



A STEP BY STEP GUIDE TO IMPLEMENTING

Good Clinical Practice Guidelines

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Glossary

Adverse Event	Any unexpected medical condition affecting a study participant.
Case Report Forms	A document on which all data is originally recorded. Once completed and checked it is then usually sent for data input.
Documentation	Any document that describes the methods, conduct and/or results of a study, the factors affecting a study, and the actions taken.
Good Clinical Practice (GCP)	A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of studies that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
Data and Safety Monitoring Board (DSMB)	An independent data monitoring committee that may be established to assess at intervals the progress of a study, the safety data, and the critical efficacy endpoints, and to recommend whether to continue, modify or stop a trial.
Informed Consent	A process by which a participant voluntarily confirms their willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the participant's decision to participate.
Investigator's Brochure	Clinical and non clinical information on the products being investigated in the study.
Institutional Review Board (IRB)	The body setup by the IMR who reviews study proposals to ensure the rights, safety and well-being of all participants. Once a study proposal is approved by the IRB it is automatically forwarded to the PNG MRAC for review.
Monitoring	The act of overseeing the progress of a study, and of ensuring that it is conducted, recorded, and reported in accordance with applicable GCP and regulatory requirement(s).
Participant	An individual, who has met specific criteria, has provided informed consent and participates in a Study.
PNG Medical Research Advisory Committee (PNG MRAC)	An ethics committee setup by the Department of Health in PNG to review all research proposals for scientific approval and ethical clearance. All study protocols or proposals involving human participants, must be submitted to and approved by the PNG MRAC prior to commencement.

Proposal	A document which provides a description of the background, rationale, objective(s), design, methodology, statistical considerations, and the organisation of a study. The protocol usually also gives the background and rationale for the study
Protocol	A document which provides the same type of information as the proposal but in more detailed format, which is generally prescribed by the sponsor and/or funding party. While every study will require an initial proposal, unless requested it is not necessary to provide a study protocol as well.
Protocol Amendment	A written description of a change(s) to, or formal clarification of a protocol.
Quality Assurance	Planned audits and reviews that are undertaken from time to time, to ensure that Study activities have complied with GCP and the applicable regulatory requirements.
Quality Control	Planned checks which are undertaken at the time of the Study activity to ensure they comply with GCP and the applicable regulatory requirements.
Quality Management	The overall plan for conducting both Quality Assurance and Quality Control activities, to ensure compliance with GCP and the applicable regulatory requirements.
Serious Adverse Events	Untoward medical conditions, in any participant which results in: <ul style="list-style-type: none"> • Death, • Life threatening situation/s, • Inpatient hospitalization or prolongation of existing hospitalisation, • Persistent or significant disability/incapacity; and/or • A congenital anomaly/birth defect.
Source Documentation	Original documents, data and records including but not limited to case report forms, laboratory logs, and health record books.
Standard Operating Procedures (SOPs)	Detailed, written instructions on how to achieve uniformity of Study activities, and comply with GCP and the applicable regulatory requirements.

About Good Clinical Practice Guidelines

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects. By implementing and then complying with the IMR GCP system we can be better assured that the rights, safety, and well-being of participants are protected and that the data are credible. This same standard is being applied in studies across the world including those conducted in Europe, Japan, and the United States.

This manual will assist Principal Investigators, Study Coordinators and other research team members to implement and maintain the IMR GCP System. It is not intended to provide details and information on the entire study, but to highlight the areas important to our GCP system. Researchers and other study staff will still have to apply their own particular skills and experience in areas that are specific to their study. Suggestions on how to obtain additional information have also been included.

To make things as easy as possible, each section will refer to generic Standard Operating Procedures (SOPs) and templates both of which have already been developed, for your convenience. A list of generic SOPs can be found in Appendix A and a list of templates in Appendix B.

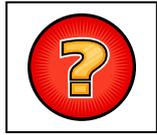
In addition, the manual provides you with tips and suggestions, as well as a summary of essential documents, at the end of each section. The following symbols will guide you along the way.



This symbol identifies when you should read a Generic SOP, or an IMR Management Policy, and take any necessary action. Generic SOPs and IMR Management Policies can be found at www.intranetaddress.imr or alternatively ask your Administration or Site Manager.



This symbol lets you know when you should take additional steps to help with implementing the GCP System.



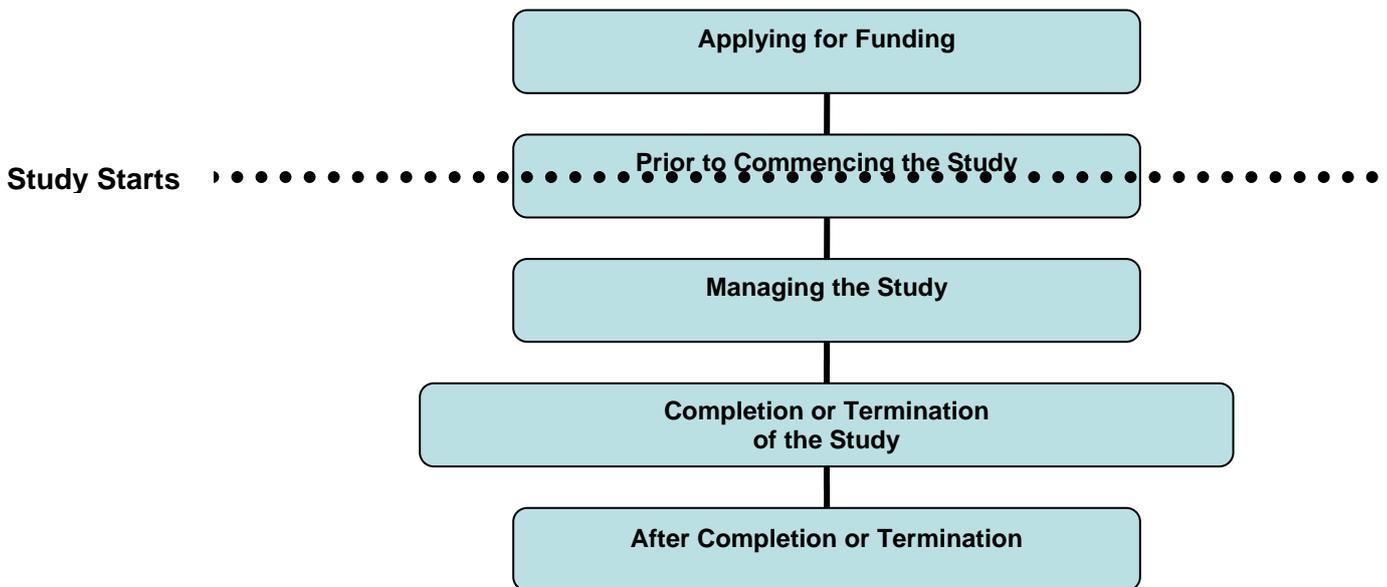
This symbol is used to identify tips and suggestions, which might help or guide you along the way.



