Study Monitoring and Assuring Data Quality

Toolkit

Make a plan

- Develop a quality management or monitoring plan for your study
- Access template plans and guidance

Why manage quality?

- This toolkit will set out why quality management and monitoring is important and how it can be easily and practically built into a study

Assess your study

- What type of quality management approach does your study require?
- Conduct a risk and complexity assessment to decide on a monitoring or quality management approach

Methodology

- What is Reciprocal monitoring?
- How can Reciprocal Monitoring be implemented in your setting?

Implement

- Explore templates and guidance documents
- Access quality management training resources

What?

- What is Quality Management?
- Reciprocal Monitoring: an introduction

How?

- Learn how to set-up an In-House Reciprocal Monitoring Scheme
- Download the Quality Assurance Plan - Template and Guide
- Webinar: How to plan and deliver quality assurance data in a clinical research study

Why?

- What is the purpose of quality management?
- Why are pragmatic monitoring and quality management systems needed?

Pragmatic Data Quality Management and Monitoring

BACKGROUND

MONITORING

Monitoring should be a helpful and fundamental part of a clinical research study. It is not an 'audit' but an ongoing process of working with the research study team to help achieve compliance to the protocol and standard operating procedures (SOPs).

The need to ensure that the question set is being answered, and that the answer can be relied upon often gets overlooked. It is possible that many clinical research studies produce answers that are either a false positive, false negative or false no difference.

This is a great cause for concern as new treatments and changes to treatments are driven by such data, and usually false results (especially if they are negative) never come to light.

MONITORS

IMPORTANCE

Whilst such errors might originate from the design or power of the study, these flaws might not be possible to predict until the study is running.

Often it is not possible to account for all eventualities when designing research studies and statistical plans are then based upon assumptions. Therefore, once the research study is up and running it is necessary that the Monitors have an inclusive role, as they need to be constantly thinking about whether any process or issues could impact on the reliability of a study endpoint.

The Monitor should be familiar with the protocol, their role is far more than just passively checking text boxes are completed.

ICH GCP

RISK ADAPTED

Monitoring need not be an arduous general task, but it should be commensurate with the risks and complexity of the research study. **ICH GCP (5.18.3)** requires the Sponsor to ensure that the research study is adequately monitored.

"The sponsor should determine the appropriate extent and nature of monitoring which should be based on the considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the research study. In general there is need for on-site monitoring, before, during and after the research study; however in exceptional circumstances the sponsor may determine that central monitoring in conjunction with procedures such as investigator's trainings and meetings, and extensive written guidance can assure appropriate conduct of the research study in accordance with GCP"

IN PRACTICE

ON-SITE OR CENTRALISED

On-site monitoring is performed at the sites at which the clinical trial is being conducted. **Centralised monitoring** is a remote evaluation of accumulating data which can complement and reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data.

Centralised monitoring can be used to:

- Identify missing/inconsistent data, outliers and protocol deviations
- Examine data trends such as the range, consistency, and variability of data within and across sites
- Evaluate for errors in data collection and reporting at a site or across sites; or potential data manipulation/ integrity problems
- Analyse site characteristics and performance metrics
- Select sites and/or processes for targeted on-site monitoring.

2. What?

Pragmatic Data Quality Management and Monitoring

BACKGROUND

DEVELOPMENT

When the reciprocal monitoring scheme was devised in 2007 The **KEMRI-Wellcome centre** had over 15 year's experience in conducting clinical studies ranging from large pharmaceutical initiated (and sponsored) regulatory research to small academic/ investigator-sponsored research studies.

As part of ensuring GCP for their trials the team had to ensure that all clinical research studies were adequately monitored. The Contract Research Organisation (CRO) model was unattractive because of the cost and non-protocol specific approach. Therefore, Trudie Lang (former Head of Clinical Trials in Kilifi) designed a scheme to harness the experience of the study coordinators and nurses and train them to be study monitors, within their day-to-day roles.

WHAT

RECIPROCAL MONITORING

Reciprocal monitoring is an in-house system where clinical research study staff are trained as research study monitors and then monitor studies for which they are completely independent.

This system has since been replicated in many settings and has been reported to raise standards across all research studies (as it creates a platform for sharing best practice), increases the profile of research study staff and has been well received by investigators, sponsors and research study staff teams (**Chilengi, Chantler et al.**).

BENEFITS

RECIPROCAL MONITORING

- Compared with industry led drug monitoring, this system is easy to set up and low cost: Training materials are available online.
- It provides an opportunity to gain research skills for clinical staff
- Best practice is shared amongst research sites i.e. hospitals, and the standard of conducting research is raised, building reputations, both at the local research site level and beyond!
- It can be implemented within a hospital, research centre or a consortia – sharing knowledge across different research teams, within regional boundaries.

