STU-SOP-TM-013 – Standard Operating Procedure on Preparation for a Good Clinical Practice Regulatory Inspection

1. Purpose

This Standard Operating Procedure (SOP) provide guidance on the requirements for a Good Clinical Practice (GCP) inspection of systems and processes within non-commercial Clinical Trials of Investigational Medicinal Products (CTIMPs) by an external regulatory body. This applies in particular to inspection by the Medicines and Healthcare products Regulatory Agency (MHRA).

2. Background

Under the UK policy framework for health and social care, any project which involves human participation, is required to promote, and follow good research practice. This includes ensuring the integrity, quality and transparency of the research project and making the project documentation available to regulatory or other external bodies for inspection when requested.

The majority of GCP inspections are carried out under the MHRA risk-based compliance programme. These can be either systems based or trial specific.

GCP systems inspections examine the systems in use by an organisation to conduct clinical research. The inspectors will select a number of clinical trials to examine how the organisations trial procedures are applied. One or two investigator sites involved in the selected trials may also be inspected.

Trial specific GCP inspections assess clinical trials that have been completed and reported.

The risk-based inspection programme uses information available to the MHRA to determine the organisations risk:

- Internal information about previous inspection history
- Organisational changes
- Intelligence from external sources.

Each organisation is risk assessed and inspections are usually prioritised for organisations considered to be the highest risk. However, a small number of the organisations in the medium and low risk categories will be randomly selected for routine-based inspections.

Departments/Vendors that may be inspected might include (but not be limited to):

- Clinical Trial Units
- Contracts
- Information Technology (IT)
- Randomisation service providers
- Laboratories
- Archive Facilities
- Clinical Research Facilities
- Research and Development
- Pharmacy
- Imaging
- Medical Records
- Financial records

3. Roles and Responsibilities

The **Sponsor** is responsible for informing relevant staff and researchers of an impending inspection and supporting staff and researchers in the preparation and participation in MHRA inspections.

Swansea Trials Unit (STU) is responsible for leading in the inspection preparation for trials they are involved with and ensuring that unit processes are compliant with regulatory requirements and available for inspection.

Inspection Coordinator (IC) where delegated, may be a member of STU and will liaise with the MHRA Inspectors regarding the regulatory inspection, communicate necessary information to relevant parties, plan and organise the inspection.

Chief Investigator (CI) is responsible for ensuring that project documentation is accurate, up to date and inspection ready at all times.

Trial Manager (TM) is responsible for maintaining the Trial Master File (TMF) including an audit and document trail (evidence trail), site communication and liaising with the IC.

External use of SOP: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

The most up to date information on MHRA expectations for conducting and participating in an inspection can be found on their website. Communication from the MHRA for an inspection will depend on the type of inspection as detailed below.

4.1 Notification of Inspection

4.1.1 Risk Based GCP Inspection

The Sponsor is formally notified by the MHRA that their organisation has been selected for a routine GCP inspection. The notice of inspection will request the preparation of a dossier to be completed within a fixed time period. The MHRA will specify a submission date (usually 30 days). Further detail on the content of the dossier and a template can be found on the MHRA website (see references).

An IC from the sponsor organisation or STU should be nominated. They will be responsible for liaising with the MHRA and all involved parties and notifying all parties when the inspection dates are confirmed.

On submission of the dossier, the MHRA will liaise with the IC to acknowledge receipt of the complete dossier and to develop and finalise an inspection plan and dates, indicating any documents and access required by them to aid the inspection e.g. SOPs, electronic databases. The IC will also be advised if any part of the inspection will be a remote desk top audit.

4.1.2 Study Specific Inspections

The Chief Investigator (CI) or a site Principal Investigator (PI) may be formally notified by the MHRA that a particular project shall be subject to a routine GCP inspection or a triggered

inspection. In such circumstances, the CI/PI should notify Sponsor and STU immediately by emailing the project Trial Manager (TM) through their usual email or emailing STU@swansea.ac.uk and inform their local R&D office.

4.1.3 Triggered/For Cause Inspections

The MHRA may arrive without prior notification to undertake a triggered inspection of an organisation or a single project. In such circumstances the person who receives the MHRA should notify the Sponsor, CI/PI, trial office, STU and local R&D department immediately.

4.2 Preparation for a routine MHRA Inspection

The MHRA will provide a proposed timetable for the inspection detailing departments to be inspected, and researchers/sponsor staff to be interviewed.

The IC will liaise with departments/individuals as soon as possible to ensure that staff are available for interview. If the proposed timetable is not suitable for key staff, the IC will advise the MHRA.

For a trials unit/vendor systems inspection, STU must ensure that all relevant staff are available and appropriately prepared for the MHRA inspection. Training files must be up to date and available for inspection.

The MHRA have published guidance on *GCP Inspections: Expectations and the dos and don'ts for hosting* (link available in references below*).*

4.3 Documentation for a MHRA Inspection

Under the regulations, a TMF should always be inspection ready. The CI, sponsor and relevant staff collectively must ensure that all appropriate documentation requested by the MHRA is available.

