THE GLOBAL HEALTH NETWORK
Enabling research by sharing knowledge

COVID-19 Quality Management and Monitoring

Toolkit

Why manage quality?

- This toolkit will set out why quality management and monitoring is important and how it can be practically built into a COVID-19 study

Make a plan

- Develop a quality management or monitoring plan for your COVID-19 study
- Access a template plan and guidance

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

- Which monitoring methodologies should you utilise for your study?
- How can monitoring be implemented in your setting?

Implement

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

What?

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

How?

- Learn how to set-up a Monitoring Scheme
- Download the Quality Assurance Plan - Template and Guide

1. What?

What is 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 quality management is to ensure that:

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

ICH-GCP, whilst developed for clinical trials, can be adapted and applied to all research on human subjects. 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 the registered products or non-drug trials, and indeed observational or sampling only studies which may be developed in the context of COVID-19.

STANDARDS

BE PRAGMATIC

RISK PROPORTIONATE

Monitoring and quality management 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 straight forward protocol that 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.

By considering which study steps or activities present risk, including participant safety, data integrity, and confidentiality teams can identify where to focus resources and reduce the burden on site staff.

COVID-19

The COVID-19 situation is evolving, and pragmatic actions may be required to deal with the challenges of conducting research (2). Special consideration needs to be made when considering study monitoring procedures due to the potential for limited access to hospitals and clinics, the risk of spreading infection, and the additional burden on healthcare professionals.

However, 'monitoring' can be adapted and applied pragmatically generally – and so absolutely can be done in this context by considering methodologies outside the norm such as alternatives to external monitors visiting sites and physical Source Document Verification (SDV).

APPROACH

2. What?

Data Quality Management and Monitoring: What does your study require?

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.

DESIGN

QUALITY BY DESIGN

In order to reduce the burden on trial participants, clinicians, and investigators it is important to consider error prevention from the outset and throughout your study.

Study feasibility and important error prevention should be factored in during protocol design and trial planning – the **Study Walk-through method** is a useful tool for working this through as a team. For example, incorporating simplified but well-justified eligibility criteria, flexible visit schedules, a variety of data capture methods, and streamlined collection of relevant clinical events with centralised review of critical safety and efficacy information, can all facilitate efficient, effective, and feasible trials. (**Enhancing clinical evidence by proactively building quality into clinical trials**).

MONITORING

ONGOING

Whilst we can try to identify and mitigate errors some 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.

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, whilst developed for clinical trials can be adapted and applied to all research on human subjects. Within these the guidelines state that the appropriate extent and nature of monitoring should be determined for each study based on considerations such as the objective, purpose, design, complexity, blinding, size and endpoints of the study.

This toolkit applies thse considerations to COVID 19 clinical research protocols with the aim of enabling sites to design and implement a pragmatic and effective monitoring strategy for their studies; be they observational, sampling or intervention trials.

IN PRACTICE

Back: Section 1. What?

Next: Section 3. COVID 19 Study Considerations

3. What?

Quality Management and Monitoring: COVID-19 Study considerations

COVID 19

CHALLENGES

The challenges faced by those conducting research related to COVID 19 may include: national legislation or guidance restricting travel and access to hospitals, clinics and labs to limit the spread of infections, the potential that trial participants being in self-isolation or quarantine and a greatly increased workload on health care professionals who are committed to critical clinical tasks in addition to other study specific challenges.

These challenges should be considered when writing your Quality Management Plan but 'monitoring' can be adapted and applied pragmatically generally – and so absolutely can be done in this context.

ALTERNATIVES

Consideration needs to be given the feasibility of on-site monitoring and routine Source Data Verification (SDV). Centralised monitoring is a remote evaluation of accumulating data which can complement and reduce the extent of on-site monitoring and help distinguish between reliable data and potentially unreliable data. It 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

ON-SITE

CRITICAL DATA

SIMPLIFY:

Any study monitoring processes which require input from the study team should be simplified to avoid putting disproportionate burden on staff.

Consider techniques which are outside the current norm e.g. could SDV be performed via video call? Photograph? Any proposed remote SDV should be clarified with authorities such as Ethics Committees and data protection agencies.

Critical data is regarded as data points that directly impact study outcomes. Endpoints such as participant death, hospital discharge or longer-term outcomes could be verified via review of medical records or linkage to medical database if practical mechanisms can be put in place.

