CHAPTER 3

THE STUDY TEAM

3.1 Who Can Be A Principal Investigator (PI)?

3.1.1 Minimum Qualifications to be a PI

The minimum requirements for being a PI of a research study is based on the risks involved in the research study.

MINIMAL RISK under the Human Biomedical Research Act Section 1(2) means the probability and magnitude of harm and discomfort anticipated in the research or removal of human tissue that are not greater, in and of themselves than those ordinarily encountered (a) in the daily life of normal and healthy persons; or (b) during the performance of routine physical or psychological examinations or tests.

Minimal risk studies – Research proposals that qualify for Exempt or Expedited review will be considered minimal risk studies. To be a PI for a minimal risk study, the individual should at least be:

a. Doctors - Fully registered medical practitioner, or a level 2 conditionally registered medical practitioner (please refer to subsequent section on “Special Considerations”)

b. Dentists - Fully registered/ conditionally registered/ temporarily registered dentists

c. Nurses - Registered nurse

d. Allied Health Staff – Registered allied health practitioner

e. Case managers, research scientists, research fellows and health services research staff, or as determined to be eligible by the DSRB

For registered pharmacists to be a PI for minimal risk HSA-regulated clinical trials and other clinical research, the following requirements should be met:

a. The research involves locally registered products;

b. The PI must have a PhD and/or PharmD and/or other appropriate Postgraduate Qualification, hold a primary appointment in a local institution and salaried by the institution, with a demonstrated track record of research for example, as evidenced by the award of nationally competitive funding, substantial publication record or a laboratory or clinical research program that carries out research in Singapore; and

c. For interventional clinical trials, a locally-registered physician(s) should be involved as co-investigator(s) to provide direct medical supervision and monitoring of the trial subjects.

Greater than minimal risk studies – Research proposals that do not qualify for Exempt / Expedited review and are reviewed by the Full Board are considered to be greater than minimal risk. To be a PI for a greater than minimal risk study that is not a HSA regulated, the individual should at least be:

a. Doctors – Fully registered Associate Consultant and above, or who is a level 3 conditionally registered Associate Consultant and above (please refer to subsequent section on "Special Considerations").

b. Dentists – Fully registered or conditionally registered or temporarily registered Associate Consultant and above.

c. Nurses – Senior Staff Nurse (SSN) – Must have an Associate Consultant and above on the research team.

d. Allied health staff - Senior therapist or pharmacist, must have an Associate Consultant and above on the research team.

For clinical trials that are HSA regulated, the PI should be:

a. A locally registered doctor who is a Fully Registered Associate Consultant and above, or

b. A level 3 Conditional Registered Associate Consultant and above, or

c. A locally registered dentist who is a Fully Registered or Conditionally Registered or Temporarily Registered Associate Consultant and above.

For research conducted in institutions under the oversight of NHG Health DSRB, the PI should be a staff of NHG Health or the partner institutions. This requirement is not solely for the purpose of the application to DSRB, as the PI has the responsibility for ensuring that the conduct of the research complies with ICH GCP and all other applicable guidelines and regulations.

3.1.2 Special Considerations

I. Visiting Consultants

If the PI holds a Visiting Consultant position within NHG Health or partner institutions, there should be at least one full time staff within the institution who is a part of the study team for that study (the designation of the study team member should follow the requirement guideline under 3.1.1). The Visiting Consultant may not be PIs of studies unless the NHG Health or partner institutions have given their approval for the Visiting Consultant to conduct studies in their respective institutions.

II. Conditionally Registered Medical Practitioners

- A level 2 conditionally registered medical practitioner is one who has fulfilled 0.5 years of practice at level 1 and has received at least an "above average" performance grading for the past 6 months.

- A level 3 conditionally registered medical practitioner is one who has fulfilled 0.5 years of practice at level 1 and has received at least an "above average" performance grading for

level 1 and after 1.0 year of practice at level 2 and has been ascertained to be ready to work independently but has yet to fulfil the specified period of supervised practice required for computation towards full registration.

The following set of conditions must be fulfilled before a level 2 or level 3 conditionally registered medical practitioner may be accepted as PI of a study:

a. The supervisor of the level 2 or level 3 practitioner must declare in writing that:
   i. He or She is aware of, and supports, the involvement of the conditionally registered doctor as PI;

   ii. He or She will provide guidance and include research activities in regular progress reports to the Singapore Medical Council (SMC); and

   iii. Based on the doctor's current progress and technical and ethical competency, the conditionally registered doctor is deemed competent to assume the role of PI and affirms that the conditionally registered doctor has adequate medical expertise to provide medical care and decisions for the safety and welfare of subjects.

b. The conditionally registered doctor declares that his or her involvement in research as PI has been provided to SMC and no objection has been received from SMC.

c. The DR and IR or Institutional Officer (IO) approve of the conditionally registered doctor to be the PI of the study.

III. Conditionally or Temporarily Registered Dentists

For a conditionally or temporarily registered dentist to be accepted as a PI for a study; the following conditions must be fulfilled:

a. The supervisor of the dentist must declare in writing that:

   i. He or she is aware of, and supports, the involvement of the conditionally/ temporarily registered dentist as PI;

   ii. He or she will provide guidance and include research activities in regular progress reports to Singapore Dental Council (SDC); and

   iii. Based on the conditionally/ temporarily registered dentist's current progress and technical and ethical competency, the conditionally or temporarily registered dentist is deemed competent to assume the role of PI and affirms that the conditionally/ temporarily registered dentist has adequate dental expertise to provide clinical care and make clinical decisions for the safety and welfare of the subjects.

b. The conditionally or temporarily registered dentist declares that his/ her involvement in research and PI has been provided to SDC and no objection has been received from SDC.

c. The DR and IR or IO approve of the conditionally temporarily registered dentist to be the PI of the study.