RESOURCES

WEBINAR & LINKS:

For information on how to develop an in-house monitoring scheme **click here**

Other useful links:

- **Quality Assurance Plan for Clinical Research Studies: A Template and Guide**
- **Chilengi R, Ogetii G, Lang T. A Sensible Approach to Monitoring Trials: Finding effective solutions in-house**
- **How to set-up an in-house monitoring scheme**
- **The Global Health Trials' tools and templates library**

Pragmatic Data Quality Management and Monitoring

WHY

QUALITY MANAGEMENT

A very fundamental, but often overlooked, element of high quality research is the planning and implementation of research quality management (often referred to as monitoring). The purpose of this is to ensure the following;

1. That the study is conducted according to the protocol
2. That the study SOPs are followed (and so helping achieve 1.)
3. That the ethical rights of the participants are being considered and protected
4. That the study is being conducted safely
5. That the data is being recorded and transcribed accurately.

BACKGROUND

All studies on human subjects should have an assured level of quality to protect the rights of the participants and to ensure data are reliable. This is not just important for those taking part in the research but for every future patient whose treatment has been determined by the results.

All clinical research should be run to ICH-GCP standards; however ICH-GCP was designed by industry and FDA primarily for new product registration and is therefore often difficult to apply to other more pragmatic trials on registered products or non-drug trials, and indeed observational or sampling only studies.

STANDARDS

BE PRAGMATIC

RISK PROPORTIONATE

Trial monitoring and quality assurance is often perceived as difficult as much experience has been based in classical industry drug monitoring. This is more than is needed for research such as an observational study with a straightforward protocol this is very low risk.

However, as with any research it is still very important to confirm that the data is correct and reliable. This can be done easily and made into an integral and beneficial part of study operations.

RECIPROCAL MONITORING

There has been a trend over recent years towards the use of expensive contract organisations to monitor research studies and this can be expensive and unnecessary.

As an academic clinical research facility the **KEMRI-Wellcome** programme in Kenya needed to find an optimum way to monitor all their studies to ensure adherence to the protocol, that high ethical standards were being maintained and that the data was being accurately captured.

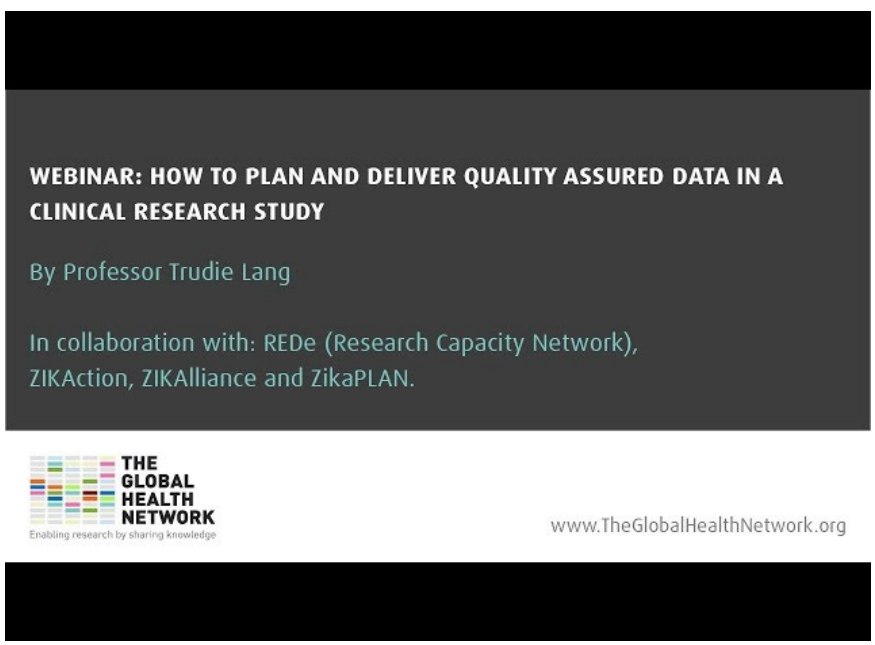
To find out more about Reciprocal Monitoring **click here** for information on how to develop an in-house monitoring plan **click here**.

APPROACH

4. How?

REDe Webinar: How to plan and deliver quality assured data in a clinical research study

WATCH



LEARN

WEBINAR

Professor Trudie Lang presents a live training webinar on data quality management using the ZIKAlliance Pregnant Women Cohort Study as a working example.

The webinar covers how to build research study monitoring, and quality assurance into a clinical study, and why it is important to do so.

DOWNLOAD:

To download the presentation, **click here**.

For further information on how to plan and deliver quality assured data in a clinical research study click '**Where to start**'.

