

Title: MHRA inspections	
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Document History


Version	Description of update	Date Effective
1	Change of number for Q-Pulse	2-10-15
2	Reformatted. Reference to Device Trials at 1.1 and 3.1 Removal of reference to Compliance report at 3.2 Definition of MHRA findings at 3.20	1-4-17
3	Change of author. Addition of commercial studies at 1.2, 3.1.3 and 3.1.4 Reference to other regulatory authorities at 1.3 Reference to GCP laboratory inspections at 1.4 Clarification of triggered inspection at 3.1.2 Clarification of dossier requirements at 3.4 Clarification of dossier review at 3.6 Addition of TMF review at 3.7	19-9-18
4	Reference to UKAS laboratory inspections at 1.4 Reference to remote inspection at 3.1	30-11-21

1. Scope

1.1 This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) and Medical Device Clinical Investigations (MDCIs), which are co-sponsored or hosted by the University of Aberdeen (UoA) and/or NHS Grampian (NHSG); which are subject to inspection by the MHRA.

1.2 This SOP applies to all research team members and departments supporting, coordinating or participating in CTIMPs or MDCIs, sponsored or hosted by UoA and/or NHSG and also any local hosted or commercial studies selected for inspection by the MHRA.



1.3 Although the MHRA is the competent authority in the UK, other regulatory authorities (eg US Food and Drug Administration (FDA)) may select a UK site for inspection. The same process detailed in this SOP may be followed for such inspections and Sponsor/R&D shall advise as appropriate.

1.4  The MHRA also conducts GCP inspections of laboratories which perform the analysis or evaluation of human samples collected in support of primary or secondary endpoint data, or where the analysis is critical to the conduct of the trial (eg specific gene mutations associated with eligibility assessments). Routine standard safety testing is **not** included in the scope of these inspections. Laboratories accredited to ISO/IEC 17025:2017 or ISO 15189:2012 shall be inspected by the United Kingdom Accreditation Service (UKAS). See SOP-IMS-35 (External audit/inspection).

2. Responsibilities

Sponsor Support researchers in preparation and participation in MHRA inspections.

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Research Governance	Inform relevant researchers and UoA/NHSG staff of impending inspections.
Chief Investigator	Ensure documentation is accurate, up to date and inspection ready at all times. Provide necessary documentation to the Sponsor for preparation of an inspection dossier or to MHRA inspectors upon request.

3. Procedure


Medicines and Healthcare products Regulatory Agency (MHRA)

3.1 The MHRA conduct different types of Good Clinical Practice (GCP) inspections. These may be on-site or conducted remotely (eg MS Teams):

3.1.1 **Risk based inspection** – uses previous inspection information, organisational changes, and any intelligence gathered, to determine an organisation’s control of their risk (high, medium or low). Inspections are prioritised for organisations with the highest risk category, although a small proportion of organisations from the medium and low risk categories shall also be randomly selected for inspection. Risk based inspections may be either system based or trial specific.

3.1.2 **Triggered inspections** (for cause) –  the site is selected for inspection due to suspicion that the law has been broken. This information may be as result of:


- A serious breach notification.
- A whistleblower
- Information from other MHRA department
- Information from the Health Research Authority

3.1.3  **Commercial study inspections** – if the Sponsor of a commercial study is notified that a local site has been selected for inspection, they should notify the site immediately. This may be through the Principal Investigator (PI) or the Commercial R&D Manager.

3.1.4 Responsibility for managing a commercial study inspection and liaison with the MHRA remains with the commercial sponsor and Commercial R&D Manager. However the local QA Manager may advise and provide input to the response provided by the commercial sponsor.

Notification of inspection by the MHRA

Trial specific or triggered inspections

3.2  The CI/PI may be notified by the MHRA that a study shall be subject to either a routine or a triggered inspection, or the MHRA may arrive unannounced to undertake a triggered inspection. The Sponsor/R&D should be notified immediately (01224 551121) and shall advise.



Systems inspections

3.3 Sponsor is notified by the MHRA that the organisation or site has been selected for inspection.

3.4 The formal notice of inspection will request a dossier detailing activities performed by the organisation. The dossier shall list the documents required by the MHRA prior to the inspection:

- A list of clinical trials.
- Organisational charts.
- Standard Operating Procedures list.
- Contact details.

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- Overview of facilities.
- Service providers.
- Clinical trials activities.