This symbol highlights some of the essential documents that must be obtained and collected prior to moving on to the next section. A full list of documents that may be applicable to your study can be found in Appendix C.

An Overview of the Process

At IMR the GCP implementation and management process is divided into 5 distinct parts, as depicted in the following flowchart:



The application process involves:

- developing the initial research proposal
- developing the study protocol (if required)
- obtaining Institutional Review Board and Ethics Approval

Prior to commencement you need to ensure that you:

- setup a hardcopy and electronic document filing system
- organise staff

- obtain resources
- obtain drugs and/or vaccines
- compile study SOPs
- create study database/s
- obtain insurance (if required)
- develop a line of communication
- prepare a Quality Management Plan
- prepare an Adverse Event Plan
- prepare a study Activity Schedule
- setup initial templates
- train and prepare study staff
- distribute appropriate documentation
- undertake pre trial monitoring (if required)

Managing the study includes:

- managing the study protocol and activities
- managing adverse and severe adverse events
- managing the SOPs
- managing the study Activity Schedule
- managing staff
- managing source documentation
- managing quality
- managing finances
- managing external monitoring (if required)
- reporting

Upon completion or termination ensure that you:

- submit final report(s)
- complete financial accounts
- organise a final monitoring visit (if required)

- dispose of supplies
- archive databases, samples and documents

After completion or termination IMR will still need to:

- manage archived databases, samples and documentation

Where Do I Find Things

SOPs Already Developed By the IMR

The IMR has already developed some Generic SOPs which are referred to throughout this Information Pack. These can be found on the IMR Intranet sites in Goroka and Madang. Alternatively a hardcopy of these SOPs can be obtained from your Administration or Site Manager.

Templates Already Developed By the IMR

The IMR has already developed some Templates which are referred to throughout this Information Pack. These can be found on the IMR Intranet sites in Goroka and Madang. Alternatively a hardcopy of these Templates can be obtained from your Administration or Site Manager.

IMR Policies and Procedures

These can be found on the IMR Intranet sites in Goroka and Madang. A hardcopy of the policy may be obtained from your Site Administrator.

Additional Information

National Institute of Health (NIH) <http://www.nih.gov/>

Division of Microbiology and Infectious Diseases (DMID) <http://www3.niaid.nih.gov/about/organization/dmid/>

U.S. Food and Drug Administration (FDA) <http://www.fda.gov/default.htm>

Office of Human Research Protection <http://www.hhs.gov/ohrp/>

World Health Organization (WHO) <http://www.who.int/>

European Forum for Good Clinical Practice http://www.fda.gov/ohrms/dockets/dockets/04n0018/04N-0018_emc-000021-01.pdf

Belmont Report	http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4178b_09_02_Belmont%20Report.pdf
Declaration of Helsinki	http://www.wma.net/e/policy/b3.htm
45CFR46-Human Subjects Protection	http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
FDA Good Clinical Practice (ICH E6)	http://www.fda.gov/cder/guidance/959fnl.pdf
What is a Clinical Trial?	http://www.niaid.nih.gov/clintrials/clinictrial.htm
General Information on Protecting Human Subjects	http://www.hhs.gov/ohrp/policy/index.html

The Application Process

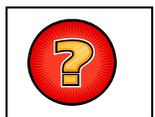
The best time to start to implement and manage a GCP system is before you start writing the study proposal. The IMR Research Policy encourages and supports the implementation of GCP compliant studies.

Developing an Initial Research Proposal



Read the following IMR Management Policies:

- Research Policy and associated procedures.
- Finance Policy and associated procedures



It's a good idea at this stage to make sure that the Principal and Sub Investigators you intend to involve are both willing to take part in, and have the necessary qualifications relevant to this study.



Read the SOP - Investigator Qualifications and Agreements.



Another tip is to ask for assistance from other staff at the IMR. For example the Database Manager might be able to assist you to identify what data to collect and how you might analyse it.



Setup a folder on the "S" Drive with the proposed name of the Study for all electronic documents. In addition setup a proposal folder within your filing cabinet, for all of the hardcopy documentation including drafts of the proposal, letters etc. Don't forget to keep a copy of all important documentation. You never know when you might need it.



