should be designed in such a way that it should act as a prompt to the investigators to perform the study specific investigations as laid out in the protocol's treatment schedule. This will help the R&D office to confirm that the protocol was followed and for the statistician to build in edit checks within the database to assist with the management and analysis of the data. As a minimum, the following should be taken into consideration during CRF design:

- The arrangement of the data fields should be clear, logical, and user friendly
- When possible, provide tick box options and keep free text to a minimum. Tick box options should be exhaustive e.g. provide an option for "other" or "NA" if appropriate
- For variables where the actual value is captured, the number of boxes required should be adequate and if appropriate reflect the number of decimal places desired
- The unit of measurement should be specified
- Consideration should be given as to how the CRF will relate to the database
- Consideration should be given as to collection of data for unscheduled patient visits

5.2.5 The design of the CRF should include some core data as minimum requirements to ensure data collected per study subject is Good Clinical Practice compliant, as follows:

- Inclusion/exclusion criteria checklist with tick boxes (with investigator's signature)
- Date informed consent taken (with investigator's signature)
- Subject demographics (e.g. age, gender, ethnicity)
- Relevant medical history
- Results of physical exam
- Baseline data
- Primary and secondary endpoints (with investigator's signature)
- Laboratory data, ECG etc.
- Dosing and compliance data

- Adverse events
- Concomitant medications
- Withdrawal/Off study form
- Serious Adverse Event Reporting Form (with investigator's signature)

5.2.6 CRFs should have a study identification number (study number, study title, sponsor). If possible, all pages should have the subject ID and initials. The date of each subject visit should be captured. There should be a place, preferably at the end of the CRF for the Principal Investigator's signature to verify that all data is complete and accurate. **To comply with the data protection laws, the CRF should not contain patient identifiable information unless this has received ethics approval and is stated within the protocol.**

5.2.7 The CRFs for WHHT sponsored CTIMP trials must be reviewed and approved by the RDSG as part of the R&D approval process (see Policy on obtaining approval to conduct clinical research).

5.2.8 When CRFs for WHHT sponsored CTIMP trials are amended this must be approved by the RDSG as a non-substantial amendment (see SOP-09).

5.3 CRF Completion and Retention

5.3.1 The CRF should be completed by an appropriate individual delegated the responsibility by the Chief Investigator/Principal Investigator and recorded on the study delegation log.

5.3.2 All staff completing the CRFs should have adequate training to ensure minimal corrections required. For multicentre studies a CRF guidance document is recommended to assist sites with accurate CRF entry.

5.3.3 To complete pCRFs, always use black ballpoint pen. **Do not use pencils.**

5.3.4 Ensure that the CRF contains only anonymised data unless it is specified in the protocol that CRFs are source documents and that patient names can be collected.
5.3.5 The CRF should be completed in a timely manner using source documents (i.e. medical notes) unless the protocol states that the CRF can be the original site of recording. Ensure that all entries are legible.

5.3.6 Do not leave CRF pages blank. If data are unavailable then the annotations not done (N/D), not applicable (N/A) or unknown (U/K) should be recorded as appropriate.

5.3.7 Do not create additional fields on the CRF i.e. Only provide information which is asked for. Do not use 'post it' notes within CRFs to include additional information.

5.3.8 Corrections should be made by crossing through the incorrect entry with a single line so that the original entry is still readable. Enter the correct data. Initial and date the correction. Never use correction fluid or obliterate entries made on the CRF.

5.3.9 The CRF should be reviewed for accuracy and completeness by the Investigator or an appropriately delegated individual and signed off before the CRF data is entered onto the statistical database.

5.3.10 The WHHT sponsored study CRFs will be subject to source data verification monitoring to ensure the data collected is accurate and verifiable and that the safety of patients is maintained. For

Phase I/II trials, 100% SDV will be conducted by the R&D office. For all other studies, 10% source data verification will be performed. The level of monitoring will however be decided by the Sponsor and detailed in the study monitoring plan.

5.3.11 The Monitoring report will identify any changes which are required to the CRF. The CRF corrections should be made by the research team within the defined timelines of the monitoring report.

5.3.12 CRFs should be stored in a secure location during the course of the study and archived when the study has finished.

