STANDARD OPERATING PROCEDURE FOR PREPARING AND PARTICIPATING IN A REGULATORY INSPECTION

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AUTHOR:	Valerie Godfrey
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1. PURPOSE

This Standard Operating Procedure (SOP) describes the process for preparing and participating in a Medicines and Healthcare products Regulatory Agency (MHRA) inspection.

2. SCOPE

This SOP applies to members of staff associated with and managing a Clinical Trial of an Investigational Medicinal Product (CTIMP) that are sponsored or co-sponsored by the University of Dundee (UoD) and/or NHS Tayside (NHST).

3. RESPONSIBILITIES

The MHRA performs Good Clinical Practice (GCP) inspections of CTIMPs to measure compliance with the principles of GCP and the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments.

The MHRA may carry out routine or triggered (for cause) inspections. Routine inspections follow a risk-based programme and organisations with a higher risk rating will be inspected more frequently than those with a lower risk rating. Triggered inspections are conducted as a result of information received by the MHRA about suspected breaches of legislation relating to the conduct of clinical trials e.g. from serious breach notifications.

The organisation's director/senior manager will delegate the preparation for a MHRA Inspection to the appropriate personnel. The inspection may be carried out onsite, remotely or as hybrid, dependent on the MHRA's request.

4. PROCEDURE

4.1 Notification of Inspection by the MHRA

4.1.1 The MHRA will formally notify the organisation's director/senior manager of a GCP inspection. The notice will ask for a dossier which details the activities performed by the organisation to be submitted by a specified date.

4.1.2 TASC senior management will be informed of the MHRA notification and timelines for dossier submission.

4.1.3 An Inspection Lead, e.g. the TASC Senior Research Governance Manager, will be nominated by the R&D Director and will request up to date information from relevant groups/individuals for completion of the dossier. Staff must respond to each request within the timelines given.

4.1.4 The Inspection Lead will be responsible for liaising with the MHRA to ensure coherent communication on matters relating to the inspection.

4.2 Preparation for the Inspection

4.2.1 The MHRA should provide a proposed timetable for the inspection. The Inspection Lead shall notify heads of staff relevant to the departments to be inspected of the proposed Inspection dates as the returned Dossier must include the names of the individuals who are available for interview. The Inspection Lead shall liaise with the MHRA regarding staff availability. The inspection may take several days.

4.2.2 For an onsite inspection, the Inspection Lead will delegate general housekeeping arrangements for the visit e.g. ensuring the availability of meeting rooms, access to photocopiers and providing refreshments for inspectors.

4.2.3 For a remote visit, the Inspection Lead will inform staff of the platform to be used e.g. MS Teams. The Inspection Lead will liaise with the MHRA to ascertain what permissions will be required to access trial IT systems e.g. clinical trial databases.

4.2.4 The Inspection Lead, on behalf of Sponsor, shall ensure that relevant staff receive support and guidance on the Inspection process.

4.3 Documentation required for Inspection

4.3.1 Sponsor, Chief Investigator (CI) and relevant staff collectively must ensure that documentation requested by the MHRA is readily available.

4.3.2 For the Trial Master File (TMF), documents may be held as paper or electronic. In either case, there must be an index with section numbers to cross reference to the corresponding paper sections or electronic folders.

4.3.3 The location of any documents that form the TMF but are held elsewhere must be clearly stated on the index.

4.3.4 The documentation which forms the Trial Master File (TMF)/Investigator Site File (ISF) may be reviewed. This includes, but is not limited to:

- Case Report Forms (CRF)
- Insurance
- Laboratories: SOPs and records of maintenance and calibration of equipment should be available.
- Patient medical records/source documentation
- Pharmacy drug accountability records
- Patient information leaflets/consent forms
- Training records: refer to TASC SOP for Training Records for further guidance.
- SOPs
- Sponsor Risk Assessment
- Trial Databases

Refer to the TASC SOP on Establishing & Maintaining a TMF or an ISF in CTIMPs, for further guidance.

4.4 During Inspection

4.4.1 The CI and trial staff must make themselves available during inspection to provide information and/or documentation.