In order to find things quickly, use a specific format for filing all electronic documents. We suggest the following filename format, which is also explained within the SOP – Filing Electronic Documents:

The filename of any Study document should comprise of:

1. Type of document – ie Protocol, Letter, Note, SOP, Report
2. Name of person receiving or name document if applicable – ie John Smith in the case of a letter, or Filing Electronic Documents for an SOP

3. First and last initial of person saving the document – ie CD for Carol Davy
4. Date of this version – ie 011205 for 1st December 2005
5. Version number – ie V1 or V2 or V3

Each item is separated by a “-“

A proposal to WHO written by Peter Siba on the 1st March 2006 would have a filename of:

Proposal-WHO-PS-010306-V1

You can automatically place this filename at the bottom of each document for easy identification. See SOP – Filing Electronic Documents to see how to create footers in word and excel documents.

Obtaining a Funding Agreement

Once the proposal has been accepted a written agreement between the funding body and the IMR must be entered into. This written agreement must be reviewed and if acceptable signed by the Director of the IMR, before continuing.



Read the IMR Research Policy and associated procedures.

Developing a Protocol (if required)

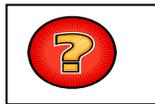
Once the proposal has been accepted, the funding body may also require you to submit a protocol. A protocol is a document that describes the objective(s), design, methodology, statistical considerations, and the organisation of a study. The protocol usually also gives the background and rationale for the study.

If applicable the following attachments should be affixed to the protocol:

- Investigator’s Brochure
- Participant Information and Consent Form
- Case Report Form
- Curriculum Vitae of all named Principal and Sub Investigators



Read the SOP entitled “Protocol Development and Approval”.



The approved Study Protocol must be adhered to at all times, and any changes will need to go through a strict and time consuming approval process. Therefore it is important that you concentrate on “what” will be done, and keep details about “how” you will do it to a minimum. Specific information about processes and procedures should be left wherever possible to the SOPs, which are easier to change if required.

Obtaining Institutional Review Board & Ethics Approval

Prior to commencing any study involving the IMR, which involves human participants, the Principal Investigator must ensure that approval from the two following ethical committees is obtained in writing.

- **IMR IRB**
Contact at the IMR is Ms Norries Pomat – Goroka Site
Meets approximately 6 times per year
Information available on the IMR Intranet at:
<http://intranet.imrgka.pngimr.org.pg/>
- **Papua New Guinea Medical Research Advisory Committee**
Contact at the IMR is Ms Norries Pomat – Goroka Site
Information available on the IMR Intranet at:
<http://intranet.imrgka.pngimr.org.pg/>

Documents should firstly be sent to the IMR IRB for review. If the IMR IRB approves the Study Protocol or Proposal, they will forward the documents to the Papua New Guinea Medical Research Advisory Committee.



Read the SOP entitled “Ethics Approval”.



The following documents where applicable, must be sent to the IMR IRB at least two weeks prior to the next scheduled meeting:

- trial protocol or proposal;
- written informed consent form(s) that;
- subject recruitment procedures (e.g. advertisements);
- written information to be provided to subjects;
- Investigator’s Brochure;
- available safety information;
- information about payments and compensation available to subjects;
- investigator(s) current curriculum vitae and/or other documentation evidencing qualifications; and
- any other documents that the IRB members may require to fulfill their responsibilities.



This process can take up to 4 months. Always allow plenty of time for obtaining both of these approvals.



Both the IRB and MRAC may ask for additional information, reject your application or approve your study. ***You must receive written approval from both committees prior to commencing the study.***



Essential Documents

You need to have copies of the following documents in your filing system before continuing:

- Proposal
- Budget
- Written agreement with funding body
- Curriculum Vitae, and applicable qualifications and licenses of all Principal and Sub Investigators
- Study Protocol (if required)
- Investigator Brochure (if required)
- Information to be provided to participants
- Informed Consent Forms in all languages
- Case Report Forms
- IMR IRB approval
- PNG MRAC approval
- All official correspondence relating to the above

Prior to Commencement

Now that you have the required approvals and agreements, it is time to start gathering resources and setting up the systems which will help ensure a successful outcome to your study.

Setting Up a Hardcopy and Electronic Filing System

To comply with our GCP system you must setup both a hardcopy and an electronic filing system which contains and limits access to, all of the **documents** listed at the end of each chapter and in Appendix C. Most of the documentation will be filed in one Study Master File, setup at the main Study site. If however, you are conducting your study at several different sites, you will need to set up a filing system at each site which will hold documentation specific to that particular study site.



Read the following SOPs:

- Filing Electronic Documents
- Filing Hardcopy Documents

Organising Your Study Staff

The things you need to ask before you start to find staff for your study, are:

- What skills, qualifications and experience do we need?
- How many people do we need in each area?
- When would we like them to start?
- How long do we need them for?
- How much will this cost the study – ask your human resource officer about additional costs which can include:
 - An additional 8.4% for superannuation
 - Accommodation costs if provided
 - Gratuity dependent on salary level
 - International or domestic market allowance if applicable



Read the SOP entitled “Defining Responsibilities”.



Don't forget that some the staff that you may need for your study could already be working for the IMR. Employing staff that are not fully utilized or are about to finish on another IMR study will be beneficial not only because you will usually know the person and their skills, but also because it will save the time and effort needed to recruit staff from outside the organization.



If you do need to recruit staff from outside the organization, read the IMR Recruitment Policy.



In addition, any research staff will need to read and sign a Research Code of Conduct. The Research Policy will provide more information about this Code.

Obtaining Resources

Apart from staff, you may need to purchase additional resources before you start such as field and laboratory supplies, equipment, consumables. As the following questions before you even start:

- What do we need?
- How much do we need?
- When do we need it?
- How much will it cost?
- Do I have the funding?



Read the following SOPs:

- Supplies Monitoring and Storing
- Supplies Shipping and Receiving
- Supplies Storage



When ordering any resources you will need to read the Procurement Policy.

