Qualité

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Qualifications and Requirements for Principal Investigators of Clinical Trials

Introduction

The conduct of clinical trials within National Healthcare Group (NHG) and partner institutions is regulated by both the Domain Specific Review Board (DSRB) and the Health Sciences Authority (HSA). The overarching intent of such regulation seeks to protect the rights, safety and well-being of subjects participating in these studies. Each authority administers a separate set of requirements for principal investigators (PIs) of clinical trials, to which researchers must comply should they wish to initiate and oversee the conduct of a clinical trial.

In addition, the DSRB has introduced several changes over the past year, with regard to the qualifications and minimum requirements for PIs of clinical trials. This article provides a summary of the PI requirements that apply.

What qualifications must an individual fulfill to be the PI of a clinical trial?

Based on DSRB's requirements, clinical trials are considered to be "greater than minimal risk" studies. As such, PI requirements for such studies are more stringent than that for minimal risk studies. To qualify as a PI for a more than minimal risk study that does not require a Clinical Trial Certificate (CTC) from HSA, the individual should be:

- A fully-registered or conditionally-registered medical practitioner who is an Associate Consultant and above; or
- A senior staff nurse and above, and where at least one member of the research team is an Associate Consultant and above; or
- An allied health staff who is a senior therapist / pharmacist, and where at least one member of the research team is an Associate Consultant and above.

For clinical trials regulated under the Medicines Act and Medicines (Clinical Trials) Regulations, the study will require a CTC from HSA and the PI must be a locally registered doctor or dentist. In most cases, the medical practitioner must be of rank Associate Consultant and above to oversee the conduct of a clinical trial. To avoid unnecessary delays in the review timelines, individuals submitting applications for regulatory and ethics approvals are strongly encouraged to ensure that both HSA's and DSRB's requirements are fulfilled in proposing the PI for a study.

When does a clinical trial require a Clinical Trial Certificate (CTC) from the Health Sciences Authority (HSA)?

Under the Medicines (Clinical Trials) Regulations, a clinical trial is as an investigation where one or more medicinal products are administered by a doctor or dentist to his patients, to ascertain any beneficial or harmful effects of the product. Please refer to the regulations for the full definition of a clinical trial.

In general, clinical trials seeking to examine the safety and/or efficacy of the following types of medicinal products will require a CTC from HSA:

- Registered and unregistered drugs;
- Radiopharmaceuticals;
- Complementary health products, e.g. health supplements, Chinese proprietary medicines, traditional medicines.

More than minimal risk studies that do not fulfill the legislative definition of a clinical trial will not require a CTC from HSA. However, an approval from DSRB will still be required to initiate conduct of the study.

When in doubt, the principal investigator is advised to write directly to HSA to clarify the need for a CTC. For clinical trials requiring HSA's approval, a study protocol should be submitted for review as part of the application dossier. The DSRB application form is not an acceptable substitution for a formal protocol document.

What are the minimum training requirements for principal investigators of clinical trials?

The Singapore Guideline for Good Clinical Practice (SGGCP) requires that the PI and all study team members be adequately trained before conducting the study. The DSRB further specifies that, with effect from 1st August 2014, PIs of clinical trials will be required to complete both the web-based Collaborative Institutional Training Initiative (CITI) and the SGGCP course, as the minimum research-related training requirements. The PI is required to provide proof of attendance or completion of both trainings to the DSRB, at the point of application for ethics approval.

References

Medicines (Clinical Trials) Regulations
Singapore Guideline for Good Clinical Practice.
NHG DSRB SOP 201-E03 – Minimum Training and Minimum Requirements for Investigators.

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DSRB Announcement: Changes to the Informed Consent Form Requirements for Studies Involving Prospective Collection of Biological Sample(s) and Re-Consenting Subjects for Ongoing Studies

Changes to the Informed Consent Form Requirements for Studies Involving Prospective Collection of Biological Sample(s)

The NHG Domain Specific Review Board (DSRB) recently handled a complaint where a subject had requested the investigator to return the tissue samples which had been collected as part of the research study. The subject had wanted to use the tissue samples for further clinical tests, and mentioned that the Informed Consent Form (ICF) did not state that she could not make such a request. However the investigator did not agree to the return of the tissue samples.

