



The REDe Resource Kit

Study Monitoring and Assuring Data Quality

Introduction

One of the tasks set to the REDe network was to devise and deliver a data quality management system in the form of reciprocal monitoring that could be implemented across the studies of all three consortia to assure data quality. The requirement for each study varies depending on the risk and complexity of the study, and therefore several approaches are offered, including reciprocal monitoring.

This resource kit provides a set of materials and guidance to enable all types of studies to implement a data quality management plan.

This resource guides the process of selecting which approach is best for which studies and then provides support, training and tools to undertake these quality management plans, including reciprocal monitoring.

- A. The first step is for each study team within the three consortia to agree what approaches they would like to implement for their component studies, if none are in place already.
- B. The next step is for the study leaders to work with their teams to set out how this approach will be implemented. Then any training can be delivered and the tools and templates can be adapted to become the operating procedures and documents for each study.

On the REDe platform there is a resource kit which comprises of the following resources, as outlined below. These are designed to support each team in assessing the requirements for their study and then implementing their approach and training their teams.

1. Managing Data Quality in Clinical Research
2. Conducting a risk and complexity assessment to decide on a monitoring or quality management approach (step 1 the study assessment task)
3. Writing a quality management or monitoring plan for your study
4. Reciprocal Monitoring: an Introduction and tool kit
5. Training resources for quality management and resources
6. Templates and guidance documents for quality management and trial monitoring

This pack contains all of the materials that can be found online within REDe:

<https://rede.tghn.org/resources/>



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Study assessment task

This is an assessment task to determine the type of quality management approach your study may require. The first task is to consider the risk and needs of your study.

(Please complete **all** sections)

Consortia name:	
WP Number:	
Study title:	
First Name:	
Surname:	
Institution:	
Role in study:	
Contact details (including email address/tel. number):	

Brief overview of the study design (e.g. cohort study)	
---	--

Briefly describe the data (including samples) that you will be collecting as part of your study?	
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What are the key data endpoints being captured? (This is data that matters to the answer generated)	
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What potential data collection errors could occur? (How likely would these be?)	
What potential errors could occur in capturing key endpoints?	
What potential errors could cause a safety risk?	
What potential errors could cause an ethical risk?	
What potential errors could harm the reputation of the study or research in general?	
How in practice could these be checked or validated? <ul style="list-style-type: none">- In person at the site?- Remotely on the database? How often would be appropriate?	





Do you already have a Quality Management Plan in place for your study?	
Do you have access to a study monitor?	
If no, do you want one of your team to be trained to do this?	
What approach to monitoring do you think your study needs and what training or support do you need to implement this?	
Any other comments:	



The REDe Guide to Clinical Research Practical Data Quality Monitoring

Background

One of the goals of the REDe network is to support the conduct of high quality research by providing tools, training and guidance in all the elements that are required. A very fundamental, but often overlooked piece in this is the planning and implementation of research quality management, which is 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 the above (point 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.

This guide will set out why quality management and monitoring is important and how it can be easily and practically built into a study. This document will also explain how this process should be proportionate to the complexity and risks associated with the study and so should be appropriate as well as being highly practical and achievable.

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.

Trial monitoring and quality assurance is often perceived as difficult as most people's experience has been classical industry drug monitoring. This is more than is needed for an observational study as the protocol is straightforward and the risks are very low. 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. This guidance paper sets out several ways this can be achieved.



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Quality Management Plan for Observational Studies

Step One:

The first step suggested is for each site to write a *simple and pragmatic quality management plan*. Appendix 1 provides a guideline and template for this and Appendix 2 is a more detailed example.

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. You might wish to consider liaising with the Sponsor, just in case they have any existing Standard Operating Procedures (SOPs) already in place, or some 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 Two:

Who will be confirming that this quality management plan is being implemented? We suggest that each site *nominates a quality manager or officer* (or whatever term they wish to use). Ideally this should be an experienced member of the research team. They might be a clinician, a nurse, a 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 quality management.

This has worked well where this system has been implemented successfully in other sites when it is seen that this is a job enhancing role, and that being offered this expresses recognition of their efforts, confirming their work is valued. It has been a useful way to extend staff's experience and give their job an extra dimension.

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.