Obtaining Study Drugs and/or Vaccines (if required)

If your study involves the use of drugs and/or vaccines, particular care must be taken, with shipping, storage and even disposal. You may need to for example obtain special authorization from the Papua New Guinea Department of Health to import particular drugs or medicines.

At a minimum:

- Keep a sample of labels attached to the drugs and/or vaccines
- Keep a copy of the instructions for handling the drugs and/or vaccines
- Make appropriate arrangements for storing drugs and/or vaccines.



Read the following SOPs:

- Supplies Monitoring and Storing
- Supplies Shipping and Receiving
- Drugs & Vaccines Storage and Handling

Compiling Study SOPs

SOPs specify how study activities must be performed. They ensure consistency, quality and accuracy in all study activities. Therefore, SOPs should be developed for all of the main processes involved in your study. For example, if it is important to your study that samples are collected in a particular way, you will need an SOP for this process.

In order to ensure that you have all of the SOPs you need for your project you will probably need to:

- use the “Generic” SOPs developed by the IMR. These have been developed for all of the common study activities (see Appendix A) and you can adopt any or all of these SOPs without any further approval, and/or
- adjust the “Generic” SOPs developed by the IMR to make them more applicable to your study. If you adjust any SOP you must obtain approval for the change from the Director and a Unit Head before using, and/or
- develop your own SOPs to describe activities which are unique to your study. You will need to ensure that the Principal Investigator and a Unit Head approve the SOPs before use.



Read the SOP – SOP Development



IMR has written the generic SOPs so that they specify the minimum acceptable standard. Therefore if you need to change a generic SOP you must ensure that it at least maintains the minimum standards. For example the SOP – Informed Consent specifies that all participants must have voluntarily agreed to participate in the study. You must ensure that if you make changes to this SOP this requirement is maintained.

Creating the Study Database/s (if required)

If you are creating database/s to collect and analyse your data, you will need to develop these before you start collecting your data. Hopefully, in accordance with the tip in Chapter 2, you have already talked to the database manager about what data to collect and how these might be analysed.



Read the SOP – Database Creation

Data Safety Monitoring Board (if required)

Some studies will require the setting up of a Data Safety Monitoring Board, which is an independent data monitoring committee that may be established to assess the:

- progress of a study
- safety of participants, and
- viability and efficacy of results.

If the Study Protocol specifies a blinded study, the Data & Safety Monitoring Board may also

- maintain a list of study codes, and
- if required, review requests to unblind of the study.

In reviewing the study, the Data & Safety Monitoring Board may if it feels necessary, recommend to modify, temporarily halt, or terminate a study. If any of these actions are taken, the IRB must be informed immediately.



Read the SOP – Data Safety Monitoring Committee

Obtaining Insurance (if required)

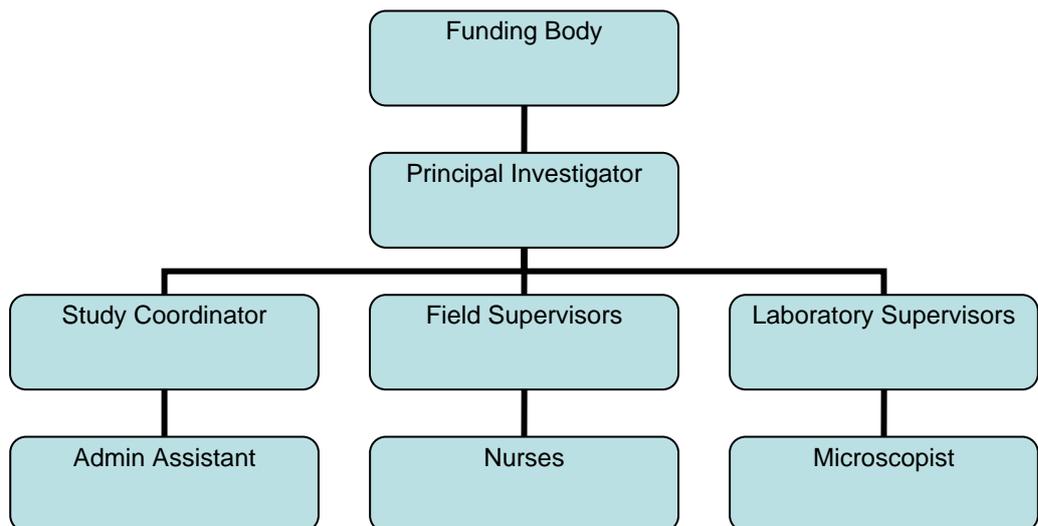
Workers compensation is already in place at the IMR. However, if the funding party also requires professional indemnity insurance, you will need to organize this for your study. The funding body will usually tell you how much you may require, and you should contact the Financial Manager to find out the contact numbers of insurance agents who can provide the IMR with a quote.



Professional indemnity insurance provides insurance cover in case the action of any study staff member causes harm.

Developing a Line of Communication

It may not seem important now, but if you have more than 3 staff working on your study it may be a good idea to develop a line of communication which ensures that people are aware of who to contact to answer questions and provide information. This includes identifying one person, normally the Principal Investigator, who communicates with the funding body. A line of communication might look like:



Preparing a Quality Management Plan

An important function of the GCP System is to ensure the quality of all study outcomes. It is necessary before you start the study to develop a Quality Management Plan which specifies how and when you are going to apply quality management measures. There are two quality activities that you will need to plan for:

1. Quality Controls

These are quality checks that occur at the time of a study activity. Quality Control checks **must be in place** for all data handling activities and may also be developed for other important study activities. They are added as a step or steps to each relevant SOP. For example, we have already added the following Quality Control step to the generic SOP – Case Report From Management and Tracking.