Patient hospital notes/source documents may be requested for review. If a patient's hospital notes cannot legitimately be available, this must be explained to the MHRA in advance of the inspection where possible.

Documentation that may be reviewed includes:

- Closed minutes from Data Monitoring Committee (DMC)
- Completed Case Report Forms
- Completed consent form(s) and associated Participant Information Sheet(s)
- Evidence of Insurance
- Investigator Site File (ISF)
- Laboratory records
- Pharmacy drug accountability records
- Publications from the research project
- Sponsor committee minutes
- Sponsor risk assessment
- Sponsor SOPs
- Training records
- Project contracts including financial records
- Project Database(s)
- Study specific SOPs

Additional supporting documentation e.g. floor plans, database extracts may also be requested either before or during the inspection. Archived documentation required for review should be available on the days of the inspection.

4.4 During a MHRA Inspection

The dossier supplied to the MHRA is used to help draft the inspection programme and identify personnel to be interviewed from the research team and sponsor or vendors.

The CI and staff from relevant departments must make themselves available during the inspection. Usually, advance notification is given of a person's involvement in the inspection, however, a role, and the relevant person to interview may only be identified during the inspection.

The MHRA Inspector(s) must be accompanied during their visit to the relevant departments. The Inspector(s) must adhere to any hand washing or dress code guidelines to allow entry into restricted or high-risk areas.

All interviews will be attended by a scribe to note the discussions. Interviewees should expect to receive a copy of the transcribed discussion for information. The MHRA do not permit the audio/video recording of any interviews or discussions.

Information provided during an interview may be updated or clarified at any time throughout the inspection via the IC.

During an interview, the MHRA inspector(s) may request a specific document or information. Any such request must be conveyed to the appropriate personnel and the document delivered to the inspector.

A record and duplicate set of all information requested by the Inspector(s) should be kept.

After the last department/organisation is inspected, a report of all findings and the expectations for a response will be issued to the IC.

4.5 Closeout of a MHRA Inspection

At the end of the inspection, a closeout meeting will take place where the Inspector(s) provide verbal feedback on the findings. All personnel involved in the inspection may attend. This will not be audio/video recorded.

A detailed written report will be provided by the MHRA, usually within 30 working days of the last inspection date. This report will document findings from the inspection as:

- **Critical** – a departure from legislation that has the potential to or adversely affects the rights, safety or well-being of patients, poses a risk to public health, represents a serious violation of applicable legislation and guidelines, clinical trial data are unreliable or there are several major con-compliances indicating a systematic quality assurance failure. All such findings are reviewed by the MHRA and may be referred to their Clinical Trial Inspection Action Group where Sponsors may be recommended for prosecution.
- **Major** – a departure from legislation or GCP guidelines that is unjustified and has the potential to develop into a critical issue or evidence of a number of departures in a single area indicating a systematic quality failure.
- **Other** – a departure from legislation/GCP guidelines or procedural requirements that is neither Critical nor Major.

An initial response to the written report is expected within the timeline specified by the Inspector(s) – usually 30 calendar days. This response should be managed by the IC.

Discussions may be held with the MHRA to clarify findings detailed in the report, proposed corrections and Corrective and Preventative Actions (CAPAs). The final written response to the MHRA will document corrections and CAPAs with a timeframe for completion.

When the MHRA are satisfied with the response they will accept the proposed timeframe and CAPA plan, close out the Inspection and issue a closing email and GCP inspection statement.

4.6 Post MHRA Inspection Follow Up

A summary of the MHRA Inspection will be disseminated to researchers and staff involved by the Sponsor or STU as appropriate.

Any corrections and CAPAs in relation to inspected projects will be discussed with the CI, STU and the Trial Management Group as appropriate.

Any corrections and CAPAs in relation to STU SOPs will be overseen by the STU Executive Group.

Any corrections and CAPAs in relation to Sponsor systems, procedures or SOPs will be addressed by the relevant Sponsor departments or committee(s).

5. References

- Health Research Authority website (HRA) - http://www.hra.nhs.uk/
- Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information
- UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
- UK Medicine for Human Use (Clinical Trials) Regulations 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made
- International Council for Harmonisation (ICH) Good Clinical Practice guideline - https://www.ich.org/page/ich-guidelines
- *MHRA GCP Inspections: Expectations and the dos and don'ts for hosting* – (https://mhrainspectorate.blog.gov.uk/2020/03/10/gcp-inspections-expectations-and-the-dos-and-donts-for-hosting/

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

6. Associated Documents

Number	Title	Location
N/A	N/A	N/A

7. Abbreviations

List of Abbreviations	
CI	Chief Investigator
CAPA	Corrective and Preventative Actions
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HRA	Health Research Authority
IT	Information Technology
ISF	Investigator Site File
MHRA	Medicines and Healthcare Products Regulatory Agency
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
R&D	Research and Development
REC	Research Ethics Committee
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
SU	Swansea University
TMG	Trial Management Group
TMF	Trial Master File

8. Appendices

Appendix 1: Document History

Version No:	4	**Effective Date:**	08 Aug 2024
Description of changes:	Update to procedure.		