IV. Multi-Centre Studies Within NHG Health and Partner Institutions

If the research study is going to be conducted in more than one site within NHG Health and/or partner institutions, the PI for one of the sites should be the submitting PI for the study for the purposes of communication with the DSRB. The rest of the PIs may be listed as site PIs. The site PIs does not relinquish their responsibility for the study at their respective institutions.

V. Mutual Recognition of IRB Reviews for Collaborative Studies

A*STAR Research Entities (ARES), NHG Health, Nanyang Technological University (NTU), National University of Singapore (NUS) and SingHealth (SHS) have entered into a Mutual Recognition Agreement streamlining the ethics review procedures for Collaborative Studies to avoid duplicative review.

With effect from 1 April 2025, all new IRB applications involving A*STAR, NHG Health, NTU, NUHS, NUS and SingHealth sites, or their Partner Institutions, are eligible to benefit from the IRBs mutual recognition arrangement (Single IRB Review) and have their studies reviewed by 1 IRB.

Research studies involving a single site, or multiple sites that are under the purview of only one (1) IRB, will continue to be reviewed by the respective cluster/ institution IRBs.

A collaborative study (“Collaborative Study”) refers to a study involving at least two or more Research Institutions (RIs) or Partner Institutions whose review purview is under one of the five (5) IRBs in the agreement. The study should be led by a Lead PI from one of the RIs and supervised by a Site PI from at least one of the other RIs.

Please refer to Chapter 4.1.5 for more information on the submission and review of collaborative studies.

3.2 Minimum Training Requirements for Investigators and Study Team Members

The intent of having minimum training requirements is for investigators and study team members involved in the design, conduct and reporting of research to appreciate and apply the underlying ethical principles to their day-to-day research practice.

The PI and delegated study team member(s) should meet the minimum training requirements set by the reviewing IRB and the Research Institution and be adequately trained on all delegated study tasks (e.g., protocol or study specific training) prior to performing any study procedure.

The documentation of completed trainings (i.e., protocol or study specific training) for all study team members, including PI and new study team member(s) should be documented and filed in the investigator file. Other additional relevant training(s) or certification(s) for study team member(s) (e.g., phlebotomy course) should also be kept in the investigator file.

3.2.1 Training Courses

The minimum training requirements comprise of **4** types of trainings:

I. Collaborative Institutional Training Initiative (CITI);
II. Good Clinical Practice (GCP) course;
III. Financial conflict of interest (FCOI) training;
IV. Research Institution (RI) Specific Training Minimum Requirements (e.g., HBRA training)

Each of these trainings is described below in more detail.

I. Collaborative Institutional Training Initiative (CITI) – The protection of human research subjects training programme

CITI is a web-based training programme covering various foundational topics on ethical research and human protection. The CITI program is available online at https://www.citiprogram.org.

All **PIs, Site PIs and Co-Is** of research conducted within NHG Health and partner institutions are required to complete the CITI Program's Investigator's Course.

When setting up the CITI account, PIs, Site-PIs, Co-Is and other study team members (if applicable) must select that they are affiliated to "National Healthcare Group – Singapore" to access the correct curriculum. The appropriate modules should be selected within CITI to correspond to the type of research study(ies) that they are intending to conduct.

Investigators conducting biomedical research or population health research are required to complete the core and elective modules listed in table 6 below.

Table 6: CITI core modules

	CITI Module Type		
Type of Study	**Core Modules**		**Elective modules**
	Research ethics modules	**NHG Health-specific modules**	
Making submissions to Biomedical Research (NHG Health DSRB Domains A to E)	(7 fundamental research ethics modules) • Belmont Report and CITI Course Introduction • History and Ethics of Human Subject Research • Informed Consent • Social and Behavioural Research (SBR) for Biomedical Researchers • Records-Based Research • Populations in Research Requiring Additional Considerations and/or Protections • Conflicts of Interest in Human Subjects Research	(3 NHG-Specific modules) • NHG-Singapore. Overview of Domain Specific Review Board (DSRB) Review Process** • NHG-Singapore. Overview of the Regulatory Framework and Guidelines in Singapore • National Healthcare Group – Singapore	Select and complete 5 elective modules from the remaining 21 modules based on the relevance to the investigators' area(s) of speciality, relevance to the study(ies) being conducted and/or individual interest.
Making submissions to Population Health (NHG Health DSRB Domain F)			Select and complete 5 elective modules out of the 11 Social, Behavioural and Educational (SBE) related modules based on the relevance to the investigators' area(s) of speciality, relevance to the study(ies) being conducted and/or individual interest. These modules are identified by 'SBE' in the suffix.

*** These two core modules also constitute the NHG Health FCOI training requirements. Please see section 3.2.1.3 below for more details.*

Waiver of Requirement to complete the CITI

If an investigator has attended any other course relevant to research ethics, he or she may apply for a waiver of the requirement to complete the CITI program. This request for a waiver to complete the CITI program will be reviewed by the DSRB. The waiver will be granted if the course content is comparable to the content of the CITI Biomedical Course or GCP Course.