Review each CRF ¹ in batch ² to ensure both legible and complete, and discuss how to correct the CRF ¹ with appropriate Field supervisor if not.	Study Coordinator	Within 2 wkng days of receiving
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2. Quality Assurance

This is an audit that looks at what has already happened, to see if study activities have been conducted in accordance with the GCP system. For example the Quality Assurance audit might include ensuring that the Master Study File has all of the essential documentation that it should have. It is suggested that you should undertake a Quality Assurance audit at least once every 6 months.



Read the following SOPs:

- Quality Management
- Quality Assurance

Preparing an Adverse Event Plan

Prior to starting the study, you will need to decide how and when you should report any medical occurrence in a study participant. The first step is to decide what will be defined as a Serious Adverse Event and what can be considered as an Adverse Event. This is because each will be treated differently. For reporting purposes:

- Serious Adverse Events must be treated in accordance with the SOP – Serious Adverse Events. In terms of notification Serious Adverse Events should for example be reported to the Data Safety Monitoring Board and IRB within a specified timeline.
- Adverse Events need amongst other things to be recorded and tracked for monitoring purposes but there is not the same urgency to report them to other parties.

While recording and notification is extremely important, the first priority is always to ensure the safety of participants.



Read the following SOPs

- Adverse Events
- Serious Adverse Events

Preparing a Study Activity Schedule

Lots of studies use what is commonly known as a Project Management System to identify what activities have to be done, by whom and when. These systems are normally very complicated and take a lot of time to develop and maintain. Instead, a simple Study Activity Schedule can be setup in Excel.

Just open up a new excel document. Name the first column “Date”, second column “Activity”, third column “Responsible Party”. Then list all of the major study activities under the column marked “Activity”. These might include interim and final reports, purchasing of supplies, quality assurance audits, external monitoring visits, the start of field trips or any other activity which needs to be started or completed by a particular date. Complete the columns entitled “Date” and “Responsible Party” with the appropriate detail for each Activity. They don’t have to be in any particular order because you can use the “Sort” function later to sort in order of “Date”, or even “Responsible Party”. An example of a Study Activity Schedule may look like:

Date	Activity	Responsible Party
1/02/2006	Place order for clinical supplies	Procurement Officer
4/03/2006	First Interim Report Due	Principal Investigator
7/03/2006	Organise meeting with Funding Body	Study Coordinator
9/04/2006	Organise field trip	Field Supervisor
10/04/2006	Attend meeting with Funding Body	Principal Investigator



If you are not sure how to use excel, ask the Data Manager or someone from the Computing Department.

On a regular basis a study staff member will need to check the Study Activity Schedule for up and coming activities, and remind the Responsible Party. They can also add and change dates of Study Activities, as required.

Setting Up Initial Templates

To make things as easy as possible, the IMR has developed some generic templates that can be used to record and disseminate information. Some of them will be helpful and some of them wont. You may even need to change these templates to suit your particular needs or develop your own. It is not necessary to obtain any approval if you change an existing template or develop your own. A list of Generic Templates can be found in Appendix B.

Training and Preparing Study Staff

There are three possible levels of training that you may need to consider.

1. GCP System Training

The IMR has developed a GCP Training Pack which can be obtained through your Human Resource Officer or Site Manager. All researchers, clinicians, study coordinators, laboratory staff, nursing staff and person who is responsible for supervising other study staff members must complete this training prior to commencing study activities.

2. SOP Specific Training

Study staff members must all be aware of their particular study responsibilities, and what procedures they need to follow in carrying these out. This can be achieved by providing them with and reviewing the SOPs relevant to them. Their direct supervisor should also be involved in this. It may be necessary to consider how to explain and continue to remind people of their responsibilities, especially if English is a second language.

3. Skills and Knowledge

You must ensure that each study staff member is appropriately qualified and has the necessary skills, experiences and knowledge to carry out their particular responsibilities. In most cases IMR would expect that Study staff are appropriately trained prior to being employed, however in certain situations it may be necessary to provide unique training. You must make sure that additional funding is provided within the Study budget, prior to authorizing this type of training.



Read the following SOPs

- Training and Qualifications
- Defining Responsibilities



Don't forget to fill in the training log whenever a staff member undertakes any study specific training.

Distributing Appropriate Documentation

One copy of each approved SOP now needs to be placed in each Study SOP Folder and distributed to the appropriate parties. It is not necessary or advisable to provide a Study SOP Folder to all study staff members. In most cases one Study SOP Folder should be provided to each of the following individuals:

- Principal Investigators
- Sub Investigators
- Clinicians
- Study coordinators
- Supervisors whether they are in the laboratory or the field.

Templates should only be provided to those people who are responsible for completing them.

A copy of all SOPs and Templates should be kept in the Master Study File.



Read the SOP – SOP Development

Undertaking Pre Trial Monitoring (if required)

The sponsoring party and/or funding body **may** a pre trial audit. This is to ensure that all of the required resources and systems are in place to ensure that the rights, safety, and well-being of participants are protected and that the data are credible.



Read the SOP – External Monitoring



Essential Documents

You need to have added the following documents to your filing system before continuing:

- Checklist GCP Documentation
- Responsibility Log
- Authorisation for import of drugs and/or vaccines (if required)
- Sample of the drug and/or vaccine labels (if required)
- Instructions for the use of drugs and/or vaccines (if required)
- Drug or Vaccine Specification (if required)
- Drugs and Vaccines Log (if required)
- Study Order Log
- Supply List
- Sample Shipping Log
- Study SOPs
- Certificate of Insurance (if required)

- Line of Communication
- Quality Management Plan
- Adverse Event Plan
- Study Activity Schedule
- Incoming Mail Log
- Outgoing Mail Log
- Signature Log
- Training Log
- External Monitors Log (if required)
- Pre Trial Monitoring Report (if required)
- Any official correspondence relating to the above

Managing the Study

Now that you have completed all of the required steps detailed in Chapter 3, you should now be in a position to commence study activities. Throughout this stage it is important to continually review and maintain the systems that you have now put in place.