5.3.13 Once the patient has finished their study treatment and the CRF has been completed they should be sent to the study's delegated study coordinator / CTU / data manager who should then check the CRF for missing or incomplete responses and if found, queried with the investigator and recorded.

5.4 Design and Use of Database for Statistical Analysis

5.4.1 Once the CRF has been designed and approved by the RDSG, the database for the statistical analysis should be designed by the study's statistician.

5.4.2 A database should be designed to ensure that it captures all the information that is required according to the protocol. It should directly reflect the content of the Case Report Form (CRF) and only include the parameters which will be included in the final analysis. Parameters collected to satisfy GCP requirements such as details of adverse events, previous medical history and concomitant medications generally do not require inclusion in the trial database. (see SOP-34)

5.4.3 The database should ensure that an electronic audit trail for the data is maintained (ICH-GCP 5.5.3) with appropriate password protection to prevent unauthorised access to the data. The database should be maintained according to user requirements with appropriate levels of access. Any upgrades or changes to systems should be managed according to local SOP.

5.4.4 There must be suitable backup for any database and if blinding is required then the data entry and processing systems must be designed so that this is not compromised (ICH GCP 5.5.3).

5.4.5 The CRF responses must be coded before they can be entered onto the statistical database therefore the codes should be determined before data entry begins, preferably when the database is being designed. It is important to ensure that codes are in place for not done, not applicable and unknown to represent where data is missing.

Adverse events also require coding using the Medical Dictionary for Regulation Activities (MedDRA)

5.4.6 For WHHT sponsored CTIMP trials, data verification is arranged by the R&D office through source data verification, as stated in the protocol/ monitoring plan.

5.4.7 Where data queries arise from CRF review, the corrected CRF should be entered onto the database by a delegated individual. For multicentre studies where the CRFs are being sent to a coordinating centre for data entry a copy should be kept in the site file. It is important for the coordinating centre data manager to keep a log of all the CRFs received.

5.4.8 The single data entry method is the most commonly used method for WHHT sponsored trials. Once the data has been entered onto the database, check is completed to ensure the accuracy of the data recorded. For each trial, the process for data entry should be standardised and documented.

5.4.9 To ensure the accuracy of the data set for the statistical analysis an important process is the 'cleaning' and validation of the data. This process should be done as defined in study protocol.

5.5 Management of Amendments to CRFs and Statistical Database

5.5.1 All amendments involving CRF collection to clinical trials require authorisation by the trial statistician prior to RDSG/R&D approval as per SOP-09.

5.5.2 The study statistician should review the amendment to assess the impact on CRF design and study database. The investigator should be advised of any potential changes required to the CRF and study database.

5.5.3 Any amendments to the CRF should conform to requested amendments to study documents and/or revised protocol.

5.5.4 The CRF page numbering and version information should be updated to reflect the current status of the document.

5.5.5 The amended CRF should be submitted for RDSG approval prior to use.
5.5.6 Any changes to a statistical database should be controlled and a clear audit trail should be present, as local SOP.

6.0 RELATED DOCUMENTS

- SOP-09 Amendments
- SOP-34 Statistics

7.0 APPENDICES

- Appendix 1 - Definitions
- Appendix 2 - Template CRF

8.0 VERSION HISTORY

Revision Chronology:		
Version Number	**Effective Date**	**Reason for Change**
SOP-15-06	**October 2021**	1. Change from general Standard Operating Procedures (gSOP) to SOP 2. Removal of the '10.0 Agreement' from the template - all agreement signatures will be collated on a new 'SOP Signature Sheet Document' 3. Other minor amendments and clarification of terms following review
gSOP-15-05	**October 2017**	Minor amendments following review
gSOP-15-04	**01/10/2015**	Minor amendments following dissolution of consortium
gSOP-15-03	**22/05/2014**	Minor amendments following review
gSOP-15-02		SOP modified for implementation at ENHT/WHHT.

gSOP-15-01 (MVCC)		SOP modified for implementation at MVCC

9.0 AUTHORSHIP & APPROVAL

Author

Signature  **Date** 28/10/2021

R & D Steering Group Approval

Signature  **Date** 28/10/2021

Appendix 1: Definitions

Adverse Event (AE)
An unfavourable outcome that occurs during or after the use of a drug or other intervention, but is not necessarily caused by it.

