NHG RESEARCH QUALITY MANAGEMENT PROGRAM

QUALITÉ

THE PROGRAM WITH A MISSION TO ENSURE AND ENFORCE THE RESPONSIBLE CONDUCT OF RESEARCH MEETING HIGH ETHICAL STANDARDS

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PROTOCOL NON-COMPLIANCE DSRB AND SUBJECTS NOT UPDATED OF STUDY CHANGES

The Principal Investigator (PI) was replaced by the Co-Investigator as the initial PI had left the institution.

UNDERSTANDING THE DIFFERENCE AND PREPARING FOR MONITORING, AUDIT AND INSPECTION

FREQUENTLY ASKED QUESTIONS (FAQS) ON TRIAL CONDUCT

FAQ: What types of changes constitute a protocol amendment and requires a submission to Domain Specific Review Board (DSRB) and/or Health Sciences Authority (HSA). And which requires only a notification or submission to DSRB?

ANSWER: If the Principal Investigator (PI) anticipates amendment(s)/ changes to a protocol, regardless of its significance - minor, major or administrative, these amendment(s)/ changes should be submitted to DSRB and HSA, if applicable. Protocol Amendments may be necessary to further protect the safety and welfare of the research subjects and to further improve the scientific and research soundness of the protocol. Therefore, DSRB receives and reviews submitted protocol amendments and determines the category of review for the changes that have been made to the approved proposal.

Administrative Amendments such as a change in the address, contacts and correction of typographical and grammatical errors should be submitted to the DSRB for review. An acknowledgment letter by the DSRB will then be sent to the Investigator/ Sponsor. If the study is a HSA approved study, submission of administrative changes is not required. However, proper records of these changes should be maintained in the study site and sponsor files and made available to HSA upon request.

Minor Amendments are determined by DSRB if the changes to the protocol affect the risk-benefit assessment. Changes to the protocol that pose any increase in risk which is not more than minimal risk, or new procedures added that fit within the categories are eligible for expedited review. The Sponsor and/or PI should contact the HSA if they are unsure if the minor amendment(s) constitute a submission to HSA.

Major Amendments that significantly increase the overall risk or negatively alter the risk-benefit ratio to the subjects of the study will be reviewed at a DSRB Full Board Review meeting (e.g. a major change to the consent document or process that increases the overall risk to the subject involved in the study must be submitted to DSRB). HSA requires the Sponsor and/or PI to submit such major amendments as well as a copy of the amendment document.

The Sponsor and PI need to obtain approval from both DSRB and HSA before the amendment can be enforced.

PIs and Sponsors should to check with DSRB and HSA for further clarifications if unsure about their protocol amendment submission and/or procedures.

References:
SGGCP 6 Clinical Trial Protocol and Protocol Amendment(s)
NHG DSRB SOP 201-C11 & NHG Investigator Manual
Health Sciences Authority Frequently Asked Questions
Good Clinical Practice: A Question & Answer Reference Guide May 2011

UNDERSTANDING THE DIFFERENCES AND PREPARING FOR MONITORING, AUDIT AND INSPECTION

Well, you may ask, why is there a need to perform all these activities (i.e. Monitoring, Audit and Inspection) when a study has already been approved by the relevant Institutional Review Boards (IRB) or Regulatory Authorities?

Imagine if your loved one was asked to participate in a research study, what type of a mental checklist would you have before encouraging your loved one to participate in it?

- Your loved one is safe and his/her rights are protected
- The data obtained will be of good quality and integrity so that it will not be a waste of his/her effort
- Your loved one is under the protection of the available guidelines and regulatory requirements
- The operations of the study are well planned

These are very similar to the following points:

Purpose of Performing Monitoring, Audit and Inspection

- To safeguard the rights, safety and well-being of subjects participating in research studies;
- To verify the quality and integrity of the research data - to ensure that the data are accurate, complete and verifiable from source documents;
- The conduct of the trial is in compliance with the currently approved protocol/amendment(s), applicable Standard Operating Procedures (SOP), SG-GCP, and the applicable regulatory requirement(s). Some of these guidelines and requirements may include the respective institutional SOP and Institutional Review Board (IRB) SOP, SG-GCP, Medicines (Clinical Trial) Regulation, Guidelines for Clinical Trials provided by Health Sciences Authority (HSA) and Proper Conduct of Research SOP provided by National Healthcare Group (NHG).
- To assess whether the systems set up to conduct the research studies are suitably designed, controlled, maintained and documented to fulfill the objectives of the study; and
- To identify areas for quality improvement in conducting research

It may be difficult to ensure all of the above through a study application. Therefore, monitoring, audits and inspections are performed. The monitor/ auditor/inspector may look into all aspects of the research study, including the approval of the study application, subject recruitment methods, informed consent process, management of investigational products, documentation of study-related procedures and safety monitoring.

The Differences of Monitoring, Audit and Inspection

The distinction lies in the responsibilities of different parties and the different frequencies for the conduct of these activities.

MONITORING

Monitoring is carried out periodically and is applicable for all clinical trials. All clinical trials should include adequate provisions for the purpose of monitoring the conduct of a research study. The monitoring plan for a particular research study would depend on the complexity of the research study and the possibility of potential harm to subjects.

For Investigator-Initiated Clinical Trials, the Principal Investigator (PI) is responsible for having a written monitoring plan prior to study initiation. Clinical trials should be monitored regularly by a monitor who is independent of the research team. You may find the Monitoring Plan Template provided by (NHG-RDO) useful in drafting your respective monitoring plan. It can be found on National Healthcare Group – Research & Development Office's research portal (*www.research.nhg.com.sg*) (Resources -> Monitoring Plan Template).

For Industry Sponsored Clinical Trials, the PI is responsible for ensuring that the sponsor provides a monitoring plan for the clinical trial.