Managing the Study Protocol

As you may remember from above, changes to the approved Study Protocol including any attached documents listed in Chapter 3, cannot be made unless approved by the IRB. Although this should be avoided, there is a protocol amendment application process. You must ensure however, unless there is a risk to an individual's safety, the application for an amendment to the protocol and/or attached document is approved prior to implementation.

In addition any deviation from the approved Study Protocol and/or attached documents should be reported to the IRB and any other required parties immediately.



Read the following SOPs

- Protocol Compliance
- Protocol Amendment
- Protocol Deviation

Managing Adverse and Severe Adverse Adverts

Previously you have identified what is considered to be an Adverse Event as opposed to a Severe Adverse Event. Adverse Events must be recorded and reported in accordance with the Adverse Events Plan. Severe Adverse Events however must always be treated in accordance with the following SOP.



Read the SOP – Severe Adverse Events

Managing SOPs

Unlike the Study Protocol, the SOPs are flexible documents. Providing that appropriate approvals are provided prior to implementing, changes can be made as required throughout the study.

Changes can be identified either through regular SOP reviews or alternatively if study staff members identifies a need, and the principal investigator agrees with the suggested change.



Read the SOP – SOP Maintenance

Managing the Study Activity Schedule

A senior study staff member, usually the Study Coordinator must review and manage the Study Activity Schedule at least once per week. This includes identifying activities that need to be undertaken and reminding the Responsible Party. They can also add new Study Activities and change dates, as required.

Managing Study Staff

When new staff join the study they will need to undertake GCP System Training and SOP Specific Training. In addition a review of the individual's qualifications, experience and knowledge should be undertaken to ensure that they are able to carry out their responsibilities.

If existing staff change roles and/or responsibilities you will also need to ensure that they receive SOP Specific Training and a review of their qualifications, experience and knowledge is undertaken, to ensure they are able to carry out their new responsibilities.



Read the following SOPs:

- Training and Qualifications
- Defining Responsibilities



Don't forget to fill in the training log whenever a staff member undertakes any study specific training.

Managing Source Documentation

All of the source documents that your study will complete and/or collect will be listed in the Protocol. These documents must be collected and filed within either the Site or Study Master Files.

Where the Study staff are creating a source document such as a Case Report Form or a Laboratory Log, we must ensure that all writing is legible and that any errors are corrected by placing a horizontal line through the word or number, writing the correct word as near as possible to the correction and signing and dating the correction.



Read SOP – Case Report Form Management as an example

Sometimes source documentation is a copy of a document produced by somebody external to the study ie a health centre in the case of the Health Record Book. As soon as you receive this copy, you must write on each page the words “**Certified Copy**”, followed by your signature and the date.

One of the most important source documents is the Informed Consent. This should be checked prior to filing or even leaving the field site, to ensure that the correct version of the informed consent has been used, in addition to ensuring that all of the required parties have signed and that they have recorded the correct date on the form. An additional note should be made on a separate document, usually the Case Report Form, to say that the informed consent process for this participant has been completed.

Managing Quality

Measures to ensure quality outcomes must be undertaken throughout the study in accordance with the Quality Management Plan, discussed in Chapter 3. This Quality Management Plan must also be reviewed and updated at least every 12 months.



Read the following SOPs:

- Quality Assurance
- Quality Management Plan

Managing Finances

At least once per month it will be necessary to check the study's Cost Centre Report and ask the following questions:

- Have we received all of the expected funding in comparison to the budget?
- Are any areas overspent in comparison to the budget?
- Are any areas under spent in comparison to the budget?
- Are there any errors or omissions in the Cost Centre Report?

If you identify any queries or potential problems, speak to the Financial Manager immediately.



The Financial Policy will provide more information including your responsibilities in regard to reviewing Cost Centre Reports.

Managing External Monitoring

The sponsoring party and/or funding body **may** require you to undertake, or alternatively they may send, an external monitor to conduct audits at intervals throughout the study. This is to ensure that all of the required resources and systems are in place to ensure that the rights, safety, and well-being of participants are protected and that the data are credible.



Read the SOP – External Monitoring

Reporting

You will need to provide the IRB with several different types of reports throughout the study:

- A written report must be provided at least every 12 months, unless otherwise specified, summarizing the status of the study.
- A written report must be provided as soon as possible, about any changes significantly affecting the conduct of the study, and/or increasing the risk to participants.
- Written notification any suspension to the study providing details of the reasons for that suspension.
- As discussed previously the IRB will need to be informed in writing of all Serious Adverse Events

In addition other parties such as your funding body or sponsor, if you have one may also need regular reports. Refer to funding and sponsor agreements for these requirements.



Read the following SOPs:

- Reporting
- Serious Adverse Events



Essential Documents

You need to have added the following documents to your filing system before continuing:

- Applications and approvals or Protocol Amendment
- Notification of Protocol Deviations
- Severe Adverse Event Reports and associated documentation
- Approved new versions of SOPs
- Curriculum Vitae, and applicable qualifications and licenses of any new Principal or Sub Investigators
- Records of Adverse Events
- Quality Assurance Audit Reports
- Cost Centre Reports
- External Monitor Reports (if required)
- All reports
- Any official correspondence relating to the above

In addition to all of the documents collected so far, you will should also have on file specific items pertaining to study activities:

- Signed informed consent forms
- Completed case report forms
- Other source documentation

Upon Completion or Termination

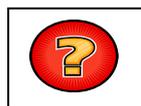
A study can end either because it has been completed or because it has been prematurely terminated. In either case your responsibility does not end there. The following chapter describes what the GCP system requires you to do upon completion or termination.

