

MRC/DH joint project to codify good practice in publicly-funded UK clinical trials with medicines

Workstream 4: Trial Management and Monitoring

B) Summary of Trial Management Systems (TMS)

It is recommended that for every clinical trial a document includes a description of the systems in place for each of the major aspects of trial management. The level of detail required will depend upon:

- (a) The clinical trial risk assessment,
- (b) The organisational structure within which the clinical trial is conducted, and
- (c) The design and methods of the clinical trial.

Where institutional policies (such as those of the Host University or NHS Trust) prevail over the arrangements for a particular trial, these could be referenced within the TMS documentation.

For some trials this may simply be an index to the relevant Standard Operating Procedures (SOPs). In others, the trial management systems may be described in sufficient detail in the study protocol.

It is recommended that the TMS description addresses the following aspects of the conduct and organisation of the clinical trial. These aspects have been identified by the MHRA as being systems routinely checked during their inspections.

1. Project management

This would include:

- The study protocol (by cross-reference)
- Organisational structure, including relevant details of the identity and responsibilities of the following (as applicable): the sponsor, chief investigator, trial management team, host institution, Trial Steering Committee, Data Monitoring Committee, endpoint adjudication committee, coordinating centre(s), central laboratory(ies).
- Details of care organisations, participating sites and investigators
- Relevant regulatory approvals (e.g. ethics committee, clinical trial authorisation)
- Name of contact individual: name of the individual who should be the first point of contact in the event of questions about the conduct of the trial (e.g. for audit/inspection purposes)

2. Contracts and financial management

This section would explain the contractual framework and identify the individual or organisation responsible for:

- a) negotiation of contracts/sub-contracts (if relevant)
- b) dealing with invoices and payments.

In many circumstances this role may be taken on by the host institution (e.g. University or NHS Trust), in which case it is helpful to describe the role of the lead investigator at the site in the contractual process.

For some trials (e.g. investigator-led single-centre trials) there may be no requirement for contracts or sub-contracts.

3 Insurance and Indemnity arrangements

The arrangements for insurance and indemnity should be stated, including arrangements to address negligent harm to the participant (e.g. NHS indemnity) and adverse consequences of the interventions and trial procedures that are not due to clinical negligence (e.g. provision for *ex gratia* payment).

4 Quality Assurance

Approaches to quality assurance including both internal and external schemes, e.g. certified laboratory standards, validation procedures, protocols for imaging or histology reporting, central reviews of end-points, etc.

5 Monitoring

It is recommended that the clinical trial risk assessment and trial design be used to inform the approach taken to monitoring as well as the intensity and focus of the monitoring process (see Section C – Monitoring of Clinical Trials for details). Particular consideration should be given to the following aspects of the trial:

- consent
- eligibility
- capturing and reporting information on Serious Adverse Events
- capturing, processing and coding of study endpoints

Further guidance on rational approaches to monitoring is given in Section C - Monitoring of Clinical Trials.

6 Training

This includes the training of all the personnel involved in the trial, including the staff of the coordinating centre as well as clinical sites. The methods used to deliver training should be described (if applicable).

For example, training meetings, arrangements for mentoring and supporting study staff, and for encouraging continuing professional development.

Consideration should be given as to how the training and monitoring procedures interact, as each may usefully inform the other.

It is helpful to describe not only the methods for delivering training but also how that training is to be documented (e.g. personal training records, registers of attendance at training meetings or investigators meetings, or formal appraisal within an employer scheme).

7 Patient information and communication

This section would detail the plans for communication with participants, including the patient information sheet, consent procedure, contact arrangements for patients with questions about the trial and the strategy for communication with participants during and at the end of the trial.

8 Pharmacovigilance

This should include definitions of Adverse Events, Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) relevant to the trial.

It should also explain procedures for capture of information, processing reports, making reports to regulatory agencies, DMC, ethics committees, investigators, etc.

Further details are provided in the [Pharmacovigilance](#) guidance.

9 Endpoint Assessment

This would outline the methods for assessing study endpoints, e.g. independent review, endpoint adjudication committee, procedures for assessing images, pathology samples, etc.

10 Computer systems

Computer systems used in clinical trials should be developed and maintained to a standard appropriate to their functionality within the trial. Particular attention should be paid to issues of confidentiality, security and access to data.

For some trials it may be necessary for computer systems to meet external standards such as the United States Code of Federal Regulations Chapter 21 Part 11 (21 CFR Pt 11) [ref].

The procedure for developing and maintaining computer systems should be described in an appropriate level of detail, with reference to external standards, if applicable.

For example, sections on security, user specification, development process, validation methods, bug-reporting, change requests and disaster recovery may all be relevant.

For complex systems it is likely that these will need to be addressed in separate documents, which should be cross-referenced.

11 Data management

Some aspects of data management may have been covered by other sections (such as the section on computer systems). It is helpful to consider:

- Source documents: What are the source documents? Where data are being collected directly from the patient (e.g. family history or quality of life) the case report form (CRF) may be the source document. In some cases source data may be held on electronic data entry systems (e.g. a computer-based case report form)
- Key documents: Location, version control and release procedures
- Data checking: Methods for data checking and corrections so that additions and corrections made to the CRFs and data can be traced and explained in a clear audit trail.

12 Investigational medicinal product management

The following aspects may be relevant and are dealt with in more detail by the **Trial Supplies Workstream**:

- Source of study drug
- Procedures for manufacture, packaging and distribution
- Disposal of unused study treatment

13 Statistical Analysis

Identity of those responsible for statistical analysis and documentation of statistical analysis plan.

14 Writing of reports and publications

Arrangements for authorship.

15 Regulatory submissions

If appropriate, describe who will be making the submission, and the arrangements for preparing data for submission and answering regulatory queries.

16 Archiving

[Archiving](#) of written material, including case report forms and other source documents to comply with relevant regulations. Archiving of electronic data.

Archiving of clinical samples, biopsies, tissue samples, genetic material, etc.