3.5 An individual from the organisation, or site, shall be nominated to be ‘**Inspection Coordinator**’ and shall be responsible for liaising with the MHRA on matters relating to the inspection.


3.6 On submission of the dossier the MHRA may decide not to proceed with the inspection, or shall acknowledge receipt and advise on a potential inspection date and may request further information.

Preparation for an MHRA inspection


3.7 The MHRA shall provide an inspection plan detailing the studies selected from the dossier for TMF review, departments which may be inspected and staff who shall be interviewed. The Inspection Coordinator shall inform departments/individuals and ensure staff shall be available for interview. If the inspection plan is not suitable, the Inspection Coordinator shall advise the MHRA.


3.8 For sponsor wide system inspections, the Sponsor shall ensure all relevant staff are appropriately prepared for the MHRA inspection by offering appropriate support and guidance.


Documentation required for an MHRA inspection


3.9  The Sponsor and CI shall ensure that all documentation requested by the MHRA is available. Some documents may have to be retrieved from archive (see SOP-QA-32 - Archiving).


During an MHRA inspection

3.10  The CI/PI and staff from relevant departments shall make themselves available during inspection; should they be required by the inspector(s) to provide information or documentation.

3.11  MHRA Inspector(s) shall be accompanied at all times during on-site visits to relevant departments. Inspector(s) shall adhere to any health and safety guidelines regarding entry into restricted or high risk areas (eg hand washing, use of PPE, use of mobile phones etc).

3.12  Interviewees shall answer MHRA Inspector(s) questions honestly and succinctly to the best of their knowledge. All interviews shall be attended by a scribe; to record the discussions.

3.13  Interviewees may update or clarify information given during an interview at any time throughout the inspection via the Inspection Coordinator.

3.14 During an interview the MHRA inspector(s) may request a specific document or piece of information. Any such request shall be conveyed to the appropriate personnel and the document provided to the inspector(s).  A record shall be kept of any documentation provided.



Close-out of an MHRA inspection

3.16 At the end of the inspection, a closeout meeting shall take place and the inspector(s) shall provide verbal feedback on the findings.

3.17 A written inspection report shall be provided by the MHRA afterwards and shall document all findings from the inspection, which shall be graded as:

Critical: a deficiency that adversely affects the rights, safety or well-being of patients, poses a potential risk to public health, or which represents a serious violation of applicable legislation and


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guidelines. All such findings are reviewed by the MHRA and may be recommended for prosecution by the Crown Office and Procurator Fiscal Service (COPFS).

Major: a deficiency that could potentially affects the rights, safety or well-being of patients, could potentially pose a risk to public health, or represents a violation of applicable legislation/guidelines.

Other: a deficiency not expected to adversely affect the rights, safety or well-being of patients.

3.18  A response to the written report, coordinated by the Inspection Coordinator, is expected within the timeline specified by the inspector(s); usually 30 calendar days.

3.19  A dialogue may be held with the MHRA to clarify findings and proposed Corrections and Corrective and Preventive Actions (CAPAs). The final written response to the MHRA shall document Corrections and CAPAs and any response timeline.

3.20 When the MHRA are satisfied with the response they will formally accept the CAPA plan, close out the Inspection and issue a **GCP Inspection Statement**.

Post MHRA inspection follow-up

3.21 An overview of the MHRA Inspection shall be disseminated to researchers by the Research Governance Manager and/or Quality Assurance Manager.

3.22 Any Corrections and CAPAs in relation to inspected projects shall be discussed with the CI and the research team as appropriate.

3.23 Any Corrections and CAPAs in relation to Sponsor systems, procedures, SOPs or other Sponsor matters shall be addressed by the relevant governance committee(s).

3.24 Appropriate close out of all CAPAs shall be overseen by Sponsor through the Clinical Research Oversight Group (CROG).

4. Abbreviations and definitions



CAPA/CCAPA	(Correction and) Corrective Action and Preventive Action
CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare products Regulatory Agency*
PI	Principal Investigator
TMF	Trial Master File

5. Related documentation and references

SOP-QA-7	Trial Master File
SOP-IMS-35	External audit/inspection

*An executive agency of the Department of Health in the United Kingdom which is responsible for regulating medicines, medical devices and blood components for transfusion in the UK. The MHRA is the competent authority in the UK responsible for human medicines and is responsible for ensuring organisations comply with good clinical practice (GCP) standards.

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