South Eastern Health and Social Care Trust

Standard Operating Procedures (SOP) Research and Development Office

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Author:	Alison Murphy, Research Manager Endorsed by Paul Carlin
Approved by:	Dr David Hill
Signed:	
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1.0	Sept 2007	Katrina Hughes	N/A
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1. INTRODUCTION

The MHRA (Medicines and Healthcare Products Regulation Agency) is an executive agency of the Department of Health. This body is currently executing a programme of Inspections into the conduct of Clinical Trials of Medicinal Products. The inspections are to measure compliance with the set of internationally legally recognised Principles for conducting Clinical Trials – Good Clinical Practice (ICH GCP Principles) and to ensure compliance with the EU Clinical Trials Directive (2001/20/EC) which came into force on 1 May 2004 and has been transposed into UK law by the Medicines for Human Use (Clinical Trials) Regulations 2004, and the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 (the Amendment Regulations) which were laid in Parliament on 20 July 2006 and came into force on 29 August 2006. Meaning those NHS organisations sponsoring and hosting CTIMPs must ensure that systems are in place so that CTIMPs can be managed and conducted in accordance with both the Research Governance Framework (2005) and the Clinical Trials Regulations.

2. OBJECTIVE

This Standard Operating Procedure (SOP) seeks to explain the procedure for facilitating an inspection by the MHRA.

3. SCOPE

This Standard Operating Procedure (SOP) applies to all Clinical Trials of an Investigational Medicinal Product (CTIMPs) where the South Eastern Health and Social Care Trust (SEHSCT) is acting as the sponsor, co-sponsor or hosting site.

4. PROCESS

4.1 MHRA GCP Inspection in Non-Commercial Organisations

One of the requirements of the EU Clinical Trials Directive is that Member States set up inspection systems to ensure compliance with the Clinical Trials regulations. Therefore, the MHRA has established a GCP Inspectorate to conduct GCP inspections, one of a range of inspections that are carried out by the MHRA.

The UK legislation defines the responsibilities of the Sponsor and the Investigator site. NHS organisations conducting clinical trials may be subject to inspection of either of these responsibilities.

4.1.1 Sponsor Inspection

Where the organisation is named as the sponsor or co-sponsor of the CTIMP, the MHRA may conduct a ‘sponsor’ inspection. The sponsor has responsibility for the initiation, management and financing (or arranging the financing) of the trial. The Sponsor is required to satisfy the MHRA that the study meets the relevant standards

and to ensure that arrangements are put and kept in place for management, monitoring and reporting. An MHRA inspection will include scrutiny of Trust-wide systems to confirm that the organisation has fulfilled its sponsor responsibilities.

4.1.2 Investigator Site Inspection

Where the organisation is hosting an investigational site, (with an external sponsor) the MHRA may conduct an 'investigator site' inspection. This is an inspection of the conduct of the trial by the investigator and of the role of the sponsor in overseeing the trial. Any NHS organisation systems that are used to conduct the trial will be scrutinised to ensure that they are "fit for purpose".

4.2 Pre-inspection Activities for Routine Inspections

The MHRA will issue a letter of notification 2-3 months in advance to the Research and Development Department. The organisation is expected to produce, within 28 days, a 'Pre-inspection Dossier' that will contain:

- Organisation details
- Contact name to manage logistics
- Details of clinical trials of medicinal products
- Index of standard Operating Procedures and processes

The inspector will then review the dossier and agree inspection dates and the agenda with the organisation. Additional updated details may be requested nearer the date of the inspection. The MHRA will provide a list of trials to be looked at in specific detail.

4.3 The Inspection

There will be an opening meeting to confirm the purpose of inspection, provide introductions and methodology. The inspection will be conducted generally in accordance with a predetermined plan, though this may be revised based upon inspection outcomes. The inspection will include a combination of staff interviews, document review and facility visits. The MHRA are likely to use study-specific examples to demonstrate the system. The MHRA will provide feedback of general findings at a closing meeting.

The inspection will be characterised by:

- Flexibility on both side
- Open dialogue from the beginning
- Ongoing verbal feedback throughout the inspection
- Opportunity to demonstrate how your systems meet the legislation
- Review of action plans already in place to address known areas of non-compliance

4.3.1 Activities of Interest

The MHRA will be interested in processes relating to:

- Regulatory submissions
- Laboratories
- Investigational medicinal product management
- Contract Management
- Project Management
- Trial-file management for selected clinical trial(s)
- Quality Assurance
- Training
- Computer systems
- Monitoring
- Pharmacovigilance
- Medical Advisors
- Data management
- Statistical Analysis
- Report writing
- Archives
- Investigational sites

4.3.2 Types of Findings

The inspection report will specify the criteria used to categories findings. However, in previous inspections, the MHRA have used the following criteria:

- Critical;
- Major; or
- Other.

A 'Critical' finding was defined as one where:

- Evidence exists that the safety, well being or confidentially of trial subjects has been (or has significant potential to be) jeopardised, and/or
- Serious doubt exists relating to the accuracy or credibility of trial data.

A 'Major' finding was a non-critical finding that:

- Reveals a significant and unjustified departure from the UK regulations
- Consists of a number of minor departures from the UK regulations or other relevant established guidance, suggesting a systematic quality assurance failure
- Reveals a failure to comply with relevant legislative requirements.

An 'Other' finding was any other inspection finding, including observations and recommendations.

The implications are:

- Critical findings require an agreed remediation plan to be put in place and re-inspection can occur.
- Major findings must be addressed but the organisation suggests to the MHRA how this is achieved.
- Other findings do require remedy where this is possible, and preventative actions should always be considered. Responsible to other findings will be requested in the inspection report. Observations and recommendations do

not require written response unless requested by the Inspector in the inspection report.

4.4 Post-inspection MHRA Report to the Organisation

A report is issued with 30 working days of the end of inspection. The MHRA will expect responses to be received within 30 calendar days of despatch. There will be an opportunity for questions and clarification, if required. The MHRA will issue a summary letter and an inspection certificate.

5. REGULATIONS, GUIDELINES, REFERENCES, SOP LINKS etc.

NHS Research and Development Forum Document "How to prepare for an inspection for Good Clinical Practice by the Medicines and Healthcare products Regulatory Agency (MHRA): a guide for NHS organisations that sponsor or host clinical trials of medicinal products". Version 2, 31 October 2006.

6. APPENDICES

None