It should be noted that approval granted for a waiver of CITI certification does not exempt investigators from the FCOI training requirements.

II. Good Clinical Practice (GCP) Course

The GCP course should equip learners with basic knowledge and understanding of how GCP principles and guidelines may be applied to the conduct of clinical trials.

The DSRB will recognise generic GCP courses (such as CITI GCP) and trainings as meeting the acceptable minimum training standard. PI, Co-Is and other study team members may participate in either local or overseas GCP training programmes, e.g., CITI GCP modules, general GCP training provided by sponsor companies.

The DSRB does not mandate a specific validity period for these GCP training certificates. However, individuals should ensure that their trainings remain relevant.

Training Requirement for Investigators and Other Study Team Members Conducting Clinical Trials Regulated by HSA

For **PIs, Site PIs and Co-Is** conducting clinical trials regulated by HSA, GCP training must be completed on top of the CITI Program.

Other study team members (e.g., clinical research coordinator, pharmacist) involved in significant trial activities (e.g., informed consent process, eligibility assessment, investigational product management, key efficacy, and safety assessments) should also complete the GCP training before any trial involvement. Refer to table 7 GCP Training Requirements.

Table 7: GCP Training Requirements

Who	Training Requirement *(Effective **1 April 2024**)*
Investigators (Conducting clinical trial regulated by HSA)	**Mandatory** for PI, Site-PIs and **Co-Is** to complete GCP prior to IRB submission.
Other **Study Team Members (STM)** (Conducting clinical trial regulated by HSA)	**Mandatory** for **STM** conducting *significant trial related tasks to complete GCP before study involvement.

**Significant trial related tasks include informed consent taking, eligibility assessment, IP management, key efficacy, and safety assessment etc. Refer to HSA website for more details.*

PIs, Site-PIs and Co-Is who have completed the ICH GCP course can use it to meet the minimum training requirements for conducting **biomedical research studies only**.

III. Financial Conflict of Interest (FCOI) Training Requirements

The FCOI training requirements aim to educate researchers on how conflicting interests may adversely affect the protection of subjects or the credibility of the human research protection programme.

With effect from 1 January 2015, all investigators and study team members who are involved in the design, conduct or reporting of research conducted under the oversight of NHG Health or its partner institutions must declare if they and/or their immediate family members have any financial interests related to their research studies.

For staff who are not from NHG Health or its partner institution but are involved in the design, conduct or reporting of research that is conducted under the oversight of NHG Health or its partner institution, the FCOI declaration is required.

The declaration would need to be done annually and within 30 days if there are any changes to the financial interest status.

The FCOI training course is a sub-component of the CITI programme, and comprises the following two core modules:

1. NHG-Singapore. Overview of Domain Specific Review Board (DSRB) Review Process (ID: 810)*
2. Conflicts of Interest in Human Subjects Research (ID: 17464 or 488)*

**Course code is subjected to change.*

Investigators and study team members who have obtained their CITI certification would have, by default, completed the FCOI training requirements, as the 2 modules for FCOI training are encompassed within the core modules in the CITI programme.

For investigators and study team members who have not obtained or are not required to obtain CITI certification:

- Where CITI is a minimum training requirement, investigators will have to complete the CITI course as stipulated above. Completion of CITI will automatically ensure that the FCOI training requirements are met, as the FCOI-related training modules are encompassed within the CITI course requirements.

- Where CITI is **not** a minimum training requirement, study team members will only be required to complete the 2 FCOI-related training modules listed above. It is not mandatory to complete the full set of 10 core modules and 5 elective modules in CITI.

IV. RI Specific Minimum Training Requirements

There may be specific minimum training requirements set by individual Research Institutions (RIs).

From 1 November 2019, all **NHG Health Institution Staff (PIs, Site-PIs, Co-Is and study team members)** involved in the design, conduct or reporting of new HBR studies or sites* approved by a NHG Health appointed IRB (i.e., DSRB, SingHealth CIRB, NUS IRB, NTU IRB, A*STAR IRB), will be required to complete the NHG Health HBR Essential Conduct of Research (ERC) Course as part of the minimum training requirements. Table 8 below summarises the NHG Health HBR Minimum Training Requirements.

Table 8: NHG Health HBR Minimum Training Requirements

Who	When
All NHG Health PI, Site PI and Co-I involved in the design, conduct or reporting of HBR studies / new sites* approved by a NHG Health appointed IRB (i.e., DSRB, SingHealth CIRB, NUS IRB, NTU IRB, A*STAR IRB).	Complete HBR Training before new HBR IRB submissions and amendments for HBR studies in ECOS^.
All NHG Health CRCs, Research Assistant (RAs) and other supporting Study Team members **involved in the design, conduct or reporting of HBR studies / new sites* approved by a NHG Health appointed IRB (i.e., DSRB, SingHealth CIRB, NUS IRB, NTU IRB, A*STAR IRB).**	Complete HBR Training prior to the commencement of their study involvement.

**sites: refers to any new sites added to any ongoing HBR research protocol.*
^ECOS was launched on 10 May 2024.

The NHG Health HBR ERC Course is also applicable to all:

- **NHG Health-based MOHH residents/doctors** who are participating in HBR studies (approved by NHG Health appointed IRB from 1 November 2019) in the capacity of NHG Health PI or Co-I or study team member, from 1 October 2020.
- **NHG Health-based SAF staff/doctors**^ who are participating in HBR studies (approved by NHG Health appointed IRB from 1 December 2021) in the capacity of NHG Health PI or Co-I or study team member, from 1 December 2021.