Once this has been decided, details such as (i) the specifics of what they will review, (ii) where they will conduct the review, and (iii) how often monitoring will take place, will all be recorded in the plan (as explained Appendix 3).

The review and reporting process should also be carefully considered and captured in the plan.



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Step Three:

Potential of *extending to reciprocal monitoring*.

Once training has been conducted (see 'Next steps' below), a good starting point will be for the quality manager(s)/officer(s) to begin by performing quality management 'visits' at their own sites, putting into practice their training and testing out their quality management plans (which of course should be amended and updated as needed).

To further enhance quality management 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. Staff reported really benefiting from visiting each other's sites and broadening their experience. See the following paper included in this kit:

Chilengi R, Ogetii G, Lang T. A Sensible Approach to Monitoring Trials: Finding effective solutions in-house. WebmedCentral CLINICAL TRIALS 2010;1(10):WMC00891

doi: 10.9754/journal.wmc.2010.00891

In this case it could work within countries, so a scheme would be established for this within the region.

Next Steps

Training would be helpful 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 REDe network and there are many resources, such as online training, materials for classroom based training and a workshop toolkit <https://rede.tghn.org/resources/>.

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 through the REDe website: REDe@theglobalhealthnetwork.org



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When sites have nominated a quality manager, The Global Health Network will also link them together to form a supportive community of practice, where ideas and approaches can be shared.

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.

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 quality management across the region would really help make this a success, and this can be facilitated on the REDe 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.



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Quality Assurance Visits

Overview

An important element of assuring data quality is comparing the entries in the database with the original source of the data (e.g. laboratory results). This procedure is known as Source Data Verification (SDV).

The process of quality assurance should be straightforward and pragmatic and easily built into a research team's operations.

Contracting an external monitoring contract organisation is not normal or warranted for these studies, yet there is a need for ensuring that data and ethical standards are met.

A good in-house or reciprocal (with other sites in a network) scheme can be put in place and carry this task out perfectly well.

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 SDV are maintained at all times.

Here we present a template tool to put in place a simple system for this.

Details of the Quality Assurance Visits

On the day of the visit the Lead Investigator or other nominated team member(s) must be available to show the Quality Assurance Manager (QAM) to their allocated space or room, and ascertain that they have everything they need (refer to Appendix 1: Details of the Quality Assurance Visits - table).

The Principal Investigator (PI) should also be available on the day of the visit for at least a proportion of each visit.

Preparation needed by study staff prior to a quality assurance 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.

Where possible, all study documents, forms and databases should be up to date prior to a QAM 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.





Reciprocal Monitoring: *A proven and practical approach to quality management within research networks and centers.*

Why Pragmatic Monitoring and Quality Management Systems are needed

There has been a trend over recent years towards the use of contract organisations to monitor research studies - this can be expensive and is not necessary. An example of this is the academic clinical research facility, the KEMRI-Wellcome programme in Kenya who needed to find an optimum way to monitor all of their studies to ensure adherence to the protocol, that high ethical standards were being maintained, and that the data was being accurately captured.

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 that false results (especially if they are negative) never come to light.

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 a cognitive role, as they need to be constantly thinking about whether any process or issues could impact on the reliability of a study endpoint. This is the light in which we insist, that the Monitor should be familiar with the protocol, and that their role is far more than just passively checking text boxes are completed.

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"*



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Introduction to Reciprocal Monitoring

When the Reciprocal Monitoring Scheme was devised in 2007, the KEMRI-Wellcome centre had more than 15 years' experience in conducting clinical studies ranging from large pharmaceutical initiated (and sponsored) regulatory research studies to small academic/investigator-sponsor research studies. As part of ensuring GCP for their trials, the team were faced with the challenge of ensuring that all their clinical research studies were adequately monitored.

The Contract Research Organisation (CRO) model was unattractive because of the cost and their non-protocol specific approach. Therefore, Trudie Lang, the Head of Clinical Trials in Kilifi at that time, 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.

The scheme that Professor Lang set up was an in-house system where clinical research study staff were trained as research study monitors and then monitored studies of which they were completely independent.