4.4.2 If onsite, the MHRA inspector(s) must be accompanied at all times during their visits to relevant departments.

4.4.3 Interviewees should answer questions honestly and succinctly to the best of their knowledge. Interviewees can update or clarify information given during an interview at any time throughout the inspection via the Inspection Lead.

4.4.4 During interview, the MHRA inspector(s) may request a specific document or piece of information. Any such request must be conveyed to delegated personnel who will deliver the document (paper or electronic) to the inspector(s). A record must be kept for the Inspection Lead of any documentation given to the inspector(s). Internal audit reports will not routinely be reviewed but may be requested.

4.4.5 Scribes, where applicable, shall be identified and will receive training on what the role entails.

4.4.6 A summary meeting will be held at the end of each day. The organisation's director/senior manager or delegate will inform who should attend this debrief session as it is important to ensure that the inspection objectives are being met and information requested has been provided.

4.5 Reporting of Inspection

4.5.1 At the end of the inspection, a closeout meeting will take place and the inspector(s) will provide verbal feedback of the findings. The organisation's director/senior manager or delegate will inform who should attend the closeout meeting. This will be followed with a detailed written report within 30 days which will typically list findings as critical, major or other.

4.5.2 A response to the written report is required within the timelines specified by the MHRA, usually 30 calendar days. The Inspection Lead or delegate should action and manage this response as appropriate.

4.5.3 A dialogue may be held between the MHRA and the Inspection Lead to clarify findings and any proposed Corrective Action/Preventative Action (CAPA). The final written response to the MHRA should document CAPA and the response timeline.

4.5.4 When the MHRA are satisfied with the response, they will issue a GCP inspection statement and cover letter/email to formally close the inspection.

4.5.5 All documentation and records of outcomes of the inspection should be kept by the Inspection Lead, Sponsor and other relevant departments as required.

4.6 Post Inspection follow up

4.6.1 An overview of the MHRA Inspection should be disseminated to relevant parties by the Inspection Lead or delegate. Any CAPAs in relation to inspected projects should be addressed with the CI and the research team. Any CAPAs in relation to Sponsor systems and/or SOPs should be addressed with the relevant Sponsor staff.

4.6.2 Appropriate closure of all CAPAs will be documented and overseen by the Inspection Lead or delegate

5. ABBREVIATIONS & DEFINITIONS

CAPA	Corrective Action/Preventative Action
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of Investigational Medicinal Product
GCP	Good Clinical Practice
ISF	Investigator Site File
MHRA	Medicines and Healthcare products Regulatory Agency
NHST	NHS Tayside
SOP	Standard Operating Procedure
TMF	Trial Master File
TASC	Tayside Medical Science Centre
UoD	University of Dundee

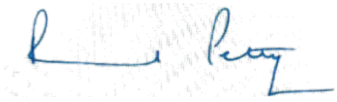
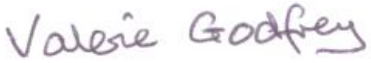
6. ASSOCIATED DOCUMENTS & REFERENCES

None

7. DOCUMENT HISTORY

Version Number:	Reviewed By (Job Title)	Effective Date:	Details of editions made:
History of reviewers prior to 2019 is detailed in the archived SOPs			
5	Valerie Godfrey (TASC QA Manager)	06/02/2019	New TASC SOP format implemented. Minor changes to text throughout, now refers to the Inspection Lead.
6	Valerie Godfrey (TASC QA Manager)	29/01/2021	Amended to include remote Inspections. Date brought forward from March to January to allow upload to new TASC SOP template which shows the new TASC website in the footer. Physical scan converted to electronic pdf as a requirement for upload to new TASC website.
7	Valerie Godfrey (TASC QA Manager)	03/02/2023	Section 3 expanded to state remote and hybrid inspections.

8. APPROVALS

Sign		Date
APPROVED BY:	Professor Russell Petty, R&D Director, NHS Tayside	
Signature		31st Jan 2023
APPROVED BY:	Dr Valerie Godfrey, TASC QA Manager, Chair of Clinical Research Guidelines Committee	
Signature		26 Jan 2023