^*Staff with formal appointment with NHG Health Institutions (including affiliate or joint appointments).*

For non-NHG Health Institutions: Research staff are advised to check with their RI to complete the specific additional RI minimum training requirements.

3.2.2 Minimum Training Requirements for Staff from NHG Health and Partner Institutions

The minimum training requirements for staff from NGH Health and partner institutions are based on their roles in the research study. Figure 3 below summarises the minimum training requirements.

Figure 3: Summary of minimum training requirements

		Minimum Training Requirements			
		IRB Minimum Training Requirements			RI HBR Minimum Training Requirements
Types of Research	**Study Role**	**NHG Health CITI**	**NHG Health FCOI**	**GCP**	**HBR**
Non-HBR	PI, Site PI, Co-I	Yes	Yes	No	No
	Other Study Team Members	No			
Human Biomedical Research (HBRA regulated)	PI, Site PI, Co-I	Yes			Yes
	Other Study Team Members	No			
Clinical Trials (HSA regulated)	PI, Site PI, Co-I	No		Yes	No
	Other Study Team Members	No		Yes	
Social, Behavioural, Education Research (submissions to NHG Health Domain F)	PI, Site PI, Co-I	Yes		No	Yes (if regulated by HBRA)
	Other Study Team Members	No			No (if **not** regulated by HBRA)

3.2.3 Minimum Training Requirements for Staff involved in Collaborative Studies under the Mutual Recognition of IRB Reviews

The minimum training requirements across the IRBs are slightly different, but training programs are cross-recognised among the 5 IRBs (A*STAR IRB, NHG Health DSRB, NTU-IRB, NUS-IRB, and SingHealth CIRB).

The PI and delegated study team member(s) should meet the minimum training requirements set by the reviewing IRB and/or the RI and be adequately trained on all delegated study tasks (e.g., protocol or study specific training) prior to performing any research procedure.

Please refer to the respective IRB or RI websites for the minimum training requirements.

IRB	Minimum Training Requirements
A*STAR IRB	Please click here for A*STAR-IRB min training requirements (accessible via A*STAR intranet only).
NHG Health DSRB	Refer to section 3.2.1
NTU	Please click here for NTU-IRB min training requirements.
NUS	Please click here for NUS-IRB min training requirements
SingHealth	Please click here for SingHealth min training requirements.

3.2.4 Minimum Training Requirements for Staff from Other External Institutions

Study team members from other external institutions (i.e., Institutions not under the 3.2.3 **Mutual Recognition of IRB Reviews**) must adhere to their own institution's guidelines regarding CITI, GCP training, or other relevant training requirements.

For staff who are not from NHG Health or its partner institution but are involved in the design, conduct or reporting of research that is conducted under the oversight of NHG Health or its partner institution, they must also comply with NHG Health's minimum training requirements for FCOI (Financial Conflict of Interest).

3.2.5 Minimum Training Certificate Validation and Labels on ECOS

In ECOS, only the **PI, Site PI and Co-Is** need to be listed under **Section B2 Study Site and Study Investigator List** of the IRB application form and submit their minimum training certificates for their Institution Minimum Training Secretariat (MTS) to validate training completion. An ECOS "label" will be issued under their ECOS user profile based on the trainings completed.

PI, Site PI and Co-Is will need the relevant "labels" to submit the corresponding study type (e.g. Clinical Trial, HBRA Study, Restricted HBR) selected in **Section D** of the IRB application form for IRB review.

ECOS Label	Type of Study	Minimum Training Requirements
Non-HBR	Non-Human Biomedical Research	CITI Biomed CITI FCOI
HBR	Human Biomedical Research	CITI Biomed CITI FCOI HBR Minimum Training*
Clinical Trials	Clinical Trials regulated by HSA	GCP CITI FCOI
SBE	Social, Behavioural, Education Research	CITI SBE CITI FCOI

*Name of HBRA Training Certification might differ for different cluster or institution

If the minimum trainings for any **investigators** listed in the IRB application are not met, the study team will not be able to submit new IRB applications and study amendments.

For Collaborative Studies under the Mutual Recognition of IRB Reviews

Although the minimum training requirements across the IRBs and RIs may differ, the IRBs will mutually recognise the training completion labels that had been granted to an investigator by their cluster. For example, an NHG Health investigator (with training completion labels) may be involved in a collaborative study submitted to the SingHealth CIRB. The NHG Health training completion will be accepted for the study reviewed by the SingHealth CIRB.

Please refer to chapter 4.2.1 Minimum Training Certificate Requirements for more information.

3.3 Responsibilities of a PI

The Principal Investigator (PI) is the individual who assumes the authority and responsibility for the conduct of a research study.

The PI has the authority to delegate responsibility to individual members of the research team or other persons or parties (e.g. service providers). However, the PI is ultimately responsible for the overall conduct of the research and should maintain appropriate oversight of the persons or parties undertaking the activities delegated to ensure the rights, safety and well-being of the research subjects and the reliability of data.