This system has since been replicated in many settings and has been reported to raise standards across all research studies (as it created a platform for sharing best practice), increased the profile of research study staff, and has been well received by investigators, sponsors and research study staff teams (Chilengi, Chantler), published 05/10/10. *Chilengi R, Ogetii G, Lang T. A Sensible Approach to Monitoring Trials: Finding effective solutions in-house. WebmedCentral CLINICAL TRIALS 2010;1(10):WMC00891*
doi: 10.9754/journal.wmc.2010.00891

Overall, a site mentoring, rather than a monitoring approach is well accepted and supports the aim of conducting high quality clinical research in accordance to the international conference on harmonisation of Good Clinical Practice (ICH GCP) and is highly pragmatic and inexpensive.

The KEMRI-Wellcome team found that training some of their staff for monitoring, and then monitoring each other's studies was a mutually beneficial exercise for the study monitored and the individual monitors.

The basic principles of clinical research study conduct are generic and applicable across studies. The process of developing monitoring tools, training and management of the monitors group turned out to be a highly rewarding experience to the monitors-cum-coordinators.

This cadre of staff became the key implementers and driving force of GCP. With a pool of at least 20 trained monitors, they managed to allocate at least 2 monitors to each study. All studies were similarly monitored and reported to the head of clinical research studies and respective PIs.



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In Kenya, the research study investigators, sponsors and funders, reported to be impressed and satisfied with the monitoring the research studies undertook.

Before this scheme was implemented, only the externally sponsored drug development research studies were monitored.

Presently all clinical research studies in the programme are subject to the in-house reciprocal monitoring scheme, even if they are externally monitored by the sponsor.

Previously, many of our locally sponsored or academic research studies were not able to finance monitoring (as CRO's would have been the only option) and they did not have the skills or capacity to monitor themselves. This reciprocal scheme has made quality and ethical standards assurance achievable and feasible.

This monitoring system became a popular activity within the KEMRI programme. This is because the staff reported that it brought additional benefit of staff motivation and skill enhancement. The opportunity to train and to join the monitoring pool allowed a research nurse from the ward, for example, to gain experience of clinical research studies in the community out in their field sites.

Another good example was that spending two days a month monitoring research studies gave the research study laboratory staff, or the research study pharmacists, hands on experience of clinical research studies from a perspective they did not normally experience.

With this system, it was important to write a monitoring plan that reflected the nature of each study and so, for example, included scheduling monitoring visits according to the complexity and risks of the research study.

In the CRO monitored research studies, such decisions would normally heavily weigh on availability of finances rather than study designs.

An additional benefit is that it creates an opportunity for mentoring of research study staff through continued interaction between the more experienced and lesser experienced research study staff during and after the monitoring activities. In the CRO model the amount of interaction would be limited to the resources available for on-site monitoring.

Benefits of setting up a Reciprocal Monitoring Scheme

A reciprocal monitoring scheme could be set up within any facility or organisation that runs several studies, be it in one location or many. The financial and wider benefits still hold even if travel costs are incurred.



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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.

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

The training for these monitors can also be organized in-house (and so for relatively less cost), as long as sufficiently experienced and senior monitors/trainers are available.

There is a plethora 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. Here, as with monitoring itself, it seems that the commercial needs of training companies and contract organisation have created a market and a perceived need for external training courses, certification and accreditation. It is perfectly appropriate and acceptable for those with strong experience in monitoring to train others. Therefore, here, within the REDe platform the monitoring courses and materials, both online and face to face will be highly robust and valid.

How to set up an In-House Monitoring Scheme

1. Get buy-in and agreement

Firstly, the scheme needs to be adopted and brought into by the research center, 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 (as described above) need to be made clear. This needs to be agreed and negotiated very early and terms set out (template agreement available - see Appendix 3). This scheme might be required for one specific study in a multi-centre setting, or within one research centre, or across a network, as a long term solution and resource for their study monitoring.

2. Set up systems

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 necessary. 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.



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3. Training your monitors

Materials and suggestion for this are available on the REDe platform.

Experienced tracking, oversight and support is key, and resources are also available for this.

4. Implementing into studies

The suggested approach is that for every study, a quality or monitoring plan is put into place (see document in Appendix 1) and this will lead to the generation of a monitoring, or quality management SOP.

Studies should have a person allocated as their quality manager and that this person should work with the reciprocal monitoring coordinator to appoint the monitors for new research studies.

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 monitoring 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.

5. On-going training of monitors

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

This is something in which REDe can help with – providing ongoing education, keeping people up-to-date with the latest methodology issues etc.