Case Record Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

Chief Investigator (CI)
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI. For Trust sponsored trials, the CI had been delegated the pharmacovigilance responsibility for identification, recording and reporting of safety events, including submission of Development Safety Update Reports (DSURs) to the MHRA and REC.

Clinical Trial
A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions. A Study Type.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004. An investigation in human subjects, other than a non-interventional trial, intended: a) to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products, b) to identify any adverse reactions, or c) to study absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products.

Delegated Individual (DI)
An individual delegated by a person of responsibility to carry out their task(s).

Good Clinical Practice (GCP)
Good Clinical Practice is a set of internationally recognised ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects.

International Conference on Harmonisation (ICH)
International Conference for Harmonisation, a collaboration between regulators and the pharmaceutical industry in Europe, the United States and Japan to establish common standards for clinical trials. ICH GCP is a widely recognised standard for Good Clinical Practice in clinical trials.

Principal Investigator (PI)
A collection of files that contain all the pharmacy relevant documents pertaining to a specific clinical trial.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR)
Any adverse event or adverse reaction that results in:

- death
- is life-threatening*

- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- or is a congenital anomaly or birth defect

Comment: Medical judgement should be exercised in deciding whether an adverse event/reaction should be classified as serious in other situations. Important adverse events/reactions that are not immediately life-threatening or do not result in death or hospitalisation, but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

* Life-threatening in the definition of a serious adverse event or serious adverse reaction refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe.

Site File

Site Files are held by the Principal Investigator at sites and contain copies of the essential documents, local approvals, signed consent forms and completed data forms.

The Regulations

Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Master File

The Trial Master File contains all essential documents held by the sponsor/Chief Investigator which individually and collectively permits the evaluation of the conduct of a trial and the quality of the data produced.

Appendix 2: Template Case Report Form

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

PATIENT ELIGIBILITY (complete only once)

INCLUSION CRITERIA

For example:

		Please tick appropriate box: Yes	No
1	Patients with advanced renal cell carcinoma suitable for 1st line therapy	☐	☐
2	Histologically or cytologically confirmed advanced renal cell carcinoma	☐	☐
3	The presence of one or more clinically or radiologically measurable lesions	☐	☐
4	ECOG performance status 0 or 1	☐	☐
5	etc	☐	☐

If any of the 'No' boxes are ticked this subject is not eligible to enter the study.

EXCLUSION CRITERIA

		Please tick appropriate box: Yes	No
1	Current signs or symptoms of severe progressive or uncontrolled hepatic, haematologic, gastrointestinal, endocrine, pulmonary or cardiac disease other than directly related to Renal Cell Carcinoma	☐	☐
2	etc	☐	☐
3		☐	☐
4		☐	☐
5		☐	☐

If any of the 'Yes' boxes are ticked this subject is not eligible to enter the study

I have reviewed the Inclusion / Exclusion criteria and I am satisfied that this patient is eligible.

Clinician's Signature: _____ Date: _____

Print Name: _____

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

REGISTRATION FORM (complete only once)

Patient Identification

Date of Birth: |__ __/__ __/__ __ __ __| Female: ☐ Male: ☐
d d m m y y y y

Registration Checklist

Date patient consented to study participation: |__ __/__ __/__ __ __ __|
d d m m y y y y

Time patient consented to study participation: |__|__| : |__|__|
hrs mins

Consented by:_____Confirm consenter is on delegation log: Yes ☐ No ☐

Version & Date of study Protocol: |__| . |__| |__ __/__ __/__ __ __ __|
d d m m y y y y

Version & Date of Consent form: |__| . |__| |__ __/__ __/__ __ __ __|
d d m m y y y y

Version & Date of Patient Information Sheet: |__| . |__| |__ __/__ __/__ __ __ __|
d d m m y y y y

Randomisation

Date of Study Randomisation: |__ __/__ __/__ __ __ __|
d d m m y y y y

Randomisation Arm: Arm A (treatment name) ☐ Arm B (treatment name) ☐

Patient's randomisation Number: |___|___|___|___|

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

DEMOGRAPHICS (complete only once)

Diagnosis:

Date of diagnosis: |__ __/__ __/__ __ __ __| Histology number: |__ __/__ __/__ __ __ __|
d d m m y y y y

Differentiation: Undifferentiated ☐ Well-differentiated ☐
Poorly differentiated ☐ Moderately differentiated ☐