Overall, PI must ensure that -

a. Written approval or notification or acknowledgement is obtained from the IRB and relevant authorities (e.g., Ministry of Health (MOH), Health Sciences Authority (HSA), where applicable) prior to the start of the study or when instituting any changes to the protocol.

b. Changes in protocol should not be initiated without prior written approval from the IRB except when it is necessary to reduce or eliminate immediate risk to the subjects. Thereafter, the PI will submit the proposed amendment to the IRB and other relevant authority(ies) for approval.

c. There is prompt reporting of any unexpected or serious adverse events, unanticipated problems or incidents that occur during the study, in accordance with applicable safety reporting guidelines.

d. The IRB and relevant regulatory authorities are provided with documents for ongoing review (e.g. study amendments, updated Investigator's Brochure or product information, deviations or any changes significantly affecting the conduct of the research and/or increasing the risk to subjects).

e. The IRB and relevant regulatory authorities are provided with written summaries of the research status (where applicable) and ensure study approvals are renewed on time. If the IRB approval has lapse, ensure no research activities, including screening, enrolment, interventions, interactions and data collection can occur after the expiry date, unless specific permission is granted by the IRB.

f. All essential records are maintained and recognise that the IRB, regulatory authorities or Sponsor may audit or inspect these records.

g. There are no conflicting interests for any of the research personnel participating in the study, as well as their immediate family members. Should there be any conflicts of interest, the PI must ensure it is declared on the IRB application form and describe the plan to remove or manage the conflict of interest.

Failure to comply with applicable regulations, institutional and IRB policies and requirements may result in the suspension or termination of his or her study.

Co-investigators are members of the research team designated and supervised by the PI at a site to perform critical research-related procedures and/or make important research-related decisions (e.g., associates, residents, research fellows).

Collaborators are members of the research team designated by the PI to assist with research-related activities that do not involve subjects contact (e.g., scientist, research fellow, data analyst, etc.).

Research assistant or clinical research coordinators or research nurses are members of the research team designated by the PI to handle the administrative and/or clinical responsibilities of a research study. Synonyms include trial coordinator, research coordinator, clinical coordinator, and clinical trial coordinator.

Research Manager or Clinical Research Unit (CRU) Manager are manager(s) of the research administration in the institution. For institutions that do not have a research manager, the duties and responsibilities of the research manager may be performed by the Research Administrator or Assistant Manager or Senior Executive or Senior Clinical Research Coordinator or Executive or Clinical Research Coordinator.

Service provider is a person or organisation (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil research-related activities.

3.3.1 Qualifications and Agreements

The PI must be qualified by education, training and experience to assume the responsibilities associated with proper conduct of a research study and should meet all qualifications specified by the applicable regulatory requirements.

For the conduct of clinical trials, a qualified practitioner under the Health Products (Clinical Trials) and Medicines (Clinical Trials) Regulations refers to an individual who is:

a. A registered medical practitioner under the Medical Registration Act (Cap. 174); or

b. A registered dentist under the Dental Registration Act (Cap. 76) whose name appears in the first division of the Register of Dentists maintained and kept under section 13(1)(a) of that Act.

The PI should maintain a list of appropriately qualified persons to whom he or she has delegated research-related responsibilities (e.g., study responsibility or delegation log). The PI should ensure that all persons assisting with the research are adequately trained about the protocol, the investigational product(s) and their research-related duties.

Where applicable, the PI should ensure that a Clinical Trial Agreement (CTA) or Research Collaboration Agreement (RCA) is in place to outline the terms and conditions under which the research is conducted. These agreements typically define the responsibilities of each party, including aspects such as funding, data management, intellectual property rights, and

compliance with regulatory requirements, thereby ensuring that the rights and obligations of all parties involved are clearly established and protected.

If a service provider is engaged, the PI should ensure that the agreements clearly define the roles, activities and responsibilities for the research and documented appropriately. Where activities have been transferred or delegated to service providers, the responsibility for the conduct of the research, including quality and integrity of the research data, resides with the sponsor or investigator, respectively.

Please refer to NHG Health PCR SOP 501-A02 Responsibilities of the Research Team for more information on the responsibilities of a PI and the research team.

3.3.2 Adequate Resources

The PI should ensure that there is –

a. Adequate number of available and qualified staff to conduct the research study

b. Adequate facilities to conduct the study

c. Adequate time to conduct and supervise the research study and complete it within the agreed period properly and safely

Please refer to NHG Health PCR SOP 501-A02 Responsibilities of the Research Team for more information on the responsibilities of a PI and the research team.

3.3.3 Medical Care of Subjects

Any qualified practitioner or pharmacist who is the PI or a co-investigator of the research study is responsible for all research related medical care and decisions and must ensure that adequate medical care is provided to a subject for any adverse event(s). This includes clinically significant laboratory values, related to the research.

Please refer to NHG Health PCR SOP 501-A02 Responsibilities of the Research Team for more information on the responsibilities of a PI and the research team.

3.3.4 Communication with DSRB

The PI should obtain written approval from the DSRB before initiating a research project involving human subjects, when the research is conducted by or under the direction of any

employee of NHG Health, or the research is conducted using the facilities of any institutions under the oversight of NHG Health DSRB.

The PI should ensure all relevant reports are submitted per DSRB's requirements. These reports may include study amendments, study status reports, safety events and non-compliance reporting.

Please refer to:

- Chapter 4 - *Submissions to DSRB for detailed information on the required submissions to DSRB*
- *NHG Health PCR SOP 501-A02 Responsibilities of the Research Team for more information on the responsibilities of a PI and the research team.*

3.3.5 Compliance with the Protocol

The PI should conduct research in compliance with the approved protocol and all applicable research SOPs, policies and regulations.
The PI should should not implement any deviation from or changes to the protocol without agreement by the sponsor and prior review and documented approval from the DSRB and relevant regulatory authorities (where applicable), except where necessary to eliminate an immediate hazard(s) to subjects.