Submission of Final Reports

Studies will need to provide a final report to the IRB. In addition the following parties may also require a final report:

- Funding party
- Sponsor
- Other collaborating parties

Do not archive any of the study material, until you have received notification preferably in writing, that they have accepted these final reports.



Don't forget that if a trial is terminated you must immediately inform the IRB in writing, giving a detailed explanation as to the reasons for the termination.



Read the SOP – Reporting

Reporting Back to the Community

In line with the Research Code of Conduct, Principal Investigators will need to make every effort to inform the study participants and/or participating community about the results of the study. Where ever available, IMR Community Liaison Officers should be involved in this process.



The Research Policy will provide more information including your responsibilities in regard to communications with the community.

Completion of Financial Accounts

Just like the acceptance of final reports, you will need to ensure that the financial accounts are complete. This includes ensuring that:

- All funding has been received and recorded
- All expenses have been received and recorded
- The Cost Centre Report is accurate and complete
-



Talk to the Financial Manager before closing the financial account. They can assist you with ensuring that the account is accurate.



The Financial Policy will provide more information including your responsibilities in regard to reviewing Cost Centre Reports.

Organising a Final Close-out Monitoring Visit

The sponsoring party and/or funding body **may** require you to undergo a Final Close-out Monitoring Visit conducted by an external monitor. This is to ensure that the study has been conducted in accordance with the GCP system, and to ensure that there are appropriate resources and systems in place to protect the rights, safety, and well-being of participants in the future.



Read the SOP – External Monitoring

Disposing of Supplies

In most cases the disposing of supplies will be determined by what the supplies are, and therefore study specific SOPs will need to be developed. In the case of dangerous drugs for example, a specific SOP for the destruction of these items will be required. In any circumstances however, a record of all supplies that have been disposed of will be required. You will need to record:

- What was disposed of
- The quantity that was disposed of
- Who disposed of the supplies
- Date of disposal
- Method of disposal

Archiving Databases, Samples and Documents

While all data, information and samples collected as a result of study activities need to be appropriately archived to ensure the privacy of the participants, it is also important to allow for easy authorised retrieval where and when appropriate. In most cases all archives should remain within IMR facilities, however if this is not possible, the location details of archives held outside of IMR facilities must be accurately recorded.

The following time limits will apply **only if** the Study Protocol does not specify time limits for destroying archived items:

- Databases – must be kept indefinitely
- Samples – must be kept indefinitely
- Documents – kept for 5 years



Read the following SOPs

- Database Archiving
- Sample Archiving
- Archiving Hardcopy and Electronic Documents



Essential Documents

You need to have added the following documents to your filing system before continuing:

- Final reports
- Written acceptance of final reports
- Complete financial cost centre report
- Close-out external monitoring report (if required)
- Record of disposed supplies
- Index of archived documents
- Any official correspondence relating to the above

Upon Completion or Termination

There is an ongoing commitment to preserving the outcomes of the study, including the archived databases, samples and documentation. These responsibilities will rest primarily with the following areas and staff:

- Database/Computer Manager – archived databases
- Laboratory Manager – archived samples
- Documentation – archive officer

These people will ensure that archived items are kept for the required time, in a way that allows for easy access by authorized staff. The Study's Principal Investigator or the Director of the IMR may authorize staff to access these archives if they feel that there is sufficient reason to do so. Appropriate reasons for accessing files may include:

- to ensure the safety and well-being of any participant;
- where access had been provided for within the approved Study Protocol; or
- where approval had subsequently been given by the IRB.

Appendix A

Generic SOPs

- Adverse Events
 - Archiving Hardcopy and Electronic Documents
 - Case Report Form Management and Tracking
 - Computer Backup
 - Data & Safety Monitoring Board
 - Data Entry and Validation
 - Database Archiving
 - Database Creation
 - Defining Responsibilities
 - Drug & Vaccine Storage and Handling
 - Ethics Approval
 - External Monitoring
 - Filing Electronic Documents
 - Filing Hardcopy Documents
 - Informed Consent
 - Investigator Qualifications and Agreement
 - Institutional Review Board
 - Microscopy Staining and Reading
 - Protocol Amendments
 - Protocol Compliance
 - Protocol Development & Approval
-

- Protocol Deviation
- Quality Assurance
- Quality Management
- Reporting
- Sample Archiving
- Sample Shipping & Tracking
- Sample Storage
- Serious Adverse Events
- SOP Development
- SOP Maintenance
- Supplies Monitoring & Ordering
- Supplies Shipping & Receiving
- Supply Storage
- Training and Qualification

Appendix B

Templates

- Adverse Event Plan
 - Backup Register Log
 - Batch Entry Log
 - Batch Header
 - Checklist For GCP Documentation
 - Database Access Log
 - Database Requirements Specification
 - Database test Specification
 - Drug or Vaccine Specification
 - Drugs and Vaccines Log
 - External Monitor's Log
 - Incoming Mail Log
 - Index of Archived Documents
 - Outgoing Mail Log
 - Protocol Amendment Form
 - Protocol Deviation Report
 - Quality Assurance Audit Report
 - Responsibility Log
 - Sample Shipping Log
 - Serious Adverse Event Report
 - Signature Log
 - SOP Template
-

