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How to get the most out of a Monitoring Visit from Sponsor QA

1. What is the purpose of a monitoring visit from Sponsor QA?

A key aspect of maintaining quality assurance for clinical research is the internal monitoring programme for Clinical Trials of an Investigational Medicinal Product (CTIMPs).

A monitoring visit from the UoL/LTHT Joint Sponsor QA Office aims to assess:

- Whether a trial is being conducted in accordance with the ethically and regulatory approved protocol.
- Whether there has been adherence to the ethical aspects of the study, and that the subject's rights and safety have been maintained.
- Compliance with Good Clinical Practice (GCP) and the clinical trial regulations.
- Whether subject confidentiality has been maintained.
- Whether any issues identified during the trial approval process have been appropriately actioned and improvements implemented.
- Compliance to trial-specific, Sponsor QA and organisational SOPs.
- Compliance to UoL / LTHT guidelines.
- Whether UoL / LTHT / Sponsor QA guidelines and policies can be improved.
- Whether actions from any previous monitoring visits have been appropriately resolved.

2. What is the benefit of a monitoring visit for researchers and their teams?

A monitoring visit is an opportunity for researchers and their teams to **showcase their work**, gain **advice and tips**, and have a "sense check" of the trial's conduct in line with the regulations.

Our monitors will often **identify areas that require improvement** and provide suggested corrective actions, but our monitors are also best placed to **recognise examples of best practice** and share such examples across LTHT to facilitate continuous improvements across the organisation.

It is also a chance for teams to **access targeted training** through the monitoring team and maintain a dialogue with the trial Sponsor to discuss any issues and concerns they may have.

A monitoring visit helps to ensure a high standard of regulatory compliance and that trial records are maintained to an 'inspection-ready' standard. This **minimises the likelihood of recurrent findings being raised in future monitoring visits and potential MHRA inspections.**

Remember: The QA Monitor will be reviewing the same documentation and dataset as an MHRA inspector. Identifying and addressing findings and areas for improvement in good time, through robust and regulatory sound Corrective and Preventative Action (CAPA), is a **good** thing!

It is better any GCP non-compliances are identified internally and rectified within the organisation, rather than an external body identifying issues during an audit or inspection.

3. How to prepare for a monitoring visit from Sponsor QA?

Always consider the following points when preparing for a monitoring visit:

☐ **Have I provided the following essential trial documentation for review?**

This will likely include:

- The Investigator Site File (ISF) or Trial Master File (TMF)
- Training files (e.g. CVs, GCP certificates, etc.) for staff listed on the site delegation log.
- Case Report Forms (CRFs) for the patients enrolled in the trial.
- Trial-specific and any departmental SOPs.
- Pharmacy will need to provide any trial-specific pharmacy file(s) during the separate visit to their department.

☐ **Have the medical notes for the trial patients (i.e. those containing source data) earmarked for review been requested from Medical Records?**

It is important that patient medical notes are requested in good time to ensure availability on the day of the visit.

Please note, should medical notes also be required for a clinical appointment, this will **always take priority** over the monitoring visit request.

However, the QA Monitor should always be notified in advance of the visit so that an alternative trial patient can be selected for review.

☐ **Has all source data relevant to the trial been filed appropriately and made available for monitoring?**

At the time of writing, isolated access to electronic health records cannot be given to monitors within LTHT.

As such, it is expected that trial source data worksheets, laboratory results, electronic annotations, clinic letters will all be printed and filed in the medical notes ready for review.

Otherwise access will need to be facilitated via an authorised individual such as a research nurse or trial coordinator.

☐ **Is the trial filing and data entry as up-to-date as possible prior to monitoring?**

Ensuring that the clinical trial records are as complete as possible ahead of time will minimise the number of findings identified during the monitoring visit.

Remember to file your correspondence and make sure your CRFs are up-to-date.

☐ **If an electronic Case Report Form (eCRF) and/or database is being used, has access been arranged for the monitors for the duration of the visit?**

Read-only access will need to be requested through the proper channels, and possibly through a third-party vendor outside of the research team. As such, it can often take several days (or even weeks) for access to be granted so start this process early.

☐ **Has a room or desk been reserved and the documents prepared in order for the monitor to conduct the visit?**

This may seem an obvious consideration, but research teams may be surprised by the delays that have been encountered (on the day of monitoring) from a room/desk not being booked or from documents not being ready upon the monitor's arrival.

The monitor will have limited time and several documents to review so it's essential that their time on the day can be maximised; good and timely preparation from the research team is key in supporting this.

4. What to expect following a monitoring visit from Sponsor QA?

Depending on the volume of queries, a formal monitoring report will usually be sent within 2 weeks of the visit being conducted.

