MANCHESTER 1824
The University of Manchester

Standard Operating Procedure

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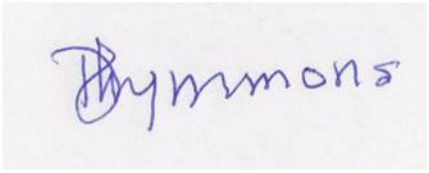
Signature: 		**Signature:** 	

Version	Date	Reason for change
1.0	**March 2018**	**First Version**

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1.0 Background

All Clinical Trials of Investigational Medicinal Products (CTIMPs) must be compliant with the European Directive on Good Clinical Practice in Clinical Trials (2001/20/EC) and The Medicines for Human Use (Clinical Trials) Regulations (2004 and subsequent amendments). A case report form (CRF) is the most common collection tool used to capture clinical data that is required for the statistical analysis of the trial.

2.0 Purpose

The purpose of this SOP is to detail the requirements and procedures that should be followed when developing case report forms, paper or electronic, for trials where the University is acting as Sponsor. This allows Chief Investigators (CI) and their trial teams to capture trial data accurately and thus to maintain scientific integrity.

3.0 Procedure

3.1 CRF Design

CRF design will be dependent on the trial protocol and statistical requirements. Key elements usually include subject identity, screening and eligibility results, information collected at baseline and subsequent trial visits, adverse events (AEs) and concomitant medication. It is imperative that the CRF is clear, unambiguous and well structured, with limited use of free text boxes. It is important to specify the units for any laboratory or clinical tests (e.g. mmol/l; mm Hg) in order to ensure consistent data collection across sites.

The CRF should be developed in parallel with trial database programming and development and should be finalised when the protocol is near finalisation. The database will then need to be tested and validated before any participant is recruited and before any data is entered from the CRF. To ensure all relevant and valid data items (and no unnecessary data items) have been incorporated into the CRF, it is highly recommended that the CRF is reviewed by several parties including the CI, trial team, Clinical Trials Unit (CTU) (where applicable), statistician, clinician and Sponsor. Following creation of the final draft, the CRF should be reviewed, approved, dated, given a version number and formally signed off by the CI and key individuals involved where appropriate.

3.2 Amendments

Following amendments to the trial, the impact on the data collected in the CRF needs to be assessed and documented. In addition, any amendment directly to the CRF should be reviewed and approved by those who provided the original sign off.

3.3 Training

Training on how to complete the CRF should be given to all relevant members at each site, including how to address errors and ensure no fields are left blank.

To ensure the validity of the data is maintained, the correction of errors should fall in line with section 4.9 of the ICH Harmonised Tripartite Guideline for GCP i.e. 'any change or correction to a CRF should be dated, initialled and explained (if necessary) and should not obscure the original entry'. This principle applies to both paper and electronic CRFs.

3.4 Collection of Source Data

Source data should be accessible and remain in a participant's medical notes, even after a trial has ended, in order to provide an audit trail for regulatory inspections or Sponsor/CTU audits. Data should be transcribed into the CRF in a timely manner. Where the CRF is to act as source data, further training on the collecting and recording of data is paramount. Associated record keeping arrangements should also be determined.

3.5 Paper CRFs

Following input into the CRF, copies of the completed pages should be faxed/posted from the trial sites to the personnel responsible for data management and data entry. A tracking system is recommended to make sure that the correct pages of the CRF are sent and received. Original CRFs will remain at the trial sites.

3.6 Electronic CRFs

Electronic CRFs allow sites to enter data through a web portal. This decreases the risk of losing data, has the potential to improve data quality and allows some data verification during data entry. Guidance detailing secure electronic data transfer should be generated.

- Further details can be found in section 4.9 of the ICH Harmonised Tripartite Guideline for GCP.

4.0 Roles and Responsibilities

4.1 Chief Investigator (CI) or delegate

The CI (or delegate) holds the responsibility for the design of the CRF based on the requirements of the protocol. Associated guidelines on how to complete the CRF should also be created and given to all sites to ensure consistency of trial data and allow it to be combined for final analysis. The CI should ensure the CRF is user friendly to the practitioner and the participants i.e. the questions should come in the order expected during a consultation. Participant completed components of the CRF have to receive ethics approval.

4.2 Statistician

It is essential to liaise with and gain input from the trial statistician and data management personnel when designing and developing the CRF.

5.0 References and Bibliography

- The Medicines for Human Use (Clinical Trials) Regulations (2004 and subsequent amendments)
- ICH Harmonised Tripartite Guideline for GCP
- Grey Guide, GCP
- Warwick Case Report Form SOP
- Oxford Case Report Form SOP