Standard Operating Procedure (SOP)

Preparing for an MHRA GCP Inspection at St George's

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The master document is posted on the JRES website and any print-off will be classed as uncontrolled.

Researchers and their teams are responsible for checking the JRES website for the most recent version.
They may print off this document for training and reference purposes.

SOP Chronology		
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V1.0	Original Version	Georgia Bullock

Associated JRES documents

SOPs	WPDs	Docs	LOGs
	JRESWPD0023 General Research Definitions		

Contents

1. Background

St George's sponsors and hosts several Clinical Trials of Investigational Medicinal Products (CTIMPs). These trials have to be set-up, managed and conducted according to the relevant UK legislation.

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department of Health and is responsible for the regulation of medicines and medical devices in the UK. The MHRA is legally required to inspect CTIMPs conducted and/or sponsored by both commercial and non-commercial organisations.

The MHRA conducts inspections to ensure compliance with Good Clinical Practice (GCP). The majority of routine MHRA GCP inspections are carried out under a risk-based compliance programme and can be systems-based (looking at the systems used by an organisation to conduct clinical trials) or trial-specific (looking at the conduct of an individual trial). Several trials may be selected for a systems-based inspection. Inspections can also be triggered, for example following the notification of a serious breach to the MHRA.

2. Joint Research and Enterprise Services (JRES) Policy

All JRES SOPs will be produced and approved in accordance with the JRES SOP on SOPs and must be used in conjunction with local NHS Trust and University policies and procedures.

The JRES acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGHFT). St George's will be the official name used on all SOPs to represent both institutions acting as Sponsor.

3. Scope

This SOP describes the process for the notification of a GCP inspection by the MHRA, and the subsequent pre-inspection preparation. It also describes the process on the inspection days and the post-inspection requirements. It does not describe the process for any other type of MHRA inspection or inspections by any other organisation.

This SOP applies to the JRES Governance team and also to all St George's researchers and departments involved in the delivery, coordination or support of CTIMPs conducted at St George's.

This SOP refers to one MHRA inspector but it should be noted that some inspections involve more than one inspector, with one of them nominated as the lead.

4. Definitions

For general research-related acronyms used in this SOP, refer to General Research Definitions Working Practice Document (JRESWPD0023).

5. Responsibilities

It is the responsibility of the JRES, when notified of an MHRA inspection, to inform the relevant personnel and departments in a timely manner.

It is the responsibility of the JRES to coordinate and manage the inspection process, including liaising with the assigned lead MHRA inspector.

It is the responsibility of the JRES to support researchers in preparing for, and participating in, an MHRA inspection.

It is the responsibility of the Chief Investigator (CI) and their research team, for the selected trial or trials, to respond to JRES requests for information in a timely manner and to ensure that all trial documentation is complete and available for the inspection.

The CI, or their appropriate delegate, is responsible for ensuring that they are available on the inspection days, as instructed by the JRES.

6. Procedure

6.1 Notification of an MHRA Inspection

For routine inspections, the MHRA will send an email to the JRES, outlining their intention to conduct an GCP inspection with their proposed timelines and dates for the inspection. The JRES will need to confirm the suitability of the dates with the MHRA.

The initial email will detail the information required by the inspector before s/he can issue the Inspection Plan. This takes the form of a GCP inspection dossier and a clinical trials spreadsheet which need to be provided to the MHRA within 30 days of notification. Templates and guidance can be found here: https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#pre-inspection-documentation.

Following confirmation of the inspection, the JRES will inform all Investigators, JRES staff and departments (eg: Research Pharmacy, Laboratories, Clinical Research Facility, Vaccine Institute), who are currently, or have previously been, involved in one or more CTIMPs, of the dates and the JRES requirements. Notification of the regulatory inspection should also be communicated via email or newsletter across the two organisations (SGUL / SGHFT) where relevant.

The JRES will compile and submit the dossier and spreadsheet with assistance as required from relevant personnel. Requests for information from the JRES to trial teams or departments must be responded to in a timely manner in order for the JRES to meet the deadline.

6.2 Inspection Plan

Following receipt of the dossier and trial spreadsheet, the inspector will send an email confirming which trial/trials s/he wishes to review during the inspection. This will include a request for the availability of the Investigators to attend an interview for their trial(s).

The inspector may also request some trial information to be sent to him/her for review prior to the inspection (eg: trial site information, SAE listings). A nominated JRES staff member must compile and submit this information on or before the deadline date specified in the email.

The JRES will inform the relevant trial teams and departments that their trials have been selected and will compile an interview schedule based on the availability of the Investigators and their teams which must be sent to the inspector to confirm. Appropriate meeting rooms should be booked for the interviews once confirmed. The dates, times and locations of the interviews must then be confirmed with the relevant personnel.