3.3.6 Informed Consent of Research Subjects

The PI and/or research staff must recruit subjects in a fair and equitable manner, weighing the potential benefits of the research to the subjects against their vulnerability and risks involved. The PI must ensure that informed consent is obtained from subjects prior to their enrolment into the research unless this requirement is waived by the DSRB. The PI must use the latest approved version of the consent documents approved by the DSRB.

Please refer to Chapter 5 - Informed Consent for more details on the informed consent process for research studies.

3.3.7 Safety Reporting

The PI must report all UPIRTSOs that occur during the conduct of a research project to the DSRB, in accordance with the timelines set by DSRB. For HBRA-regulated studies, Expected SAE(s) should also be reported to DSRB.

PI should evaluate and report events to other relevant parties e.g., RI, sponsor and/or regulatory authorities in accordance with the protocol and or applicable timelines and requirements, including supplementing additional information when available.

Please refer to Chapter 4.7 Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs) and Expected Serious Adverse Events (SAE) for more information.

3.3.8 Other Obligatory Reporting Requirements

The PI must report to relevant authorities if any research subject is suspected of having a notifiable disease according to relevant regulations and institutional requirements.

If abuse or neglect of a child or an elderly person is detected, the PI must ensure that this is reported to relevant authorities and in accordance with institutional requirements.

3.3.9 Records and Reports

Essential records are those records which individually and collectively permit evaluation of the conduct of research and the quality of data produced. These records serve to demonstrate the compliance during the conduct of research to applicable regulatory requirements and institutional policies.

The PI must maintain all essential records for the research study and make available to monitors, auditors, IRB and regulatory authority(ies) direct access to all requested research related records.

The PI must ensure the accuracy and completeness of data in all study databases and reports.

Please refer to the PCR SOP Investigator File Contents Template for the essential records that should be maintained in a research study.

Duration of Record-Keeping

The PI should ensure that essential records are archived in a safe location for the time period required for the study and notify the relevant parties (e.g., sponsor or institution) of the person responsible for the essential records retained.

For clinical trials regulated by HSA, the essential records should be retained at least until the later or the latest, as the case may be, of the following:

a. the date where there is no more pending or contemplated application for registration under the Health Products Act of the therapeutic product or for a product licence for the medicinal product being tested in the clinical trial;

b. the expiry of 2 years after the last of such registrations is granted or after the last approval of such application for the medicinal product to be tested in Singapore;

c. where the clinical trial is terminated, the expiry of 2 years after HSA has been informed of the termination of the trial under regulation 12 of the Health Products or Medicines (Clinical Trials) Regulations 2016;

d. the expiry of 6 years after the conclusion of the clinical trial;

e. the expiry of such other period as HSA may direct in any particular case.

For all other research studies, essential records should be retained for at least 6 years after completion of the research study.

Nonetheless, essential records should be retained for a longer period, if required by the applicable regulatory requirements, or by an agreement with the sponsor. PI should also check their institutional requirements for the minimum archival period.

For more information on the essential records required for research, please refer:

- *NHG Health PCR SOP 501-B05 Documentation*
- *NHG Health PCR Template 507-002 Investigator File Contents Template*
- *ICH GCP E6 (R3) Appendix C – Essential Records For The Conduct of A Clinical Trial*

3.3.10 Investigational Products (IP)

The PI must ensure appropriate process for the handling, shipping, storage, dispensing, returning and destroying or disposing of the IP (in accordance with protocol and applicable requirements). PI may assign some or all duties related to IP management at the study site to a study pharmacist or another appropriately trained individual.

Essential records should be maintained to accurately document the receipt, storage, use and destruction of IP.

3.3.11 Randomisation Procedures and Unblinding

The PI should follow the study randomisation procedures (if any) and ensure that the randomisation code is broken only in accordance with the protocol.

PI should identify the roles, responsibilities and procedures for access to unblinded information and implement mitigation strategies to reduce the risk of inadvertent unblinding of the blinded investigator site staff.

The PI should promptly document and explain to any instances of premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s).

3.3.12 Premature Termination or Suspension of a Research Study

The PI should promptly inform the research subjects and ensure appropriate therapy and follow-up for the subject if the study is prematurely terminated or suspended for any reason.

The PI should inform DSRB and the relevant regulatory authorities if the study is prematurely terminated or suspended for any reason.

3.3.13 Conflict of Interest

The PI and each member of the research team must declare to the DSRB whether the study team members or their immediate family members have any financial conflicts of interest related to the research study. The declaration should give full disclosure of the facts giving rise to the financial interest and detail the proposed steps to eliminate any conflicts of interest that arise from the financial interest.

Conflicting interests may also arise during the conduct of the study. If such interests arise, the PI and each member of the research team should declare these to DSRB.

Please refer to:

- *Chapter 3.5 Financial Conflict of Interest (FCOI) for more information on declaring and managing financial conflicts of interest.*
- *NHG Health PCR SOP 501-A02 Responsibilities of the Research Team for more information on the responsibilities of a PI and the research team*

3.4 Change of PI and/or Study Team Members

3.4.1 Change of PI

If the PI is resigning from his or her institution or is going away for an extended duration of time, the oversight of the research study should be formally delegated to another investigator (e.g., a co-investigator). This investigator should fulfill all qualifications for a being a PI as per DSRB requirements. The incoming investigator will assume all the responsibilities as the PI for the conduct of the research study, until the original PI returns.

i. For more than minimal risk studies, the study should be formally transferred to another investigator if the PI will be away for more than 3 months.

ii. For less than minimal risk studies, where subject recruitment and follow-up activities are still ongoing, the study should be formally transferred to another PI, if the original PI will be away for more than 6 months.