- Study Order Log
- Supply List
- Training Log

Appendix C

List of GCP Documents

Document Name:	To Be Kept In:	Notes
Category - Agreements		
Submission Letter	Study Master File	
Principal Agreement	Study Master File	
Principal Financial Agreement	Study Master File	If not in Agreement
Insurance Statement	Study Master File	If required
Associated Agreement/s	Study Master File	
Associated Financial Agreement	Study Master File	If required
Category – Study Information		
PNG IMR Directors approval of Study Protocol	Study Master File	
Letters of support from PIs and collaborating organisations	Study Master File	
Protocol	Study Master File	Approved and signed by IRB & MRAC
Protocol Amendment Form	Study Master File	
Protocol Deviation Reports	Study Master File	
Case Report Form/s Blank Example	Study Master File	Approved and signed by IRB & MRAC, Original and Amendments
Informed Consent Forms Blank Example – Original	Study Master File	Approved and signed by IRB & MRAC, Original and Amendments
Informed Consent Forms Blank Example – Translations	Study Master File	Approved and signed by IRB & MRAC, Original and Amendments
Advertisements & Information to Participants	Study Master File	Approved and signed by IRB & MRAC, Original and Amendments
Category – Regulatory		
Membership of IMR Institutional Review Board (IRB)		
IMR IRB Approvals	Study Master File	Original and Amendments
PNG Medical Research Advisory Board (MRAC) Approvals	Study Master File	Original and Amendments
Form FDA 1572	Study Master File	Original and Amendments

Document Name:	To Be Kept In:	Notes
Other IRBs and/or Ethics Committees Approvals	Study Master File	If Required, Original and Amendments
Data and Safety Monitoring Board Terms of Reference	Study Master File	If Required, Original and Amendments
Other Regulatory Authorities Approvals	Study Master File	If Required, Original and Amendments
Periodic Principal Investigators Reports to IRBs and ethics committees	Study Master File	
Final Principal Investigators Report to IRBs and ethics committees	Study Master File	

Category - Supplies

Study Order Log		
Study Supply List	Study Master File	
Supply Disposal Log	Study Master File	
Shipping Log	Study Master File and Site Files	
Shipping Receipts	Study Master File and Site Files	

Category – Drug and Vaccine Specific (If applicable)

Investigator Brochures and updates	Study Master File	Original & Amendments
Safety Information on Investigation Products and updates	Study Master File	Original & Amendments
Drugs and Vaccines Log	Study Master File	
Drug and Vaccine Specifications	Study Master File	
Copy of Investigational Product Labels	Study Master File	
Certificates of analysis of Investigational Products	Study Master File	

Category - Staffing

Responsibility Log	Study Master File	
Signature Log	Study Master File	
Curricula Vitas	Study Master File	Principal & Sub Investigators
Copies of qualifications/licences etc	Study Master File	Principal & Sub Investigators
Copies of Investigator of Record Agreement	Study Master File	If required, Principal & Sub Investigators
Copies of Financial Disclosure Form	Study Master File	If required, Principal & Sub Investigators
Training Log	Study Master File	

Document Name:	To Be Kept In:	Notes
Category - Operational		
Study SOPs All Versions	Study Master File	
Study SOPs Copy of most recent version	Site Files	
Participant Screening Log	Site Files	
Participant Enrolment Log	Site Files	
Participant Identification Code List	Study Master File	
Normal Values or Ranges	Study Master File	
Certification of medical, laboratory or technical procedures	Study Master File	If required
External quality assessment of medical, laboratory or technical procedures	Study Master File	If required
Sample Shipping Log	Study Master File and Site Files	
Temperature Log Fridge and Freezers	Study Master File and Site Files	If applicable
Signed Informed Consent Forms	Study Master File	

Category – Data Collection

Completed Case Report Forms Originals	Site Files	
Completed Case Report Forms Duplicates	Study Master File	
Completed Case Report Forms Originals	Site Files	
Other completed forms used to collect study data Duplicates	Study Master File	
Other source information on participants Originals	Site Files	
Other source information on participants Duplicates	Study Master File	
Documentation of changes to source documentation Original	Site Files	Only if instigated by the Site, otherwise file only an original in the Study Master File
Documentation of changes to source documentation Duplicates	Study Master File	
Sample Inventory	Laboratory Manager	

Category – Data Analysis

Decoding procedure for blinded trials	Study Master File	
Master randomization List	Study Master File	
Database Access Log	Data Management Dept	
Database Requirements Specification	Study Master File	
Database Test Specifications	Study Master File	

Document Name:	To Be Kept In:	Notes
Data Entry Log	Data Management Dept	

Category – Serious Adverse and Adverse Events

Adverse Event Plan	Study Master File	
Serious Adverse Event Reports	Study Master File	
Serious Adverse Event Correspondence to Sponsor	Study Master File	
Serious Adverse Event Correspondence from Sponsor	Study Master File	
Serious Adverse Event Correspondence to Institutional Review Board	Study Master File	
Serious Adverse Event Correspondence from Institutional Review Board (IRB)	Study Master File	
Serious Adverse event Correspondence to Independent Ethics Committee	Study Master File	
Serious Adverse event Correspondence to Independent Ethics Committee (IEC)	Study Master File	
Adverse Event Reports	Study Master File	

Category – Quality and Monitoring

Quality Management Plans	Study Master File	
Quality Assurance Audits	Study Master File	
External Monitor Reports	Study Master File	If required
External Monitor Log	Study Master File	If required

Category – General Correspondence and Communication

Correspondence to sponsor	Study Master File	
Correspondence from sponsor	Study Master File	
Correspondence to collaborating parties	Study Master File	
Correspondence from collaborating parties	Study Master File	
Minutes of Meetings	Study Master File	
Notes to File	Study Master File	
Telephone Contact Reports	Study Master File and Site Files	
Outgoing Mail Log	Study Master File and Site Files	
Incoming Mail Log	Study Master File and	

Document Name:	To Be Kept In:	Notes
	Site Files	

Category - Monitoring

Pre Trial Monitoring Report		
Internal Review Report		
External Monitor's Log		
External Monitor's Visit Report		

Category – Study Reports

Periodic Reports		
Final Reports		