There could be a space made available on the REDe website for a 'mini-network' of monitors within REDe.



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Appendix 1:

Quality Assurance Plan for Clinical Research Studies



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Guideline summary sheet

Tool: Quality Assurance Plan for Clinical Research Studies.

Purpose: All research studies on human subjects should have a level of quality and ethical standard assurance built into their operations to ensure that the rights and well-being of human subjects are protected and that the data are reliable.

ICH GCP (1) applies to all research on human subjects and states 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 document applies those considerations to the WHO protocol for surveillance of the therapeutic efficacy of antimalarial medicines (2) with the aim of enabling sites to design and implement a pragmatic and effective quality assurance plan for their antimalarial drug surveillance studies.

This template guides the investigator in preparing and operationalising a quality assurance plan. Therefore, whether an external sponsor is responsible, or the investigator is putting in place their own quality assurance procedure, we recommend this document is used to ensure a simple, pragmatic process that is specially designed for this type of study to assure valid data and ethical practices.

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

Details: The template should be customised to the protocol, the study's special needs / circumstances, and the requirements of the data capture system. Sections may be edited or deleted as needed.

References:

1. http://whqlibdoc.who.int/publications/2009/9789241597531_eng.pdf
2. <http://www.ich.org/LOB/media/MEDIA482.pdf>





How to use this document: The following steps are written to guide a study team in planning how to assure that high ethical and data standards are met for their antimalarial surveillance study.

- Items in *blue italics* and enclosed in braces [] are instructional text that should be deleted prior to approval.
- Items enclosed in single <> are placeholders. Replace as clarified in the enclosed text.
- Please retain the Template identifier in the lower left hand section of the footer.
- Remove this Tool Summary Sheet prior to use of this template.
- Please ensure that you acknowledge REDe in your document / publication.



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Quality Assurance Plan for Clinical Research Studies

Protocol Title: <Protocol Title>

Protocol Number: <#>

Version Number and Date:	Version <x.x>, <DDMMYYYY>
Funder:	<xxx>
Sponsor:	<xxx>
Sample size	<###>
Study Principal Investigator:	<PI Name and credentials>
Data Coordinating Center Data Management Contact(s):	

Summary of Changes:

Version Number	Version Date	Affected Section(s)	Summary of Revisions Made:

Template Version <e.g. 1.0.>, <Date>



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1. Procedure

Name of person(s) or organisation that will be performing the quality assurance:

[It is quite acceptable for a member of the study team to be assigned the task of study Quality Assurance Manager (QAM). 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. An external sponsor may have contracted this out to a Contract Research Organisation (CRO), or have their own QAM. If the study is being run within a network, it might be advantageous for a reciprocal monitoring scheme to be established. Whoever is conducting this study it is advisable for the investigator, and their study team to write this plan so that it is specific and appropriate for their study and circumstances.]

Details of timing of quality assurance activities

[This should begin as soon as possible after the study begins and the timing of this should be agreed between the investigator and the QAM and detailed here. Subsequent 'visits' should also be planned and recorded here. This will be a pragmatic decision based on whether it is someone internal or external.

The volume of work will be dictated by the frequency and time needed for these 'visits' it will depend on the number of participants, and how quickly they are enrolled.

An initial plan can be put in place based on estimated recruitment times - this can be adjusted as the study progresses, if needed. For the first 30 participants 100% SDV checking is recommended for all visits. For the remaining participants it is recommended that 25% of the data points are checked against the source data. Describe here which data points, for which visits will be checked, and how they will be selected.]

The documents and information needed should be thought about and detailed here 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 as detailed in the next section.

Details of the Quality Assurance Visits

[Detail here which people and what departments should be visited. This should include checking the storage of the study medication and drug accountability e.g. review drug accountability logs / stock management. For anti-malarial surveillance studies the laboratory data is key, and should be visited at appropriate intervals to observe PCR and microscopy procedures.

Template Version <e.g. 1.0.>, <Date>



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Appropriate arrangements with applicable personnel should be made in advance. If the healthcare facility where the study is being conducted does not have a system for patient notes, clinic diary, or drug accountability then you can design and provide a source data form.