Any change in the PI should be documented in a new study responsibility or delegation log. This change in the PI should also be reviewed and approved by the DSRB, and regulatory authorities as needed.

Please refer to the NHG Health PCR SOP 501-B03: Study Initiation for more information on Delegation of Study Tasks.

3.4.2 Changes in Study Team Members

DSRB must be kept informed of any change(s) to the following study team members:

- PI
- Site-PI
- Co-I(s)

Any changes to the abovementioned study team members must be submitted to the DSRB through a study amendment for approval prior to implementation. The existing PI is responsible for submitting this amendment for review. If other non-investigator staff (e.g., research manager, study coordinator) or sponsor representatives (e.g., Clinical Research Associate) wishes to have access to the study information (e.g., IRB application form, study documents), they could be assigned the following roles on the ECOS Clinical Research Management System (CRMS).

- Study Sponsor
- Study Administrator – Not directly involved in research but only provides administrative support to the study
- Study Team Member – Directly involved in research

Addition or removal of the Study Sponsor, Study Administrator and Study Team Member on ECOS CRMS will not require IRB review and approval. Changes can be managed by the research team.

PI must ensure that access to study information is removed for individuals who have left the research team.

3.5 Financial Conflict of Interest (FCOI)

Conflicting interest – A conflicting interest can be broadly defined to refer to any interest of the investigator and/or study team member(s) or any immediate family (includes spouse, children, parent(s) and sibling(s)) that competes with the investigator's and/or study team member's obligation to protect the rights and welfare of research subjects.

Financial interest – Financial interest related to the research means financial interest in the sponsor, product or service being tested. Significant Financial Interest means anything of monetary value, including but not limited to, salary or payments for services (e.g., consulting fees or honoraria); equity interests (e.g. stocks, stock options or other ownership interests); intellectual property rights (e.g., patents, copyrights and royalties from such rights), and board or executive relationships.

Investigators and study team members should not have conflicting interests that may adversely affect the protection of subjects or the credibility of the human subject protection programme.

3.5.1 Identifying FCOI

The PI must reveal to DSRB if any of the investigators, study team members or their immediate family members have any financial interest related to the research study as follows:

a. Financial interests (e.g., stocks, stock options or other ownership interests) in the assets or liabilities of any company that may benefit from the research activity.

b. Payments (e.g., salary, consultation fees, speaking fees, or honoraria) from any company that may benefit from the research activity.

c. Employment or executive relationships with any company that may benefit from the research activity.

d. Intellectual property rights or proprietary interests (e.g., patents, copyrights and royalties from such rights) related to the research.

e. Options or other compensation arrangements that could be affected by the outcome of the research.

3.5.2 Disclosure of Financial Interests to DSRB

With effect from 1 January 2015, all investigators and study team members who are involved in the design conducting or reporting of research conducted under the oversight of NHG Health or its partner institution have to declare if they and/or their immediate family members have any financial interests related to their research studies.

For staff who are not from NHG Health or its partner institution but are involved in the design, conduct or reporting of research that is conducted under the oversight of NHG Health or its partner institution, the FCOI declaration is required.

The PI must reveal on the initial application to the DSRB, annually and at any point arising during the conduct of the study if any of the investigators, study team members or their immediate family members have any financial interests related to the research study as follows:

a. Any compensation by any commercial sponsor company of the study in which the value of compensation could be affected by study outcome.

b. A proprietary interest in the tested product including, but not limited to, a patent, trademark, copyright or licensing agreement.

c. Any equity interest in any commercial sponsor of the study, i.e., any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices. The requirement applies to interests held during the time the investigator or study team member is carrying out the study and for one year following completion of the study.

d. Any equity interest in any commercial sponsor of the covered study if the commercial sponsor is a publicly held company and the interest exceed $10,000 in value or 10% of the voting stock or controlling interest of the commercial company (whichever is lower). The requirement applies to interests held during the time the investigator or study team member is carrying out the study and for one year following completion of the study.

e. Significant payments of other sorts (SPOOS) that have a cumulative monetary value of $10,000 and are made by any commercial sponsor of the study to the investigator, study team member or their institution during the time the investigator or study team member is carrying out the study and for one year following completion of the study. This would include payments that support activities of the investigator or study team member (e.g., a grant to the investigator or to the institution to specifically fund the investigator's other ongoing research or compensation in the form of equipment that is not meant to be used for the study), or to provide other reimbursements such as retainers for ongoing consultation or honoraria. Payments for the cost of conducting the study or other studies which are already under a contractual arrangement with the commercial sponsor(s), as well as miscellaneous payments that would be controlled by the institution's finance/HR department (e.g., transportation and accommodation costs to attend investigators' meetings) are excluded.

Researchers and research staff members who are reviewing and endorsing study applications in the role of a DR or IR must reveal to the DSRB if they or their immediate family members have any financial interests related to the research being endorsed.

The declaration should give full disclosure of the facts giving rise to the financial interest and to detail the steps proposed to eliminate any conflict of interest that arises from the financial interest.