Stage: T1☐ N0☐
T2☐ N1☐ M0☐
T3☐ N2☐
T4☐ N3☐
TX☐ NX☐

Medical History

		Date started (if known) dd/mm/yyyy	**Date stopped (if known)** dd/mm/yyyy	**Currently ongoing**
1		| __ __/__ __/__ __ __ __|	|__ __/__ __/__ __ __ __|	☐
2		| __ __/__ __/__ __ __ __|	|__ __/__ __/__ __ __ __|	☐
3		| __ __/__ __/__ __ __ __|	| __ __/__ __/__ __ __ __|	☐
4		| __ __/__ __/__ __ __ __|	|__ __/__ __/__ __ __ __|	☐
5		| __ __/__ __/__ __ __ __|	|__ __/__ __/__ __ __ __|	☐

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

START OF TREATMENT FORM (complete only once)

Date of treatment: |__ __/__ __/__ __ __ __|
d d m m y y y y

Weight (Kg): |__|__|__| . |__| **Height (m):** |__| . |__|__|

Surface area (m^2): |__| . |__|__|

Performance status (0-4): |__|

Drug	Dose	Dose prescribed
Drug name	|__|__|__| mg/m^2	|__|__|__| mg
Drug name	|__|__|__| mg/m^2	|__|__|__| mg

Baseline Toxicities

Please state the current worst toxicity observed using CTCAE v4. Please remember to record any Serious Adverse events on the SAE form/log as well.

Standard toxicities	Grade (0-5)	SAE	Specific toxicities	Grade (0-5)	SAE
Nausea		Yes |_| No|_|	Peripheral Neuropathy		Yes |_| No|_|
Vomiting		Yes |_| No|_|	Constipation		Yes |_| No|_|
Diarrhoea		Yes |_| No|_|	Other 1:		Yes |_| No|_|
Alopecia		Yes |_| No|_|	Other 2:		Yes |_| No|_|

Blood test results **(all blood results should be assessed by a delegated clinician for potential toxicities)**

Date of sample	WCC $x10^9/l$	Haemoglobin g/dl	Platelets $x10^9/l$	Neutrophils $x10^9/l$	ALT (U/L)

Please note if any are of clinical significance: _____
_____
_____

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

ON TREATMENT FORM

(complete this form and the Concomitant medications log at every clinic visit whilst the patient is on treatment)

Date of visit: |__ __/__ __/__ __ __ __| Cycle number: |__|__|
d d m m y y y y

PS (0-4): |__| Weight (Kg): |__|__|__| . |__| Surface area: |__| . |__|__|

Treatment modifications

Treatment delay: ☐ Yes ☐No Length of Delay (days): |__|__|

Reason for Delay: ☐ Toxicity ☐ Awaiting investigation ☐Other_____

Dose Modifications (express as % of baseline dose):

Drug name |__|__|__| **%** reduction Dose administered |__|__|__| . |__| mg/m^2

Drug name |__|__|__| **%** reduction Dose administered |__|__|__| . |__| mg/m^2

Toxicities

Please state the worst toxicity observed since Day 1 of the previous cycle using CTCAE v4. Please remember to record any Serious Adverse events on the SAE form/log as well.

Standard toxicities	Grade (0-5)	SAE	Specific toxicities	Grade (0-5)	SAE
Nausea		Yes |_| No|_|	Peripheral Neuropathy		Yes |_| No|_|
Vomiting		Yes |_| No|_|	Constipation		Yes |_| No|_|
Diarrhoea		Yes |_| No|_|	Other 1:		Yes |_| No|_|
Alopecia		Yes |_| No|_|	Other 2:		Yes |_| No|_|

Blood test results (all blood results should be assessed by a delegated clinician for potential toxicities)

Date of sample	WCC x10^9/l	Haemoglobin g/dl	Platelets x10^9/l	Neutrophils x10^9/l	ALT (U/L)

Please note if any are of clinical significance**:** _____

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

IMAGING ASSESSMENT FORM
(Complete this form every time the patient has a scan)

4.5 Tumour Measurements

Target Lesions: Please record the exact location and the longest diameter of each lesion in mm