For PCR and blood-slide reading quality standards procedures should be followed and compliance to these should be observed. These might be local standards or others and should be simply and concisely described here. Below is a table as a guide for each visit - this has been written specifically for a malaria drug surveillance study, using the WHO example protocol (Reference 2); it can be amended as considered appropriate and pragmatic for each study following an assessment of risk and complexity of the research.

For each visit the QAM should complete a 'Quality Assurance Visit Form'.]

Data point or Activity	Location/Source/People	100% Validation / Notes
Inclusion/exclusion Criteria: <i>[List criteria from the protocol]</i>	Clinic Patients notes / Laboratory records Other <i>(detail)</i>	100% of all participants
Informed consent provided	Signed Consent forms	100% of all participants
Blood test results PCR results	Laboratory records	100% of first 30 participants then 25% of subsequent participants enrolled. <i>Consider using a random selection system. Decide what is appropriate</i>
Serious adverse events Protocol violations Loss to follow up Withdrawals	Laboratory records, clinic records	100% validation checks.
Intervention administration and accountability – if applicable?	Patient notes Drug accountability records	100% of first 30 participants then 20% randomly selection of following
Participant attendance	Clinic Diary/patient notes	100% of first 30 participants then 20% randomly selection of following

Abbreviations

CRO	Contract Research Organisation	PI	Principal Investigator
GCP	Good Clinical Practice	QAM	Quality Assurance Manager
ICH	International Conference for Harmonisation	SDV	Source Document Verification

Template Version <e.g. 1.0.>, <Date>



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Appendix 2:

Data Management Plan



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STUDY TITLE

ISRCTN <####>

DATA MANAGEMENT PLAN

Version <1.1>

Authorised by:

Name:

Role:

Signature:

Date:

Prepared by

Name:

Role:

Signature:

Date:

<Study tile> Data Management Plan, Version <1.1>



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1. Key Personnel

[A section that details the name, their function in the trial, email address, telephone/fax number for all the staff involved in the trial including the sponsor, the project coordinator, the project manager, the investigators, study staff involved in the data management (including computing staff responsibilities for maintaining hardware and software), the monitors and anyone else associated with the trial]

2. Study Milestones

[All activities are listed from the protocol development till the end of the study analysis and finalisation of a study report and especially first and last patients enrolled, first and last CRFs sent to the data management, data validated and locked. This includes dates for when key milestones should be and have been reached, and can help to organise day to day data management activities in order to relate them to the planned timelines.]

Example

Activity	Planned date	Achieved date
Final protocol		
Final CRF		
Edit check designed and finalised		
Validation checks specified and finalised		
Database (field edition) specifications finalised		
Database application and testing		
First patient's first visit centre X centre XX		
First monitoring visit (FMV) centre X centre XX		
First CRF in data management centre (LDM) centre X centre XX		
Last patient's last visit		
Last CRF in data management centre		
Last query resolved – data cleaned		

<Study tile> Data Management Plan, Version <1.1>



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3. Data Flow

[A section that details the **flow of the data** from the field to the final storage.]

4. CRF Completion Guidelines

[A section that details how to **complete the paper CRFs** or how to enter data electronically. This document will be used to train investigators]

- This can be a separate document and included in the DMP as an appendix.]

5. Monitoring Plan

[A section that details the **monitoring plan** if monitors are involved in the trial. It will detail for example, the frequency of the monitoring visits, how the Source Data Verification will be done, what are the laboratory ranges for verification/clinical interpretation.]

6. Data Entry Guidelines

[A section that details **data entry**

- How to use the data entry system set up?
- Double or single data entry?
- What are the role and responsibilities of the study staff? For example, who has the responsibility for entering the data first, with which computer, who will enter data for the 2nd time? Who will merge the file to check for discrepancies? What are the procedures in case of discrepancy?]

<Study tile> Data Management Plan, Version <1.1>



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7. Data Edit Checks

[A section that details **edit checks** (data entry checks and post-entering data checks specifications) as described previously in this Session.]

8. Coding

[A section that details **coding** – the system you have implemented to assign standard codes using a classification system to clinical statements.]

9. Data Validation

[A section that describes the **post-data entry validation system**. With for example:

- Who checks the consistency of the data?
- Who queries the investigator?
- What is the format of a query form?
- How many days are allowed to answer to a query?
- Who decides that a query is resolved?]

