SingHealth CIRB: Illuminaté
"To Énlighten... Ethics, above all"
Adapted version for researchers, investigator and study coordinators
SingHealth
Defining Tomorrow's Medicine
Issue 8
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In this issue >>>

1. Who Can be PI? >>>

UPDATED

Principal Investigator (PI)'s requirements are based on the risk involved in the research study.

1.1 Minumum Risk Studies >>>

For minimal risk studies, the PI should at least be:

a) Clinician – Fully/ Conditionally Registered medical practitioner
b) Dentist – Fully/ Conditionally/ Temporarily Registered dentist
c) Nursing - Registered nurse
d) Allied Health staff - Registered allied health practitioner
e) Research scientists, research fellows and health services research staff, or as determined to be eligible by the CIRB

1.2 Greater than Minimum Risk Studies (Non-HSA regulated trial) >>>

For greater than minimal risk studies that <u>are not regulated by HSA</u>, the PI should at least be:

a) Clinician – Associate Consultant and above.
b) Dentist – Fully/ Conditionally/ Temporarily Registered dentist who are Associate Consultants and above.
c) Nursing – Senior Staff Nurse (Must have an Associate Consultant and above on the research team.)
d) Allied Health staff – Senior therapist/pharmacist (Must have an Associate Consultant and above on the research team.)

1.3 Greater than Minimum Risk Studies (HSA regulated trial) >>>

For clinical trial or other clinical research that requires CTC and CTA, the PI should be a:

a) Locally registered doctor or dentist who is an Associate Consultant and above.
b) Locally registered pharmacist:
   i. Only for lower risk clinical trial involving locally registered products.
   ii. Must have locally registered doctor as Co-I on the research team.

2. PI's Responsibility >>>

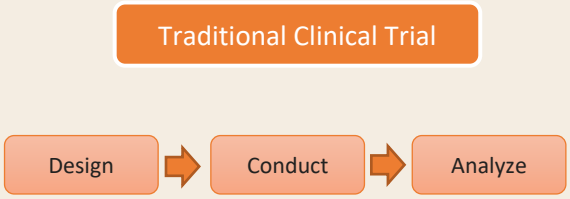
The PI is responsible for:

- ✓ Ensuring proper conduct of research
- ✓ Ensuring adequate resources to conduct the study
- ✓ Communicate with CIRB (obtaining CIRB approval to conduct research, reporting of Local Serious Adverse Events, Protocol Deviations and Non-Compliance, etc…)
- ✓ Protect rights and welfare of research participants
- ✓ Comply with CIRB policies, applicable guidelines and regulatory requirements

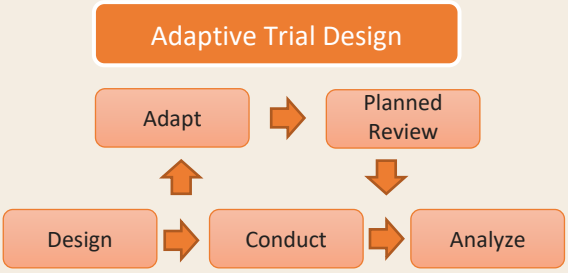
Please refer to SHS-RSH-CIRB-231 Responsibilities of Principal Investigators for details on the responsibilities of a PI.

3. *Adaptive Designs for Clinical Trials >>>*

What is an Adaptive Trial Design?
An adaptive design is defined as a clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.



Traditionally, clinical trials were performed in the following steps: (1) design clinical trial, (2) conduct clinical trial as per designed and (3) data analyzed accordingly to pre-specificed analysis plan.



Adaptive trial design: Trials were designed with planned interim analyses which allows changes to key elements of study design in a way that preserves scientific validity.

Types of Adaptive Trial Design		
Adaptive design based on non-comparative data	Adaptive design based on comparative data	Group Sequential Design
Adaption to sample size	Adaptations to the Patient Population	Adaptations to Treatment Arm Selection
Adaptations to Patient Allocation	Adaptations to Endpoint Selection	Adaptations to Multiple Design Features

Potential Advantage:
- ✓ Statistical efficiency
- ✓ Ethical considerations
- ✓ Improved understanding of drug effects
- ✓ Acceptability to stakeholders

Limitations:
- × Adaptive designs require specific analytical methods to avoid increasing the chance of erroneous conclusions and introducing bias in estimates.
- × Gains in efficiency in some respects may be offset by losses in other respects.
- × Logistical challenges to ensuring appropriate trial conduct and trial integrity.
- × The opportunity for efficiency gains through adaptation may be limited by important scientific constraints or in certain clinical settings.

Submission to IRB (Adaptive Trial Design)

- **Overall adaptive trial design**

It is important to inform the IRB on the adaptive nature of the study. The overall adaptive trial design should include the planned interim analysis and the possible adaptations (e.g. sample size, patient population, patient allocation, treatment arm, etc). This could be in a form of flow chart or diagram.

- **Adaptions while study is ongoing**

Adaptions would require study amendment to be submitted while the study is ongoing. Any adaptations should be submitted to IRB for review and approval before implementation.

- **Role of independent Data Safety Monitoring Board (DSMBs) and internal safety monitoring boards**

The review process, monitoring panel information and timepoints for evaluation by independent DSMB and internal safety monitoring boards should be stated clearly in the CIRB Application form.

References:
1) Center for Biologics Evaluation and Research & Center for Drug Evaluation and Research. (2019, November). Adaptive Designs for Clinical Trials of Drugs and Biologics Guidance for Industry. https://docisolation.prod.fire.glass/?guid=f55cb1b2-8339-4724-1bb0-7a7a75b63603)
2) Pallmann, P., Bedding, A. W., Choodari-Oskooei, B., Dimairo, M., Flight, L., Hampson, L. V., Holmes, J., Mander, A. P., Odondi, L., Sydes, M. R., Villar, S. S., Wason, J. M. S., Weir, C. J., Wheeler, G. M., Yap, C., & Jaki, T. (2018). Adaptive designs in clinical trials: why use them, and how to run and report them. BMC Medicine, 16(1). https://doi.org/10.1186/s12916-018-1017-7

Takeaway message...

The PI of a study must be qualified by education, training and experience as the PI is responsible for ensuring the proper conduct of research. CIRB policies and applicable regulatory requirements must also be complied with.

If you have any questions, please contact CIRB at irb@singhealth.com.sg