The monitoring report will document all findings from the visit and will consist of:

- A '*Monitoring Report Cover Sheet*' (summarising the visit and key findings)
- A '*Monitoring Action Report*' detailing all findings from the Trial Master File (TMF) / Investigator Site File (ISF), Source Data Verification (SDV) and Pharmacy review (where applicable).
- The monitoring action report will list all queries (graded as *minor*, *major* or *critical*) and a recommended corrective action to guide researchers.

The QA Monitor will specify a date for the research team to submit a formal response to the findings. This is usually one month from circulation of the report.

A deadline can also be agreed via discussion between the QA Monitor and the research team, and may be extended depending on the volume and complexity of queries to be actioned.

5. How should researchers and their teams respond to a monitoring report?

There are different ways in which you can provide responses to the monitoring action reports depending on personal preference.

You may wish to:

- Complete the '*action completed*' column on the reports - e.g. by:
  - Requesting an editable MS Word version of the report and typing directly onto the document.
  - Annotating the document by hand.
- Collate responses on a separate document (*e.g. within an email or MS Word document*), utilising a numbered list corresponding to each of the points on the report table(s).

The written response and associated emails should capture **all** actions undertaken and serve as an audit trail for completion. **It is not acceptable to only tick or date / initial the monitoring report.**

The QA Monitor will review the corrective action(s) and all correspondence submitted as evidence of completion and will follow up all queries until confirmation of resolution is received.

Responding to and resolving monitoring queries is a jointly owned and collaborative process between the research team and QA Monitor. It is expected that a back-and-forth dialogue will be maintained as both teams work together to achieve the same goal.

6. How can follow-up queries be minimised?

- ☐ **Have I responded to all actions at the same time?** All actions must be responded to at the same time unless previously agreed with QA (*e.g. if an urgent response is required to a particular point, a response may need to be provided by a specified earlier deadline*).
- ☐ **Is my response as detailed as possible and states the specific action(s) taken?** Provide as detailed a response as possible to evidence how the finding has been actioned. It is not sufficient to say *'done'* or to tick and/or sign the *'action completed'* column.
- ☐ **Have I checked whether there is more than one action required for a single point?** Ensure you respond to all actions on the reports in full; some findings may require more than one action.

- ☐ **Will I be able to meet the deadline set?** If you anticipate any difficulties meeting a deadline (*e.g. due to upcoming annual leave, staffing issues*) please contact your monitor as soon as possible to discuss an alternative date.
- ☐ **Have I checked the '*Person Responsible*' column and arranged for the requested individual to provide their input?** For example, a query that requires clinical opinion must always be responded to by a medically qualified doctor. This can be evidenced in various ways (*e.g. attaching a supporting email from them responding to the query*).
- ☐ **I am unsure how to respond to a query, who do I contact?** If you are unsure about how to respond to any of the points raised, please contact the Sponsor QA Office who will be happy to provide guidance.
- ☐ **I have received a QA Follow Up letter telling me the visit is closed, do I need to do anything else?** Once closed, please ensure that all documentation, reports, responses and correspondence relating to the visit is filed in the TMF / ISF for audit trail purposes.

7. What happens once I have completed the necessary actions and submitted my responses back to Sponsor QA?

Once a satisfactory response to all findings is received and considered complete by the QA Monitor, a '*Monitoring Visit Follow Up Report'* confirming the visit as closed is forwarded to the Chief/Principal Investigator and all other relevant members of the research team alongside the Sponsor Representative and CSU/R&I Leads.

This follow-up letter, along with the original notification of monitoring visit letter, monitoring plan, completed monitoring action reports and all associated correspondence should be printed and filed in the Trial Master File (TMF) / Investigator Site File (ISF).

If the monitor has concerns regarding any of the completed responses, a close out letter will not be issued and the visit may be escalated to the QA Manager or Sponsor representatives where required.

Monitoring re-visits to check completion may be required in the event the written response received lacks sufficient detail to confirm that all actions have been implemented.

This documentation will be reviewed at subsequent monitoring visits, and most likely by the MHRA at inspection, to determine whether all actions from the report have been appropriately resolved.

Remember, monitoring is an **ongoing** process and it is important that the recommendations, preventative actions, and lessons learned following a visit are evidenced throughout the trial's **future** conduct.

Key Resources & Further Reading:

LTU_QM_24: A Researcher's Guide to Trial Documentation	*Sponsor QA (LTHT / UoL)*	http://lthweb.leedsth.nhs.uk/sites/research-and-development/research-and-development-homepage/qa-documents/standard-operating-procedures/
Good Clinical Practice Guide	*MHRA*	https://www.tsoshop.co.uk/MHRA/Good-Clinical-Practice-Guide/

Should you have any queries or concerns, or would like further information regarding the content of this bulletin, then please do not hesitate to contact the Sponsor Quality Assurance Office on Tel: 0113 20 60454