10. Data Back-up and Archiving

[A section that describes procedures in place to ensure **data protection** including back-up system (if you don't do this you could lose the data!)]

<Study tile> Data Management Plan, Version <1.1>



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Appendix 3:

Standard Operating Procedure for Trial Monitoring / Quality Management



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Guideline summary sheet

- Tool:** Standard Operating Procedure for Trial Monitoring / Quality Management.
- Purpose:** To create a set of step-by-step instructions to help carry out routine monitoring at sites.
- Scope:** This document is designed specifically for investigators running all types of studies to guide the development of an operational tool to confirm quality and ethical standards within their studies. Therefore, this is a pragmatic approach that could be adapted for all non-interventional clinical research studies.
- Details:** The template should be customised to the protocol, the study's special needs / circumstances, and the requirements of the data capture system. Sections may be edited or deleted as needed.
- How to use this document:** The following steps are written to guide a study team in planning how to assure that high ethical and data standards are met for their antimalarial surveillance study.
- Items enclosed in single <> are placeholders. Replace as clarified in the enclosed text.
 - Please retain the Template identifier in the lower left hand section of the footer.
 - Remove this Tool Summary Sheet prior to use of this template.
 - Please ensure that you acknowledge REDe in your document / publication.



Standard Operating Procedure

SOP Ref No:	<xxx>
SOP title:	Trial Monitoring/Quality Management
Category:	General
Version	1.0
Date issued:	<<xx/xx/xx>
Valid until:	<xx/xx/xx>
Author(s):	Name: Signature: Date:
Approved by:	Name: Signature: Date:

Modification history:

Version Number	Version Date	Author(s)	Date reissued to previous recipients

<SOP Name>, Version <e.g. 1.0.>, <Date>



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1. Purpose

ICH GCP (1996) states that the Sponsor should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size and endpoints of the trial. In general, there is a need for on-site monitoring before, during and after the trial: however, in exceptional circumstances the sponsor may determine that central monitoring in conjunction with procedures such as Investigator's meetings and training, and extensive written guidance, can assure appropriate conduct of the trial in accordance with ICH GCP.

An important part of a monitoring visit is comparing the entries in the Case Report Forms (CRFs) with the original source documents (e.g. laboratory results, patient hospital notes, ECG printouts). This procedure is known as Source Data Verification (SDV).

At present it is extremely rare to be monitored by a non-commercial research body. Therefore, it is the responsibility of Medical Staff in particular the Investigator for the study, and appropriate staff team members to ensure high standards of data collection and SDV are maintained at all times.

This procedure describes the preparation for, and the procedure to follow, during and following monitoring visits.

2. Scope

This SOP applies to trials being led by _____ and sponsored by _____ and details the role of the investigators in governing trial monitoring.

3. Responsibility

Principal Investigators are responsible for ensuring that the trial is monitored correctly.

4. Procedure

4.1. Who?

Normally monitoring visits will be arranged in advance by the Monitor with the PI/Team Members as soon as possible after the first patient has been enrolled. If a patient is not entered within a reasonable time from study initiation, a visit should be planned to ascertain the reasons.

4.2. When?

Depending on the clinical trial, visits will probably take place approximately every six to eight weeks during the study. Depending on the length of the study and its progress, this interval may be prolonged or shortened.

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4.3. How?

All relevant documents should generally be gathered together before each monitoring visit.

4.4. Preparation

Where possible, all CRFs and the Study Master File (SMF) should be up to date, including any outstanding corrections from the last visit.

Source documents should be available in readiness for the monitoring visit. If a large number of subjects have been entered into a particular clinical trial the PI/other team member should agree with the Monitor, prior to each visit, on which subjects they wish to perform SDV.

During the visit a room or quiet desk should be booked for the use of the monitor. Details of the date of the next monitoring visit should be placed in the trial diary, to ensure meeting rooms are booked in advance.

4.5. During the visit

On the day of the monitoring visit the Lead Investigator or other nominated team member must be available to show the Monitor to their allocated meeting room and ascertain that the Monitor has all the required CRFs and source documents.

The PI should also be available on the day of the visit and preferably is available for at least a proportion of each monitoring visit.

The Monitor will normally require time to go through the CRF and associated source documents alone, with a meeting with the appropriate staff members afterwards to discuss any problems or outstanding business. Staff members should agree with the Monitor when to make themselves available for such a discussion.