3.5.3 Timelines for FCOI Declarations to DSRB

I. At Initial Application to DSRB

The Principal Investigator must reveal on the initial study application to the DSRB if any of the investigators, study team members or their immediate family members have any financial interests related to the research study.

I. Annual FCOI Declaration

The FCOI declaration cycle is an annual process and will be held from 01 December (of the current year) to 31 January (of the next year). The validity will be from the date the FCOI declaration form is submitted during the cycle, till 31 December. Principal investigator(s) and all study team members involved in the design, conduct or reporting of research will each need to complete and submit their individual FCOI form on ECOS for their declaration of their financial status.

If any study team member had missed the period for the annual FCOI declaration cycle, he or she can still submit the declaration form at any time on ECOS throughout the year. However, the declaration will only be valid until the next declaration cycle. For example, if the declaration form was submitted on 1 August 2025, this declaration would be valid only from 1 August 2025 till 31 December 2025.

If the PI, Site PI or Co-I **do not** have the required **minimum training requirements** or **valid FCOI declaration**, ECOS will **not** allow submissions of new study applications and amendments of the corresponding study type (e.g., HBR, Clinical Trial study) selected in the IRB Application Form.

II. FCOI Arising During Conduct of the Study

FCOI may also arise during the conduct of the study. If such interests arise, the investigator and / or affected study team member(s) should submit an updated FCOI declaration form as soon as possible, but not later than 30 calendar days following first knowledge of these conflicting interests. The updated FCOI declaration form should be submitted on ECOS to the DSRB.

Researchers and research staff members who are reviewing and endorsing study applications in the role of a DR or IR must also reveal to the DSRB if they or their immediate family members have any financial interests related to the research being endorsed. The DRs and IRs will be prompted to make the declaration every time they review a study that is due for submission to the DSRB. If the DR and / or IR has a conflict of interest, he / she will need to inform the DSRB and the study will be routed to another DR / IR who does not have a conflict of interest, for endorsement.

The FCOI Declaration Form should be submitted on ECOS, via the FCOI module. Table 9 below summaries submission of FCOI Declarations.

Table 9: Submission of FCOI Declarations

Who should Submit?	All ^Investigators and ^study team members who are involved in the design, conduct of reporting of research conducted under the oversight of NHG Health or its partner institutions. *^includes newly added investigators and study team members while the research is ongoing*		
What to Do?	• Complete the NHG CITI FCOI (ID: 810, 17464 or 488) **and** • Submit the FCOI Declaration on ECOS *(Please refer to Chapter 3.2.1 Training Courses, III. Financial Conflict of Interest Training for more details)*		
When to Submit?	At initial application to DSRB *(if no FCOI was declared before)*	Annually *(follow declaration cycle)*	Changes to financial interest submit within 30 days
Where to Submit?	**On ECOS FCOI Module**		

Please refer to section 3.5.2 Disclosure of Financial Interests to DSRB for more details.

3.5.4 Review and Management of FCOI

The DSRB will review the disclosed financial interests to determine their impact on the integrity of the research and whether the management plan to eliminate any conflict of interest is appropriate. The DSRB may impose a management plan to eliminate, mitigate or manage the financial interests. Possible measures that may be taken to resolve the financial conflicts of interest may include (but are not limited to):

a. Disclosure of the conflict in the consent document;

b. Modification of research plan;

c. Divestiture of financial interest;

d. Severance of the relationship that created the conflict;

e. Training on conflicts of interest for all personnel involved in the research;

f. Disqualification from participation in all or a portion of the research; and/or

g. Audit of research by independent reviewers or review committees.

Investigators who are also the inventors of the investigational product or device should not be prohibited from participating in the research as they would be most familiar with the investigational product or device. It should first be considered if additional mitigation measures could be put in place to mitigate the financial conflict. These measures may include, but is not limited to:

a. Increased monitoring or audit frequency by the Research Institution(s) or independent reviewer(s) or review committee(s);

b. Preventing the investigator(s) from receiving any Intellectual Property-related payouts during the interim period before there is sufficient evidence-based recommended usage of the investigational product or device;

c. Restricting the investigator(s)'s involvement in the research (e.g., he or she should not participate in the safety and efficacy assessments, data analysis, and/or report writing); and/or

d. Allowing the investigator(s)'s to conduct only the initial proof-of-concept study on a limited number of subjects (e.g., no more than 20 subjects in the study).

The PI will be informed by the DSRB if any modifications are required to the management plan to eliminate or mitigate the identified conflicts of interest.

3.6 Institutional Conflict of Interest (ICOI)

ICOI in human subjects' research is defined as a situation in which the relevant financial investments or holdings of NHG Health, or the personal financial interests or holdings of institutional officials might affect or reasonably appear to affect institutional processes for the design, conduct, reporting, review, or oversight of human subjects research.

Under the NHG Health Policy on Institutional Conflicts of Interest in Human Subjects Research, a financial interest is deemed significant when it exceeds the applicable threshold for each specific category of financial interest, as established and periodically disseminated by the NHG Health Research Committee.

Since 01 January 2015, the institution and Institutional Officials are required to declare the financial interests annually via a Declaration Form. The declaration should also include the financial interests of their immediate family members (includes spouse and dependent children) if known. The institution and Institutional Officials will be reminded at the 6-month interval to submit an updated declaration if there is a change in the circumstance that alters the previous declaration.

Potential ICOI will be reviewed to determine its impact and whether mitigation measures (if required) are appropriate.