MRC Clinical Trials Unit

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CLINICAL INPUT IN MRC CTU AT UCL TRIALS

VERSION 2.0

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STANDARD OPERATING PROCEDURE TITLE

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The following symbols may be used in this SOP:

Indicates a link to a related document

Indicates instructions to document trial-specific processes elsewhere

Throughout this document the MRC Clinical Trials Unit at UCL, will either be referred to as 'MRC CTU at UCL' or 'the unit'. In instances where neither read well in the sentence, 'the CTU' may be used.

1 PURPOSE

The purpose of this SOP is:

- To define the aspects of clinical trials conducted by MRC CTU at UCL where clinical expertise is required
- To define the training requirements for clinicians involved in CTU trials
- To describe how and where clinical input into trials should be documented

2 RESPONSIBILITY AND ROLES

All clinical trials conducted by MRC CTU at UCL require physician input to the protocol, procedures and oversight. There are however, different models of clinical input depending on the needs of the trial, the collaborative arrangements and the distribution of expertise among the partners. In some trials the Chief Investigator and/or trial physician is internal to the MRC CTU at UCL and in others all the clinical staff on the trial are employed by other organisations in the partnership. Irrespective of the employer, the roles and responsibilities of clinical members of the Trial Management Group remain the same.

The following table lists the roles relevant to this SOP and a brief description of their responsibilities.

This SOP will be circulated to be Read and Understood to all appropriate roles identified in the training matrix.

ROLE	RESPONSIBILITIES
Chief Investigator (clinical)	Overall responsibility for all medical components of the protocol and trial conduct
Trial physician	Undertakes medical aspects of the conduct of the trial under the leadership of the Chief Investigator
Clinical Reviewer	Only responsible for medical review of participant data and relevant clinical information during the conduct of the trial as per the direction of the Chief Investigator and/or Trial Physician

3 PROCEDURES

3.1 TRAINING REQUIREMENTS

The training requirements for clinicians may vary depending on their level of involvement, but at a minimum the training should consist of the following:

- Good Clinical Practice training
- Read and understand the MRC CTU Safety Management SOP
- Read and understand any relevant trial specific documentation including in particular the trial protocol, Safety Management Plan and Pharmacovigilance checklist
- Read and understand MedDRA training slides

All training should be documented in either a training record or CV

For clinicians employed by the MRC CTU at UCL (regardless of their percentage of time allocated to their role) training will also include having read and understood the relevant MRC CTU SOPs. MRC CTU at UCL staff employed in the Chief Investigator or Trial Physician roles have a full set of SOPs that must be read and understood. Staff employed in the Clinical Reviewer role have a more limited set of SOPs to be read and understood. The specific SOPs to be read and understand by the various roles are defined in the Trial in Matrix available on SOPbox.

The Clinical Science Function group leads will periodically check (and document) whether any of the clinicians in this group in the more limited role of 'Clinical Reviewer' have expanded their role, such as they need to complete the Read and Understood of all the SOPs allocated to the Chief Investigator (clinical) and/or Trial physician

3.2 TRIAL DEVELOPMENT

Clinical input is required to ensure that the protocol and other trial documents reflect appropriate and achievable standards of medical practice. During the development of a trial clinician input, normally led by the Chief Investigator, is expected at a minimum for:

- Eligibility criteria
- Safety endpoints and analysis
- Criteria for interrupting, modifying and discontinuing treatment
- Collection and reporting procedures for adverse events
- Risk assessment with particular respect to participant safety including risks related to pregnancy
- Pharmacovigilance procedures and safety management plan
- Selection of the reference safety information, and frequency of review
- Unblinding procedures, if applicable
- Site selection and training

This input should be documented in meeting minutes, and the senior clinician responsible should sign off any relevant documents.

3.3 DURING THE TRIAL

In an active trial clinical involvement is required for medical oversight, safety monitoring, pharmacovigilance, as well as some operational issues. The degree to which one or more clinicians are involved will vary between trials. The extent of involvement and assignment of clinical responsibilities should be documented clearly to allow auditing of trial performance, if necessary. Possible clinical responsibilities include:

3.3.1 CLINICAL OVERSIGHT

- Write and/or review trial documents or sections of documents (e.g. protocol, trial specific working instructions) relating to the clinical management of patients in the trial
- Respond to clinical queries relating to the trial protocol and conduct of the trial
- Maintain awareness of developments in the field and draw the attention of the Trial Management Group to any that may impact the trial

3.3.2 SAFETY MONITORING AND PHARMACOVIGILANCE

- Annual review of risk assessment with particular focus on participant safety
- Review of clinical cover for the trial to ensure that it is adequate
- Review of clinical coding
- Clinical review of SAEs
- Review of safety data and potential safety signals
- Review of the reference safety information to ensure that it is up-to-date
- Oversight of the unblinding process, if applicable

3.3.3 OPERATIONAL INVOLVEMENT

- Participate in Trial Management Group meetings
- Provide clinical input to data query generation and resolution
- Provide clinical input to Site Initiation Visits, Investigator Meetings and/or site training

3.4 END OF TRIAL

The Chief Investigator (and Trial Physician, if applicable) will normally be involved in the analysis stage of the trial, and the degree to which they are to be involved should be documented in relevant places (e.g. the SAP for the trial). The involvement may be informal in many areas, but aspects of the trial data analysis that should document clinical input include:

- Review of trial endpoints, where undertaken
- Clinical input to the interpretation of the analyses
- Input to the main trial report for publication, with authorship as agreed by the Trial Management Group