The Monitor may also wish to visit other departments such as the pharmacy department to check storage of the study medication and drug accountability. If so, appropriate arrangements should be made in advance with the clinical trial pharmacist. It is the responsibility of the Monitor to request this in advance of the monitoring visit.

If the visit is because of a severe or serious adverse event, or some other specific problem, the Monitor should inform you of any special requirements beforehand.

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4.6. Following the visit:

Source documents should be returned to the respective departments.

CRF queries should be addressed promptly – they are easier to do when queries raised are fresh in your mind. Don't leave it until the day before the next visit.

Following each visit, it is the Monitors responsibility to provide a written report to the Investigator. The PI or other nominated team member must ensure any highlighted issues following the visit are dealt with promptly.

If the Monitor identifies issues related to non-GCP compliance, it is their responsibility to contact the Principal Investigator as soon as possible, by phone or email. It is the responsibility of the Principal Investigator to ensure that any issues relating to non-GCP compliance are dealt with promptly.

The written report must be filed in the appropriate section of the SMF.

5. References

None.

Abbreviations

GCP	Good Clinical Practice	PI	Principal Investigator
ICH	International Conference for Harmonisation	SDV	Source Document Verification
		SMF	Study Master File

<SOP Name>, Version <e.g. 1.0.>, <Date>



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Appendix 4:

**Template: Quality Assurance Visit Form
 Contents list for Study Master File**



[TEMPLATE] Quality Assurance Visit Form

Protocol Title:	
Quality Assurance Manager:	
Principle investigator:	
Date of visit:	

Study Summary

Planned enrolment	N. screened	N. enrolled	Ongoing	Complete	N. withdrawn	Drop out / Losses to FU

General Queries

Date	Nature of Query	Investigators Comment	Resolved/ongoing

Protocol Violations*

Event	Date	Description of violation; Action taken / will be taken:



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Enrolment, Consent, Follow-up visits and General Study Issues

Data point or Activity	Comment	% Validation
Inclusion/exclusion Criteria		
Informed consent forms		
Serious adverse events		
Participant attendance		
Intervention: adherence & accountability		
Study file		
Other		

Laboratory Sampling, handling and Procedures

Procedures	Comment
Processes for collection, identification, handling and timely delivery to the designated laboratory of samples	
Labelling and storage	
Microscopy standard procedures; including validation steps	
PCR standard procedures	
Are laboratory supplies sufficient with adequate shelf life?	
Microscope and other equipment (fridges) servicing, maintenance and calibration	
Data entry and data cleaning	



Others:

General Comments and visit review

Overall Comments and sign-off

Reported by:	Reviewed by:
Signature:	Signature:
Date:	Date:



[TEMPLATE] Contents List for Study Master File

1. Contact

[Front sheet with study title and a list of investigators]

2. Study Materials

- i. Final research protocol and previous amended protocols with version numbers
- ii. Current and previous versions of subject information materials given to study subjects
- iii. Copy of the informed consent agreement signed by subjects

3. Ethics

- i. Ethics approval letters
- ii. Any other ethics committee correspondences *[e.g. amendments, trial updates / annual progress report etc.]*

4. Agreements, Contracts & Finance

- i. Study agreements
- ii. Copy of insurance indemnity agreement / certificate / letter
- iii. Copy of financial information relating to the study

5. Study Logs

- i. Duty delegation logs
- ii. Enrolment logs
- iii. Training logs

6. Quality Assurance

- i. Quality Assurance Plan
- ii. Quality Assurance Report
- iii. Record of all reported SAEs and SUSARs

7. Laboratory details

- i. Lab documentation forms
- ii. Lab quality standards procedures

8. Data Management

- i. Data entry and validation checks procedures





ii. Data entry logs

[This is not exhaustive and other items you may wish to consider, and are not limited to:

- A section for Case Report Forms (CRFs), Dummy Tables, Statistical Analysis Plan – could be included in Section 8,*
- A section for the Investigational Product, e.g. Investigator's Brochure, any product information, Accountability etc.*
- A section for the Study Team, to include copies of CVs/GCP etc.]*

For more examples, please view the REDe website:

<https://rede.tghn.org/resources/>



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