To access the Quality Assurance Plan tool and template **click here**.

RESOURCES

Pragmatic Data Quality Management and Monitoring

ASSESS - HOW?

STUDY ASSESSMENT TOOL

To assist with planning one of the first tasks is to conduct a risk and complexity assessment.

This is an assessment task to determine the type of monitoring or quality management approach your study may require. For a tool to assist you with this **click here.**

PLAN - HOW?

QUALITY ASSURANCE PLAN TEMPLATE AND GUIDE

This document is designed specifically for investigators running all types of clinical studies to guide the development of an operational tool to confirm quality and ethical standards within their studies. Therefore, it is a pragmatic approach that could be adapted for all non-interventional clinical research studies.

To download an interactive Quality Assurance Plan template and Guide for use in your own study **click here**.

SET-UP - HOW?

IN HOUSE MONITORING SCHEME

Contracting an external monitoring organisation is not normal or warranted for low risk studies with a straightforward protocol. A good in-house or reciprocal scheme (with other sites in a network) can be put in place and carry this task out perfectly well.

For a step-by-step example of how to set-up a monitoring scheme for an observational study **click here**.

To read how to achieve 'buy-in', set-up appropriate systems, train staff and implement your planned monitoring scheme **click here**.

RESOURCES

WEBINAR & LINKS:

Professor Trudie Lang presents a live training webinar on data quality management using the ZIKAlliance Pregnant Women Cohort Study as a working example. To watch it **click here**.

Other useful links:

- **Study Assessment Task**
- **Quality Assurance Plan for Clinical Research Studies: A Template and Guide**
- **Quality Management Plan for Observational Studies example**
- **How to set-up an In-house Monitoring Scheme**

How to set-up a Monitoring Scheme - Observational study example

STEP 1

PLAN:

The first step suggested is for each site to write a simple and pragmatic **Quality Assurance (QM) Plan**.

This could be done by (i) individual investigators or, (ii) in a group, as long as the specific detail is appropriate for the sites. The aim should be to establish a positive and simple process that brings broad benefit and establishes quality management as a normal and integrated part of how the site operates. Consider liaising with the Sponsor, they have existing Standard Operating Procedures (SOPs) already in place, or to seek further advice.

The objective of this step is for each site to have in place a straightforward operational plan that will confirm data reliability and high ethical practice

STEP 2

SOP

Who will confirm that this quality management plan is implemented? We suggest each site nominates a Quality Manager or officer. Ideally this should be an experienced member of the research team such as a clinician, nurse or laboratory technician – anyone who is valued, appropriately experienced and interested in taking on this important extra role. They do not need to have any previous experience in monitoring or QM. It is important that this role is viewed positively and that the person taking it on is clear about the remit and motivated in the task.

Details such as what they will review, where they will conduct the review, and monitoring frequency, will all be recorded in the plan and associated **Standard Operating Procedure**. The review and reporting process should also be carefully considered and captured.

STEP 3

TRAINING:

Training can be organised through the The Global Health Network and it may be possible to send an experienced monitor or trainer to your site to deliver a workshop or teaching session, or this could be set up online; Please get in touch: **info@theglobalhealthnetwork.org**

Please see the **Training** section for further information.

Research study monitoring can be built into people's roles so they do not have to do this full time. This is a good way to give staff an extra dimension to their role and is an excellent continuous personal development experience.

STEP 4

RECIPROCAL MONITORING

Once training has been conducted, a good starting point will be for the Quality Manager(s)/officer(s) to begin by performing QM 'visits' at their own sites, putting into practice their training and testing out their QM Plan and SOP (which of course should be amended and updated as needed).

To further enhance QM and increase credibility a beneficial next step would be to set up a Reciprocal System. Here quality managers from within the network monitor each other's studies.

When sites in Africa used this approach they experienced wide reaching benefits such as sharing best practice and standardisation.

For further information on Reciprocal Monitoring **click here**.

7. How?

How to effectively implement your Quality Monitoring Scheme

STEP 1

BUY-IN:

Firstly, the scheme needs to be adopted and bought into by the research centre, organisation, study group or network and agreed as their chosen approach to quality management and monitoring.

A key element of this 'buy in' is that specific time is made available for those selected by the study teams to be monitors. Here the significant benefits need to be made clear. This needs to be agreed and negotiated very early and terms set out. This scheme might be required for one specific study in a multi-centre setting or might be being put into place within one research centre, or across a network as a long term solution and resource for their study monitoring.

STEP 2

SET-UP:

Once agreed in principle the leading organisation/facility network needs to establish a management system for the scheme, and a coordinator is likely to be needed.