The MHRA inspector will email a draft Inspection Plan to the JRES (the original plan can be amended during the inspection if deemed necessary by the inspector). This will outline the proposed timings and activity for each day of the inspection, including an opening meeting on the first day and a closing meeting on the final day.

The relevant personnel will be informed of the plan by the JRES and guidance will be given as to what they will need to attend or be available for.

6.3 Pre-Inspection Preparation

The following preparation must take place prior to the inspection:

- An appropriate, lockable room must be booked by the JRES for the inspector for the duration of the inspection and security will need to be informed of his/her visit to facilitate access.
- TMFs, ISFs, Pharmacy Files and any other trial documentation for the selected trials must be checked for completeness.
- TMFs must be ready and available for review by the inspector and **must contain all required documentation.** Where sections of the TMF are stored in different locations, (eg: the TMF is paper but the email correspondence is stored electronically), it must be clear that this is the case. The inspector will require access to all of the TMF systems so this must be arranged in advance of the inspection. **Incomplete or inaccessible TMFs will result in an inspection finding.**

  'While we don't expect that the TMF is a single system that holds every document and we are happy to review a number of systems on inspection, it is expected that the organisation identifies all of these systems and has a clear understanding of the content of the TMF and where all of the essential documents are located' **(MHRA Inspectorate Blog).**
- Access to patients' medical records, whether paper or electronic, must be considered prior to the inspection, as the inspector will most likely wish to view a selection of these. Any paper records for selected patients will need to be requested from Health Records and authorised access to electronic records will need to be arranged.
- Staff involved in the inspection interviews must ensure that they are appropriately prepared for these and understand how the interviews will be conducted. This may require training to be provided.

- SOPs for the JRES and other related departments should be readily available as they may need to be provided to the inspector.
- Training records for the relevant staff, including the JRES team, should be up-to-date and available to be provided to the inspector if requested.
- The Inspection Plan may include a tour of a specific department (eg: pharmacy) so appropriate staff must be available to do this.
- The JRES should prepare any Sponsor presentations required for the opening meeting. Investigators may also be asked to present a summary of their trial so will need to prepare this.
- The inspector must be sent directions to St George's and details of who to contact on the first day.

6.4 During the Inspection

- On arrival on the inspection days, the inspector must be met at Reception and taken to their allocated room. The key for the room can be given to the inspector who should return it at the end of each day. The room must be kept locked when unoccupied.
- The trial files must be made available in the room for the inspector and they should be returned to the relevant department at the end of each day (it may be acceptable to leave some in the locked room overnight).
- Where copies of documents are requested by the inspector, these should be photocopied and the copy and original handed to the inspector. Electronic versions of documents may be provided by email. A record should be kept of all documents provided.
- Any documents/files highlighted as missing by the Inspector must be requested from the relevant trial team or department and provided to the inspector.
- Interviewees should be clear on where they need to be for their interviews and should endeavour to arrive on time. Any unforeseen required changes to the timetable, eg: due to clinical commitments, must be discussed with the inspector as soon as possible so that the Inspection Plan can be reviewed.
- All interviews must be minuted by a member of staff who is not involved in the interview. Any departmental visits must also be minuted. The minutes should be an accurate, clear written record of the discussions.
- The inspector must be accompanied at all times when visiting departments, relocating to an interview room or accessing electronic records. All departments must ensure that the inspector adheres to their health and safety requirements, where applicable.
- The inspector may require lunch and refreshments to be provided on each of the inspection days.

- The inspector may request a brief meeting at the end of each day with relevant JRES personnel to review, and possibly request, any outstanding documentation.

6.5 After the Inspection

At the closing meeting on the final day, the inspector will provide a verbal summary of any findings, which are graded as Critical, Major or Other. Definitions of these categories can be found here: https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#actions-after-the-inspection.

The inspector will then provide a written report within 25 days of the closing meeting. For any critical findings, a letter will be sent prior to the final report and a response to this will be required within 7 days of receipt.

All findings listed in the final report will need to be addressed by the JRES and the relevant trial teams. The JRES must provide a response to the inspection report in the form of a corrective action and preventative action (CAPA) plan. This plan can include or reference the previous responses to the critical findings, where applicable.

Once submitted, the MHRA may request further clarification or information on the responses provided. When adequate responses have been received, they will issue a GCP inspection statement by email which closes the inspection.

7. References

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https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials

http://www.rdforum.nhs.uk/content/wp-content/uploads/2014/07/RDFguidance.pdf

https://mhrainspectorate.blog.gov.uk/2020/03/10/gcp-inspections-expectations-and-the-dos-and-donts-for-hosting/

8. Appendices

None associated with this SOP.