The NHG Research Ethics Committee deliberated over this case and concluded that biological sample(s) collected for research are deemed to be gifted to the study team for the research study. Therefore, the biological sample(s) should not be returned to subjects and subjects should be made aware of this during the consent process. However, subjects should be allowed to request that the investigators discard or destroy the biological sample(s) (e.g. upon withdrawal) if it has not already been anonymised (i.e. the sample can still be traced) and their wishes must be respected.

In order to avoid potential disputes between the subjects and the investigators regarding the return of biological sample(s), the DSRB has revised the ICF requirements for studies involving prospective collection of biological sample(s).

With effect from 01 April 2014, studies that involve the prospective collection of biological materials must include a statement in the ICF to seek consent from subjects that all biological samples collected for the study will be gifted to the institution/sponsor for the purposes as described in the ICF and will not be returned to them, and to inform subjects that they retain their rights to ask the Principal Investigator to discard or destroy any remaining sample(s) if it has not been anonymised.

Re-consenting Subjects for Ongoing Studies that Involve the Prospective Collection of Biological Sample(s)

As this change is being implemented to protect the interest of both the subjects and study teams, investigators of ongoing studies where the subjects will be returning for study visits are also required to make the same changes to the ICF over a one year period.

The Principal Investigator must submit a study amendment to DSRB to update the ICF(s) and re-consent returning subjects BEFORE **01 April 2015**. A tracked change copy and a clean copy of the amended ICF(s) will have to be uploaded for the acknowledgement from DSRB prior to its use.

Please refer to Section 11 "Voluntary Participation" in the updated DSRB Informed Consent Form Template (Document No. 207-001, Version 5, dated 3 Mar 14).

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GCP FAQ: Guidelines on Source Documentation of Subjects' Study Progress

Inadequate documentation of subjects' study involvement and progress in the source documents and/or medical case notes is a common issue noted during study reviews. Documentation is important as it allows reconstruction of study events, which in turn helps to support the evaluation and validation of research findings.

The following are some tips on how you can improve the source documentation practice at your site and ensure that sufficient information is captured to substantiate the integrity of your study data.

Source documents to be used for the study should be pre-determined

Source documents are all documents that contain original records and certified copies of original records of clinical findings, observations, or other activities in a study that is necessary for the reconstruction of the research.

Prior to study initiation, the Principal Investigator (PI) should clearly identify the types of source documents required in the research and ensure that they are accessible by the study team.

Examples of source documents: Hospital records, clinical and office charts, laboratory notes, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, microfilm or magnetic media, x rays, subject files, and records kept at the pharmacy and laboratories.

Develop appropriate templates and/or tools to capture pertinent study information

The study team may also develop and utilise source document templates or stamps for the study, to ensure that all study-related procedures are carried out and appropriately documented.

Study templates developed for the study should also include:

i. A document version control (e.g. version number and/or date)
ii. Page numbering (e.g. page 1 of 2)
iii. Space/line for the person performing the data entry to initial and date to document that he/she was responsible for completing the information.

Examples of templates / tools: Subject eligibility assessment checklist, source document templates to record specific study assessments, stamps to capture information on informed consent process and adverse event reviews.

Ensure study documentation is maintained by an appropriate personnel

Only personnel who has been adequately trained on the protocol (i.e. training recorded in a training log / record form) and delegated by the PI (i.e. delegated tasks specified in the study responsibility / delegation log) should perform study related activities and maintain documentation at site.

Guidance Table on Documentation in Source Documents / Subject Medical Records:
The table on the next page aims to provide guidance on the study documentation required when recording a subject's study involvement and progress in source documents and / or medical case notes.

References

1. Singapore Guideline for Good Clinical Practice (SG GCP)
2. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-B05- Documentation available at: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops
3. NHG Proper Conduct of Research Standard Operating Procedures (PCR SOP) 501-C01 - Informed Consent Form and Process available at: https://www.research.nhg.com.sg/wps/wcm/connect/romp/nhgromp/resources/research+sops

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