Lesion Location (Anatomical description)	**Baseline** Date of Scan :	**€On treatment €Follow up** Date of Scan :	**€On treatment €Follow up** Date of Scan :	**€On treatment €Follow up** Date of Scan :	**€On treatment €Follow up** Date of Scan :
Lesion 1:	mm	mm	mm	mm	mm
Lesion 2:	mm	mm	mm	mm	mm
Lesion 3:	mm	mm	mm	mm	mm
Lesion 4:	mm	mm	mm	mm	mm
Lesion 5:	mm	mm	mm	mm	mm
Lesion 6:	mm	mm	mm	mm	mm
Lesion 7:	mm	mm	mm	mm	mm
Lesion 8:	mm	mm	mm	mm	mm
Lesion 9:	mm	mm	mm	mm	mm
Lesion 10:	mm	mm	mm	mm	mm
TOTAL:	**mm**	**mm**	**mm**	**mm**	**mm**
Target lesions response by RECIST criteria(CR/PR/SD/PD)	**N/A**				
RECIST Version					

Non-Target Lesions Please indicate either: **P**=present (use at baseline only)
U=unchanged or improved **W**= clearly worse **A**= absent

Lesion 1:					
Lesion 2:					
Site of new lesion(s) (Please tick all that apply	€ Local node € Liver € Peritoneum € Distant node €Other(specify) _____	€ Local node € Liver € Peritoneum € Distant node €Other(specify) _____	€ Local node € Liver € Peritoneum € Distant node €Other(specify) _____	€ Local node € Liver € Peritoneum € Distant node €Other(specify) _____	€ Local node € Liver € Peritoneum € Distant node €Other(specify) _____
Non-target lesions response by RECIST criteria(CR/SD/PD)	**N/A**				
Overall Response BY RECIST	**N/A**				

Name of assessor and date					
Investigator Signature and date					

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

CONCOMITANT MEDICATIONS LOG

Please complete at screening and update at every visit. The treating physician is responsible for ensuring that no concomitant medications are contraindicated in this study (please refer to protocol)

Date of visit (dd/mm/yyyy)	**Medication name**	**Dosage and Frequency**	**Start date** (dd/mm/yyyy)	**Signature**	**Stop date** (dd/mm/yyyy)	**Signature**

EXAMPLE: TO BE MODIFIED ACCORDING TO PROTOCOL REQUIREMENTS

FOLLOW UP FORM
(Complete this form to record the follow up once the patient is no longer attending trial visits)

Date of last contact: | __ __/__ __/__ __ __ __|
d d m m y y y y

Type of contact:

☐ Hospital visit

☐ Telephone call to clinical team

☐ Telephone call enquiry made to GP

☐ Other _____

Patient lost to follow up after this visit: Yes ☐ No ☐

NOTIFICATION OF DEATH FORM

Date of death: |__ __/__ __/__ __ __ __|
d d m m y y y y

Cause of death:
☐ **Disease**
☐ **Adverse Event/Toxicity (please provide details below)**
☐ **Other (please provide details below)**

Details of Adverse Event/Toxicity:

Specify "other" cause of death:

Autopsy performed: Yes ☐ No ☐

Autopsy Findings (if applicable):

STUDY WITHDRAWAL FORM

Date of study withdrawal: | __ __/__ __/__ __ __ __|
d d m m y y y y

Reason for withdrawal:

- ☐ **Lack of efficacy**
- ☐ **Adverse Event/Toxicity**
- ☐ **Patient choice**
- ☐ **Clinician decision**
- ☐ **Non-compliance**
- ☐ **Other (please state)** _____

Patient agrees to continued study follow-up: ☐ Yes ☐ No

PROTOCOL VIOLATION FORM

Date of protocol violation: |__ __/__ __/__ __ __ __|
d d m m y y y y

Details of the protocol violation:

Action Taken:

DATA COMPLETION FORM

CRF sign off by PI or delegated individual:

Date: |__ __/__ __/__ __ __ __|
d d m m y y y y

All the information in this patient's CRF is complete and accurate: ☐ Yes ☐ No

All reported SAEs are also included in the CRF toxicity section: ☐ Yes ☐ No

(Both answers should be "yes" before sign off)

Name: _____

Signature:_____

Database completion:

Date: |__ __/__ __/__ __ __ __|
d d m m y y y y

Data Manager Name: _____

Data Manager Signature: _____