SPONSOR/FUNDER

The FDA and EMEA allow for data base level monitoring (ref) here this can be built in within the data management system and the eCRF. Later further checks can be performed remotely to pick up wider concerns in regard to recruitment, safety, visit and sampling adherence, intervention administration, compliance and reconciliation.

If direct quality checking or monitoring remains both necessary and feasible, it should be possible to nominate a member of the team or someone from another team to undertake that role. In this situation an external monitor would not be appropriate and they could review the work of the locally appointed monitor remotely depending on sponsor or funder requirements.

All plans should be details in your **Quality Assurance Plan** which should be updated as the COVID 19 situation evolves.

REQUIREMENTS

Back: Section 2. What does your study require?

Next: Section 4. How?

4. How?

Pragmatic Data Quality Management and Monitoring: How?

IDENTIFY RISKS

STUDY WALK-THROUGH

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

Consider which study steps or activities present risk, ensuring you include participant safety, data integrity, and confidentiality. Use the **Study Walk-though** method to assist you with identifying these areas and how to mitigate them. This assessment of risk can be used to identify where to focus resources in order reduce the burden on site staff.

This **Study Assessment Tool** can help you work through this task and determine the type of monitoring or quality management approach your study may require.

MAKE A PLAN

QUALITY ASSURANCE PLAN

The next step suggested is for each site to write a simple and pragmatic **Quality Assurance Plan**. Take the risks you have identified and document how you will mitigate them and monitor quality.

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.

This document is designed with COVID-19 studies in mind but can be adapted for all types of clinical studies to guide the development of an operational tool to confirm quality and ethical standards. It is a pragmatic approach that could also be adapted for all non-interventional clinical research studies.

WHO?

QA MANAGER

Who will confirm that this quality management plan is implemented? We suggest each site nominates a Quality Manager. 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.

This is typically a role given to someone separate from the study team, which has advantages as this brings independence - perhaps someone working for another study team at the same centre could be considered. For studies involving a network consider a **Reciprocal Monitoring Scheme**.

IMPLEMENT

SOP

Contracting an external monitoring organisation is not normal or warranted for low risk studies with a straight forward protocol. It is quite acceptable for a member of the study team to be assigned the task of study Quality Manager (QM).

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 (SOP). The review and reporting process should also be carefully considered and captured.

Whoever is conducting this study it is advisable for the investigator, and their study team to write this plan and the associated SOPs so that it is specific and appropriate for their study and circumstances.

What?

Pragmatic Data Quality Management and Monitoring: Reciprocal Monitoring

BACKGROUND

DEVELOPMENT

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.

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.

BACKGROUND

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.**).

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.

BENEFITS

5. How?

How to identify and deliver monitoring 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 sites.

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

TRAINING

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

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.**

NEXT STEPS

ONGOING

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

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

6. 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.

Consider a **Reciprocal Monitoring** Scheme.

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 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**.

7. How?

How to conduct Quality Assurance/Monitoring Activities

OVERVIEW

QA ACTIVITIES:

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

The Quality Manager will conduct quality management activities in accordance with the QM Plan.

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 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 quality management checks. 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 quality management activity. A room or quiet desk should be booked if any on-site visit is required/feasible. The study team should be aware of the any planned visits or the timings of any virtual sessions and session should be kept simple and be well managed to reduce burden on site staff.

ON THE DAY

SDV

To confirm data is valid and correct, it is necessary to cross check against the original record. This is called Source Data Verification (SDV). In order to confirm a patient attended a clinic, for example, the clinic records can be checked; to ensure a correct temperature or virology result is as is recorded on the database, the original lab record sheet or hospital notes should be cross referenced.

Only critical data (data points that directly impact study outcomes. Endpoints such as participant death, hospital discharge or longer-term outcomes) should be included in SDV there is no need to cross check every data point. Consider techniques which are outside the current norm e.g. could SDV be performed via video call? Photograph? Any proposed remote SDV should be clarified with authorities such as Ethics Committees and data protection agencies.

FOLLOW-UP

DOCUMENTATION

The outcome of Quality Management activities and checks such as site visits or virtual SDV sessions should be documented and followed-up on as specified in the Quality Assurance Plan.

Follow-up may be as simple refresher training on aspects of the study which are generating errors or more formal escalation depending on the nature of the findings.

By defining thresholds for escalation in your Quality Assurance Plan the next steps are clear for all parties.

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