Here the systems required will include the following:

- Reciprocal monitoring scheme membership agreements
- Monitoring assignment and planning tools
- A training plan for monitors
- Template SOPs for scheme including review and feedback from monitoring visits

STEP 3

COORDINATE:

Coordination is key, especially in large and collaborative studies where data is to be pooled.

Whether sites choose the in-house system, or move to a reciprocal scheme within countries (or a mixture of both being the most likely outcome?), coordinating information exchange on QM across the region can be facilitated on the platform, and involve the following:

- Support and review of quality management plans
- Review and support with quality report visit (and implementing any actions)
- Coordination of any reciprocal schemes
- Coordination of training
- Implementing an evaluation process for both in-house and reciprocal schemes.

STEP 4

IMPLEMENT

The Coordinator drafts a periodic schedule detailing which research studies are to be monitored within that period.

The frequency of monitoring for each study is determined based on the complexity of the study, the extent of external monitoring and specific protocol requirements. This is clearly documented in the study specific **Quality Assurance Plan**, this plan should include what the data point or activity is and the people and departments, which should be visited, along with details of appropriate percentages of outputs to be validated/reviewed.

For guidance on how to implement training **click here**.

For details on Quality Assurance visits please **click here**.

8. How?

How to identify and deliver training

NETWORK

RESOURCES

Training is required in both setting up and then implementing a Quality Management Plan, whether quality management is performed at an in-house level, or if this is extended into a reciprocal scheme in one or more of the countries within the region.

This can be organised through The Global Health Network and there are many resources, such as online training, materials for classroom based training on the platform.

It may be possible to send an experienced monitor or trainer to your site to deliver a workshop or teaching session, or this could be set up online; Please get in touch: info@theglobalhealthnetwork.org

FOCUS

Typical training courses (virtual or face-to-face) would encompass the following:

- Review and development of draft quality management plans (sites would bring their draft versions)
- Basic GCP
- Introduction to quality management for clinical research
- How to conduct a quality management visit
- How to report a quality management visit
- Processes for handling any issues to be reported

TRAINING

TRAINERS

IN-HOUSE

Any member of a clinical research study team can train as a monitor. Nurses, data managers, pharmacists and research study coordinators all make excellent research study monitors.

There is a vast range of expensive courses for research study monitors but nowhere in ICH GCP, or in any other regulations, are there specific requirements or certification for monitors (or their trainers). What can be found are statements around appropriate experience and qualifications.

It seems that the commercial needs of training companies and contract organisations have created a market and a perceived need for external training courses, certification and accreditation. **It is perfectly appropriate and acceptable for sufficiently experienced and senior monitors/ trainers to train others in-house.**

ONGOING

Finally, it's important to consider how you will ensure the ongoing high quality of reciprocal monitoring.

This is something in which **The Global Health Network** can help with – providing ongoing education, and access to relevant resources.

NEXT STEPS

9. How?

How to conduct Quality Assurance/Monitoring Visits

OVERVIEW

QA VISITS:

Quality Assurance (QA) activities should begin as soon as possible after the study begins and the timing of any visits should be documented in the **Quality Assurance Plan**.

The Quality Manager will conduct QA visits in accordance with the QA Plan and associated **SOP**.

Irrespective of who it is that is tasked with carrying out this important role, they should be considered positively as part of standard research practice with objectives of guiding and supporting the study. This is not audit, policing, but helpful and constructive. It is the responsibility of the Investigator for the study and appropriate staff team members to ensure high standards of data collection and Source Document Verification (SDV) are maintained at all times.

PREPARATION

DETAILS

Appropriate arrangements with applicable personnel should be made in advance. The documents and information needed are detailed in the **Quality Assurance Plan** so they can be ready for this validation process. Informed consent forms are an important component. Not every single data point needs to be verified.

Where possible, all study documents, forms and databases should be up to date prior to a QM visit. A room or quiet desk should be booked for the use during the visit.

The study team should be aware of the planned visits and be able to make available the necessary time and assistance.

ON THE DAY

THE SITE VISIT

On the day of the visit the Lead Investigator or other nominated team member(s) must be available to show the Quality Manager to their allocated space or room, and ascertain that they have everything they need. The Principal Investigator (PI) should also be available on the day of the visit for at least a proportion of each visit.

To confirm data is valid and correct, it is necessary to cross check against the original record. This is called the source data. In order to confirm a patient attended a clinic, for example, the clinic records can be checked; to ensure a correct blood sample or PCR result is as is recorded on the database, the original lab record sheet should be cross referenced.

For each visit the QM should complete a **Quality Assurance Visit Form.**

RESOURCES

DOCUMENTS

Quality Assurance Plan tool and template

Standard Operating Procedure for Trial Monitoring / Quality Management

Quality Assurance Visit Form